World Health Organization

Department of Immunization, Vaccines and Biologicals (IVB)

SAGE

October 2019

Strategic Advisory Group of Experts on Immunization
08 - 10 October 2019

Executive Board Room, WHO
Geneva, Switzerland

SAGE October 2019

This booklet contains key background documents for the meeting of the
Strategic Advisory Group of Experts (SAGE) on Immunization
08 - 10 October 2019

Further documents can be found online at the SAGE work space web site:

SAGE/meetings/2019/October

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17 September 2019

World Health Organization

Meeting of the Strategic Advisory Group of Experts (SAGE) on Immunization
08 - 10 October 2019
Executive Board Room, Geneva, Switzerland

Draft Agenda

Tuesday, 08 October 2019

Time	Session	Purpose of session, target outcomes and questions for SAGE	Duration
10:00	**Welcome – introduction of participants** A. CRAVIOTO. Chair of SAGE.		20 min.
10:20	**Report from Director, IVB and Regional Updates - Session 1** Global report including key updates and challenges from regions. K. O'BRIEN. WHO. 30 min.	**FOR INFORMATION**	1h 30 min.
10:50	**Coffee/Tea break**	**Break**	**30 min.**
11:20	Cont. Session 1 Key updates and challenges from regions. Regional Advisers. WHO. 15 min. Discussion: 45 min.	**FOR INFORMATION**	
12:20	**Report from Gavi, the Vaccine Alliance - Session 2** Report from Gavi, the Vaccine Alliance. S. BERKLEY. Gavi, the Vaccine Alliance. 15 min. Discussion: 25 min.	**FOR INFORMATION**	40 min.
13:00	**Lunch**	**Break**	**1h**

14:00	**Immunization Partners - Session 3** Report from the Vaccine Innovation Prioritisation Strategy (VIPS). M. MENOZZI-ARNAUD. Gavi, the Vaccine Alliance. 15 min. Discussion: 15 min.	**FOR INFORMATION**	30 min.
14:30	**Measles and Rubella - Session 4** Session introduction. N. TURNER. Chair of SAGE Measles and Rubella Vaccines Working Group. 5 min. **Rubella and CRS Control and Elimination** Rubella vaccine policy update. S. DESAI. WHO. 10 min. Discussion: 10 min. Recommendations. N. TURNER. Chair of SAGE Measles and Rubella Vaccines Working Group. 5 min. Discussion: 10 min. **Global update on measles and rubella, including on outbreaks** K. KRETSINGER. WHO. 10 min. Discussion: 20 min.	**FOR INFORMATION, DISCUSSION AND DECISION** **FOR DECISION** • Presentation of programmatic evidence to support policy amendments to recommendations for rubella and CRS control and elimination SAGE is requested to consider the following question: • Can the recommendation to only target vaccination of women of reproductive age as part of a CRS prevention/rubella control strategy be removed? **FOR INFORMATION** • Global and regional update	3h
15:40	**Coffee/tea break**	**Break**	**30 min.**
16:10	Cont. Session 4 **Measles and Rubella Elimination** Modelling the epidemiologic impact and cost-effectiveness of different MR programme performance scenarios. M. FERRARI. Penn State University and M. Jit. Member of Measles and Rubella Working Group. 20 min. Questions and answers: 20 min. Feasibility of MR eradication. B. MOSS. JHSPH. 15 min. Questions and answers: 10 min. Recommendations. N. TURNER. Chair of SAGE Measles and Rubella Vaccines Working Group. 5 min. Discussion: 40 min.	**FOR DISCUSSION AND DECISION** • Presentation of modelling and economic analysis of measles and rubella elimination • Presentation of the proposed response to the World Health Assembly request to report on the feasibility and financial resource requirements for measles and rubella eradication SAGE is requested to consider the assessment of the feasibility of measles and rubella eradication for endorsement.	
18:00	**End of Day**		
18:15	**Cocktail**		

Wednesday, 09 October 2019

9:30	**Human papillomavirus (HPV) vaccine - Session 5** Session introduction and key questions. R. AGGARWAL. Chair of SAGE HPV Vaccines Working Group. 5 min. Update on access to HPV vaccine. P. BLOEM. WHO. 10 min. Systematic review of evidence on different HPV immunization strategies. N. HENSCHKE. Cochrane Response. 15 min. Ongoing trials on single-dose HPV vaccine schedule. A. KREIMER. National Cancer Institute. 10 min. Global analysis of HPV vaccine supply and demand. T. CERNUSHI. WHO. 10 min. Impact of different HPV immunization strategies in the context of supply constraint. M. BRISSON. Laval University. 15 min. Conclusions and proposed recommendations by SAGE Working Group. R. AGGARWAL. Chair of SAGE HPV Vaccines Working Group. 15 min. Discussion: 1h 10 min	**FOR DISCUSSION AND DECISION** Present SAGE with updated information on HPV vaccination schedules and barriers, and modelling of impact of HPV vaccination schedules and strategies in the context of the constrained supply. SAGE is requested to consider the following evidence: 1. What is the current HPV vaccine uptake and what are the main barriers for access to HPV vaccines? 2. What does current evidence show on the immunogenicity and efficacy of a single dose of HPV vaccine and different intervals between the first and second doses of HPV vaccine? And what are the risks of bias of these studies? 3. What are the potential demand scenarios and the supply of HPV vaccines (short and mid-term outlook) and what could the enhanced HPV vaccine supply allocation be? Overall question to SAGE: In light of the current HPV vaccine supply and the above analyses, how should HPV vaccination be prioritized with respect to impact, feasibility, and equity?	2h 30 min.
11:00	**Coffee/tea break**	**Break**	**30 min.**
11:30	Cont. Session 5		
12:30	**Post-2020 Global Immunization Strategy/ Global Vaccine Action Plan (GVAP) - Session 6** Presentation of draft GVAP review and lessons learned report, including recommendations. N. MACDONALD. Chair of SAGE Decade of Vaccines Working Group. 20 min. Discussion: 40 min.	**FOR DISCUSSION AND DECISION** SAGE is asked to consider the GVAP review and recommendations for endorsement. *Note: The GVAP review and lessons learned report replaces the annual GVAP assessment report. It encompasses an analysis of the 2018 data.*	3h
13:30	**Lunch**	**Break**	**1h**
14:30	Cont. Session 6 Presentation of the draft post-2020 global immunization strategy ("Immunization Agenda 2030")	SAGE is asked to consider the draft Immunization Agenda 2030 for endorsement.	

	K. O'BRIEN. WHO. 45 min. Discussion: 1h 15 min.		
16:30	**Coffee/tea break**	**Break**	**30 min.**
17:00	**Ebola vaccines - Session 7** Overview of SAGE recommendations and introduction to the session. F. WERE. Co-Chair of SAGE Working Group on Ebola Vaccines. 10 min. Update on outbreak epidemiology. B. ARCHER. WHO. 10 min. Status of implementation of SAGE interim recommendations. A. DIALLO. WHO. 10 min. Preliminary observations regarding effect of rVSV ZEBOV vaccination in the Democratic Republic of the Congo (DRC). A.-M. HENAO RESTREPO. WHO. 10 min. Update on status of Ebola candidate vaccines and ongoing efforts towards global vaccine security. A. COSTA. WHO. 10 min. Conclusions and next steps. H. REES. Co-Chair of SAGE Working Group on Ebola Vaccines. 10 min. Discussion: 30 min.	**FOR INFORMATION AND DISCUSSION** Update on implementation of the interim Ebola vaccine recommendations and the ongoing response to the DRC outbreak.	1h 30 min.
18:30	**End of day**		

Thursday, 10 October 2019

09:30	**Quality and Use of Immunization and Surveillance Data - Session 8** SAGE Immunization Data WG summary. H. SCOBIE. Members of SAGE Working Group on Quality and Use of Immunization and Surveillance Data. 15 min. India: Utilization of Immunization Data to Improve Evidence-based Decision-Making. TBD. 10 min Western Pacific Region: data in the Regional Strategic Framework for Vaccine-preventable Diseases and Immunization 2021-2030. D.A.C. AMARASINGHE. WHO. 15 min. SAGE Immunization Data WG proposed recommendations. J. JAWAD. Chair of SAGE Working Group on Quality and Use of Immunization and Surveillance Data. 5 min.	**FOR DISCUSSION AND DECISION** Following the April 2019 SAGE meeting, actionable recommendations were developed. SAGE is asked to consider the draft recommendations for endorsement.	1h 30 min.

	Discussion: 45 min.		
10:30	**Coffee/tea break**	**Break**	**30 min.**
11:00	Cont. Session 8		
11:30	**Polio – Session 9** Update from the Global Polio Eradication Initiative R. SUTTER. WHO. 30 min. Presentation of clinical data from novel type 2 oral polio vaccine (nOPV2) trials and plan for Emergency Use Listing (EUL). A. BANDYOPADHYAY. BMGF. 20 min. Report from SAGE Polio Working Group including presentation of results from "One-drop monovalent type 2 oral polio vaccine (mOPV2) study"; and call for acceleration of assessment of nOPV2 under EUL. I. JANI. Co-Chair of SAGE Polio Working Group. 30 min. Discussion: 40 min.	**FOR DISCUSSION AND DECISION** Update on the current status of the polio eradication program, including circulating vaccine-derived poliovirus (cVDPV) outbreaks, and on proposed revised strategies to respond to cVDPV2 outbreaks. SAGE is asked to discuss and consider endorsement of recommendations on: • Acceleration of the clinical development of nOPV2 • Use of one-drop mOPV2 vaccination	2h
13:30	**Closing**		**20 min.**
13:50	**End of meeting**		

World Health Organization

Current SAGE Members

Aggarwal, Prof Rakesh Professor Department of Gastroenterology Lucknow India
Cravioto, Prof Alejandro (SAGE chair) Professor Facultad de Medicina Universidad Nacional Autónoma de México Puerto Vallarta Mexico
Jani, Dr Ilesh Director General Instituto Nacional de Saúde Maputo Mozambique
Jawad, Dr Jaleela Head of immunization group Public Health Directorate, Ministry of Health Manama Bahrain
Jee, Dr Youngmee Director General Center for Infectious Disease Research Cheongju Republic of Korea
Johansen, Dr Kari (SAGE vice-chair) Expert in Vaccinology European Centre for Disease Prevention and Control Solna Sweden
MacDonald, Prof Noni Professor of Pediatrics Division of Pediatric Infectious Diseases, Dalhousie University Halifax, Nova Scotia Canada
Madhi, Prof Shabir Professor of Vaccinology University of the Witwatersrand Johannesburg South Africa
McIntyre, Prof Peter Professor in the Discipline of Child and Adolescent Health and the School of Public Health University of Sydney Australia
Mohsni, Dr Ezzeddine Senior Technical Adviser Global Health Development (GHD) The Eastern Mediterranean Public Health Network (EMPHNET) Amman Jordan

Neuzil, Prof Kathleen Director Center for Vaccine Development and Global Health University of Maryland School of Medicine Baltimore, Maryland USA
Pollard, Prof Andrew J. Professor Department of Paediatrics, University of Oxford Oxford United Kingdom
Qadri, Dr Firdausi Senior Director Infectious Diseases Division Dhaka Bangladesh
Turner, Dr Nikki Associate Professor General Practice and Primary Care Wellington New Zealand
Were, Prof Fredrick Dean School of Medicine Nairobi Kenya

Strategic Advisory Group of Experts (SAGE)
Terms of reference

Functions

SAGE is the principal advisory group to WHO for vaccines and immunization. It is charged with advising WHO on overall global vaccination policies and strategies, ranging from vaccines and technology, research and development, to delivery of vaccination and its linkages with other health interventions. SAGE's remit extends to the control of all vaccine-preventable diseases as part of an integrated, people centred platform of disease prevention that spans the human life-course and in the context of health systems strengthening.

SAGE advises the WHO Director-General specifically on the:

1. adequacy of progress towards the achievement of the goals of control of vaccine-preventable diseases worldwide such as those laid out in the Decade of Vaccines Global Vaccine Action Plan 2011-2020.
2. major issues and challenges to be addressed with respect to achieving the disease control goals, including issues and challenges to achieving and sustaining high and equitable vaccination coverage;
3. immunization programme response to current public health priorities;
4. major general policies, goals and targets including those related to vaccine research and development;
5. adequacy of WHO's strategic plan and priority activities consistent with its mandate and considering the comparative advantages and the respective roles of partner organizations;
6. engagement of WHO in partnerships that will enhance achievement of global immunization goals.

Membership

SAGE comprises 15 independent experts, who shall serve in their personal capacity and represent a broad range of affiliations and a broad range of disciplines encompassing many aspects of immunization and vaccines. Members should refrain from promoting the policies and views and products of the institution for which they work.

SAGE members are recruited and selected as acknowledged experts from around the world in the fields of epidemiology, public health, vaccinology, paediatrics, internal medicine, infectious diseases, immunology, drug regulation, programme management, immunization delivery, health-care administration, health economics, and vaccine safety.

The membership of SAGE shall seek to reflect a representation of:

1. professional affiliation (e.g., academia, medical profession, clinical practice, research institutes, and governmental bodies including national immunization programmes, public health departments and regulatory authorities);
2. major areas of expertise (e.g., vaccine research, vaccine and immunization safety, optimization of immunization schedules, vaccine delivery, disease control strategies, impact monitoring); and
3. the strategic focus areas of the WHO's vaccine and immunization work including vaccines norms and standards, vaccine regulation, vaccine programme management, delivery and surveillance and monitoring, and vaccine research & development.

SAGE members, including the Chairperson and the Vice-Chairperson, are appointed by the WHO Director-General. Members are selected upon the proposal of an independent selection panel including representatives of key partner organizations. A public call for nominations is issued. After determination of eligibility, nominations are submitted to the selection panel. Members will be selected on the basis of their qualifications and ability to contribute to the accomplishment of SAGE's objectives. Renewals of term are also submitted to the selection panel.

Consideration will be given to ensuring appropriate geographic representation and gender balance. Chairs of regional technical immunization advisory groups are not eligible to serve on SAGE but are invited to attend SAGE meetings. WHO staff and United Nations staff members are not eligible to serve on SAGE.

Members of SAGE shall be appointed to serve for an initial term of three years. This three-year term may only be renewed once. To allow for continuity and efficiency, the Chairperson of SAGE is expected to act as Chairperson for a minimum of three years, not taking into account if he/she has already served three years or has been renewed for a further three years as a member of SAGE. He/she needs however, to be a member of SAGE for a minimum of one year before taking up Chairpersonship.

Prior to being considered for SAGE membership, nominees shall be required to complete a WHO Declaration of Interests form as per the attached form (Annex 1).

All papers presented to SAGE, which may include pre-publication copies of research reports or documents of commercial significance, shall be treated as confidential. SAGE deliberations are confidential and may not be publicly disclosed by SAGE members. Therefore, prior to confirmation by WHO of their appointment as SAGE members, SAGE nominees shall be required to sign a Confidentiality Undertaking (Annex 2).

A register of members' interests and signed confidentiality agreements shall be maintained by WHO.

Membership in SAGE may be terminated for any of the following reasons:

1. failure to attend two consecutive SAGE meetings;

2. change in affiliation resulting in a conflict of interest or involvement in activities resulting in a conflict of interest incompatible with serving on SAGE; and
3. a lack of professionalism involving, for example, a breach of confidentiality.

Meetings and operational procedures

SAGE meetings occur biannually, in April and October, and are scheduled 3 years ahead. The frequency of meetings may, however, be adjusted as necessary. The WHO Secretariat will work with SAGE members and key global stakeholders to develop SAGE priorities and workplans as well as specific meeting agendas.

SAGE members are asked to update their declared interests before each meeting. SAGE members with potentially conflicting interests will not participate in deliberations on the specific topic(s) for which they would have a conflict of interest. SAGE member's relevant interests will be made publically available four weeks in advance of the meeting for public comments. Background documents, presentations, final agenda and final list of participants are posted after the meeting are posted on the SAGE public website after the meeting.

Decisions or recommendations by SAGE will, as a rule, be taken by consensus.

The WHO Regional Offices, Chairs of regional technical immunization advisory groups and Chairs of relevant WHO technical advisory committees will be invited to participate in SAGE meetings and contribute to the discussions. The major global immunization stakeholders such as UNICEF, the Secretariat of Gavi, the Vaccine Alliance, and representatives of civil society organizations will also be invited to attend and contribute to SAGE meetings.

WHO may also invite other observers to SAGE meetings, including representatives from non-governmental organizations, international professional organizations, technical agencies, partner organizations, Chairs and members of national technical advisory groups on immunization as well as associations of manufacturers of vaccines and immunization technologies and representatives from the manufacturing companies.

Additional experts may be invited to meetings, as appropriate, to further contribute to specific agenda items. Observers and invited experts will not participate in the decision making process but will be allowed to contribute to the discussions as directed by the Chairperson.

SAGE reports to the WHO Director-General. The SAGE Chairperson will debrief the Director-General (or designee) following each SAGE meeting. The conclusions and recommendations of SAGE meetings shall be published in the Weekly Epidemiological Record and posted on the website within two months of each SAGE meeting. These conclusions and recommendations and will be translated into all the WHO headquarters official languages. A brief summary report of the meeting shall also be posted on the SAGE website the day after the SAGE meeting.

Roles and responsibilities of SAGE members

Members of SAGE have a responsibility to provide WHO with high quality, well considered advice and recommendations on matters described in these SAGE terms of reference. Members play a critical role in ensuring the reputation of SAGE as an internationally recognized advisory group in the field of immunization. In keeping with SAGE's mandate to provide strategic advice rather than technical input, members will be committed to the development and improvement of public health policies.

SAGE has no executive or regulatory function. Its role is solely to provide advice and recommendations to the Director-General of WHO. This includes providing advice and recommendations on urgent public health issues as needed.

SAGE members may be approached by non-WHO sources for their views, comments and statements on particular matters of public health concern and asked to state the views of SAGE. SAGE members shall refer such enquiries to WHO.

SAGE members will not be remunerated for their participation in SAGE; however, reasonable expenses such as travel expenses incurred by attendance at SAGE or related meetings will be compensated by WHO.

SAGE members are expected to endeavour to attend all biannual meetings. Further active participation will be expected from all SAGE members throughout the year, including participation in SAGE Working Groups, video and telephone conferences as well as frequent interactions via e-mail. Review of documents may also be solicited. SAGE members may be requested to participate as observers in other important WHO or partners meetings. As a result SAGE members are expected to commit to invest a substantial amount of their time to SAGE.

The secretariat of SAGE is ensured by the Immunization Policy Unit of the Department of Immunization, Vaccines and Biologicals. The function of Executive Secretary is ensured by the Senior Health Advisor who directs this Unit.

SAGE will be kept informed by WHO and partner agencies on progress concerning implementation of strategies and the attainment of objectives at country and regional level. SAGE will also be informed of conclusions and recommendations from WHO relevant technical advisory groups including regional technical advisory groups.

SAGE Working Groups are established as resources intended to increase the effectiveness of SAGE deliberations by reviewing and providing evidence-based information and options for recommendations together with implications of the various options to be discussed by SAGE during one of its biannual meetings. These Working Groups are normally established on a time-limited basis to help address specific questions identified by SAGE when the issue is particularly

complicated or time-consuming and could not be addressed by an existing standing WHO advisory committee. The need and charge for a Working Group is discussed and agreed during SAGE meetings. The purpose, structure and functioning of the Working Groups is described in detail in Annex 3 (Purpose, structure and functioning of the Strategic Advisory Group of Experts on Immunization (SAGE) Working Groups).

For its proceedings, SAGE shall follow an evidence-based review process as outlined in the SAGE guidance document on evidence-based vaccine-related recommendations (http://www.who.int/immunization/sage/Guidelines_development_recommendations.pdf?ua=1).

More detailed information on SAGE operating procedures is available on the SAGE website (http://www.who.int/immunization/sage/working_mechanisms/en/).

DECLARATION OF INTERESTS FOR WHO EXPERTS

WHO's work on global health issues requires the assistance of external experts who **may have interests related to their expertise.** To ensure the highest integrity and public confidence in its activities, WHO requires that experts serving in an advisory role disclose any circumstances that could give rise to a potential conflict of interest related to the subject of the activity in which they will be involved.

All experts serving in an advisory role must disclose any circumstances that could represent a **potential conflict of interest** (i.e., any interest that may affect, or may reasonably be perceived to affect, the expert's objectivity and independence). You must disclose on this Declaration of Interest (DOI) form any financial, professional or other interest relevant to the subject of the work or meeting in which you have been asked to participate in or contribute towards and any interest that could be affected by the outcome of the meeting or work. You must also declare relevant interests of your immediate family members (see definition below) and, if you are aware of it, relevant interests of other parties with whom you have substantial common interests and which may be perceived as unduly influencing your judgement (e.g. employer, close professional associates, administrative unit or department).

Please complete this form and submit it to WHO Secretariat if possible at least 5 weeks before the meeting or work. You must also promptly inform the Secretariat if there is any change in this information prior to, or during the course of, the meeting or work. All experts must complete this form before participation in a WHO activity can be confirmed. Please note that not fully completing and disclosing all relevant information on this form may, depending on the circumstances, lead WHO to decide not to appoint you to WHO advisory bodies / functions in the future.

Answering "Yes" to a question on this form does not automatically disqualify you or limit your participation in a WHO activity. Your answers will be reviewed by the Secretariat to determine whether you have a conflict of interest relevant to the subject at hand. One of the outcomes listed in the next paragraph can occur depending on the circumstances (e.g, nature and magnitude of the interest, timeframe and duration of the interest).

The Secretariat may conclude that no potential conflict exists or that the interest is irrelevant or insignificant. If, however, a declared interest is determined to be potentially or clearly significant, one or more of the following three measures for managing the conflict of interest may be applied. The Secretariat (i) allows full participation, with public disclosure of your interest; (ii) mandates partial exclusion (i.e., you will be excluded from that portion of the meeting or work related to the declared interest and from the corresponding decision making process); or (iii) mandates total exclusion (i.e., you will not be able to participate in any part of the meeting or work).

All potentially significant interests will be **disclosed** to the other participants at the start of the activity and you will be asked if there have been any changes. Whereas this form is confidential, a summary of declarations and actions taken to manage any declared interests will be **published** on the SAGE public website). Furthermore, if the objectivity of the work or meeting in which you are involved is subsequently questioned, the contents of your DOI form may be made available by the Secretariat to persons outside WHO if the Director-General considers such disclosure to be in the best interest of the Organization, after consulting with you. Completing this DOI form means that you agree to these conditions.

If you are unable or unwilling to disclose the details of an interest that may pose a real or perceived conflict, you must disclose that a conflict of interest may exist and the Secretariat may decide that you be totally recused from the meeting work or process concerned, after consulting with you.

Name: Institution: Email:

Date and title of meeting or work, including description of subject matter to be considered (if a number of substances or processes are to be evaluated, a list should be attached by the organizer of the activity):

_____

_____

Please answer each of the questions below. If the answer to any of the questions is "yes", briefly describe the circumstances on the last page of the form.

The term "you" refers to yourself and your immediate family members (i.e., spouse (or partner with whom you have a similar close personal relationship) and your children). "Commercial entity" includes any commercial business, an industry association, research institution or other enterprise whose funding is significantly derived from commercial sources with an interest related to the subject of the meeting or work. "Organization" includes a governmental, international or non-profit organization. "Meeting" includes a series or cycle of meetings.

EMPLOYMENT AND CONSULTING

Within the past 4 years, have you received remuneration in excess of US$ 5,000 from a commercial entity or other organization with an interest related to the subject of the meeting, work or process?

1a	Employment	Yes ☐ No ☐
1b	Consulting, including service as a technical or other advisor	Yes ☐ No ☐

RESEARCH SUPPORT
Within the past 4 years, have you or has your research unit received support from a commercial entity or other organization with an interest related to the subject of the meeting, work or process?

2a	Research support, including grants, collaborations, sponsorships, and other funding	Yes ☐ No ☐
2b	Non-monetary support valued at more than US $1000 overall (include equipment, facilities, research assistants, paid travel to meetings, etc.)	Yes ☐ No ☐
2c	Support (including honoraria) for being on a speakers panel, giving speeches or training for a commercial entity or other organization with an interest related to the subject of the meeting, work or process?	Yes ☐ No ☐

INVESTMENT INTERESTS
Do you have current investments (valued at more than US$5,000 overall) in a commercial entity with an interest related to the subject of the meeting, work or process? Please also include indirect investments such as a trust or holding company. You may exclude mutual funds, pension funds or similar investments that are broadly diversified and on which you exercise no control.

3a	Stocks, bonds, stock options, other securities (e.g., short sales)	Yes ☐ No ☐
3b	Commercial business interests (e.g., proprietorships, partnerships, joint ventures, board memberships, controlling interest in a company)	Yes ☐ No ☐

INTELLECTUAL PROPERTY
Do you have any intellectual property rights that might be enhanced or diminished by the outcome of the meeting, work or process?

4a	Patents, trademarks, copyrights or other intellectual property (including pending applications)	Yes ☐ No ☐
4b	Proprietary know-how in a substance, technology or process	Yes ☐ No ☐

PUBLIC STATEMENTS AND POSITIONS (during the past 4 years)

5a	As part of a regulatory, legislative or judicial process, have you provided an expert opinion or testimony, related to the subject of the meeting, work or process, for a commercial entity or other organization?	Yes ☐ No ☐
5b	Have you held an office or other position, paid or unpaid, where you represented interests or defended a position related to the subject of the meeting, work or process?	Yes ☐ No ☐

ADDITIONAL INFORMATION

6a	If not already disclosed above, have you worked for the competitor of a product that is the subject of the meeting or work, or will your participation in the meeting, work or process enable you to obtain access to a competitor's confidential proprietary information, or create for you a personal, professional, financial or business competitive advantage? if so, please elaborate?	Yes ☐ No ☐
6b	To your knowledge, would the outcome of the meeting, work or process benefit or adversely affect interests of others with whom you have substantial common personal, professional, financial or business interests (such as your adult children or siblings, close professional colleagues, administrative unit or department)?	Yes ☐ No ☐
6c	Excluding WHO, has any person or entity paid or contributed towards your travel costs in connection with this WHO meeting, work or process?	Yes ☐ No ☐
6d	Have you received any payments (other than for travel costs) or honoraria for speaking publicly on the subject of this WHO meeting, work or process?	Yes ☐ No ☐
6e	Is there any other aspect of your background or present circumstances not addressed above that might be perceived as affecting your objectivity or independence?	Yes ☐ No ☐

7. **TOBACCO OR TOBACCO PRODUCTS** *(answer without regard to relevance to the subject of the meeting or work)*

Within the past 4 years, have you had employment or received research support or other funding from, or had any other professional relationship with, an entity directly involved in the production, manufacture, distribution or sale of tobacco or tobacco products or representing the interests of any such entity? Yes ☐ No ☐

EXPLANATION OF "YES" RESPONSES: If the answer to any of the above questions is **"yes", check above and briefly describe the circumstances on this page. If you do not describe the nature of an interest or if you do not provide the amount or value involved where relevant, the conflict will be assumed to be significant.**

Nos. 1 - 4: **Type of interest, question number and category (e.g., Intellectual Property 4.a copyrights) and basic descriptive details.**	**Name of company, organization, or institution**	**Belongs to you, a family member, employer, research unit or other?**	**Amount of income or value of interest (if not disclosed, is assumed to be significant)**	**Current interest (or year ceased)**
Nos. 5-8: Describe the subject, specific circumstances, parties involved, time frame and other relevant details				

CONSENT TO DISCLOSURE. By completing and signing this form, you consent to the disclosure of any relevant conflicts to other meeting participants and in the resulting report or work product.

DECLARATION. I hereby declare on my honour that the disclosed information is true and complete to the best of my knowledge.

Should there be any change to the above information, I will promptly notify the responsible staff of WHO and complete a new declaration of interest form that describes the changes. This includes any change that occurs before or during the meeting or work itself and through the period up to the publication of the final results or completion of the activity concerned.

Date: _____ Signature_____

World Health Organization

CONFIDENTIALITY UNDERTAKING

1. Commercial, academic and other research institutions and individual scientists often submit or present for discussion by committees or groups of WHO on research, products and processes (hereafter referred to as "Information") which the institutions and individuals consider proprietary. To help ensure the appropriate use by WHO of such Information whilst protecting the institutions' or individual's proprietary rights, WHO undertakes to release such Information only to persons who have signed this agreement.

2. Information submitted by such institutions or individuals through WHO to committees or groups for review, discussion or comment, whether at meetings, on internet-based collaborative workspaces, during telephone conferences or otherwise, shall be regarded by the Undersigned as confidential, unless clearly stated otherwise, by the institution, individual concerned and/or the WHO Secretariat.

3. The Undersigned undertakes to treat such confidential Information as proprietary information and agrees not to make copies of it, nor to disclose or use the same in whole or in part.

4. If requested to do so, the Undersigned agrees to return to WHO any and all Information identified as confidential.

5. The Undersigned shall not be bound by confidentiality if he/she is able to demonstrate that the Information:

   (a) was known to him/her prior to any disclosure to him/her by the institution or individual or WHO;

   (b) was in the public domain at the time of disclosure by the institution or individual;

   (c) becomes part of the public domain through no fault of the Undersigned; or

   (d) becomes available to the Undersigned from a third party not in breach of any legal obligations of confidentiality to the institution, individual or WHO.

6. This Confidentiality Undertaking is valid during the entire time the Undersigned participates in the work of the committee or group, in whatever capacity, and for a period of ten (10) years thereafter.

Signed:

Signature ...

Name .
(print or type)

Purpose, structure and functioning of the Strategic Advisory Group of Experts on Immunization (SAGE) Working Groups

Purpose and decision to establish a SAGE Working Group

SAGE Working Groups are established as resources intended to increase the effectiveness of SAGE deliberations by reviewing and providing evidence-based information and options for recommendations together with implications of the various options to be discussed by SAGE in an open public forum.

These Working Groups are normally established on a time limited basis to help address specific questions identified by SAGE when the issue cannot be addressed by existing standing WHO advisory committees. Some Working Groups such as that on polio eradication or the Decade of Vaccines Working Group can be established for a number of years.

The need for and creation of a Working Group is discussed and agreed during SAGE meetings, preparatory teleconferences for SAGE meetings, or in case of urgency via email interaction.

Terms of reference of the Working Groups and identification of needed expertise to serve on the Working Group
Each Working Group operates under specific terms of reference (TORs). These TORs are defined within 30 days of the SAGE decision to establish the Working Group.

Proposed TORs and related expertise to serve on the Working Group are developed jointly by the SAGE member serving as Working Group Chair, the Lead WHO technical staff and SAGE Executive Secretary. Draft TORs and related expertise are reviewed by SAGE members. Final decision is taken jointly by the SAGE Chair, Working Group Chair, SAGE Executive Secretary, and the Director of the Department of Immunization, Vaccines and Biologicals.

Working Group composition and selection of membership

Each Working Group should include two or more SAGE members (one of whom functions as Chair), and additional subject matter experts serving in their own individual capacity and with a view to meet the identified needed expertise for the group. SAGE members and other experts who have identified conflicts of interest cannot serve on the Working Group charged with responsibility in the identified areas of conflict. WHO staff (one of whom functions as the Working Group technical lead serve as secretariat to the Working Group. In some instances other UN or non UN agencies can be co-opted as part of the secretariat.
For the selection of experts to serve on a Working Group, a public call for nomination for Working Group members will be posted on the SAGE website together with the relevant TORs of the Working Group and indication of the desirable expertise. SAGE members, regional offices, diplomatic missions, WHO staff and key partner organizations will also be approached to propose potential nominations. Nominees will be requested to provide both a Curriculum Vitae and a completed Declaration of Interests form prior to being considered for membership on the Working Group.

The selection panel, comprised of the SAGE Chair (or Vice-Chair), the Working Group Chair, the SAGE Executive Secretary and lead WHO technical staff will select Working Group members from the pool of nominees. In addition to meeting the required expertise and avoidance of nominating individuals with conflicts of interest, attention will be given to ensure proper diversity including geographic and gender representation. In general, Chairs of regional technical immunization advisory groups are not eligible to serve on SAGE Working Groups. Should experts be appointed as Chair of a regional technical immunization advisory group after their nomination as member of a Working Group and for SAGE members while still serving on the group after they rotate out of SAGE, they may continue to serve on the Working Group.

For Working Groups which terms of reference require proceedings over a number of years, if a SAGE member rotates out of SAGE while the Working Group is still active, then he/she remains on the Working Group but a new SAGE member should be enrolled to serve on the group. A new SAGE member should be appointed as Working Group Chair when the previous Chair rotates out of SAGE. For Working Groups having proceedings spanning over a number of years, the same rotation process as applied to SAGE membership should be applied i.e. two 3–year terms. The renewal is being determined by a selection panel comprised of the SAGE Chair (or Vice-Chair), the Working Group Chair, lead WHO technical staff and the SAGE Executive Secretary and is based on the contribution of the member to the group. If members resign for personal reasons, are no longer eligible to serve on the group due to arising conflicts of interest, or are unable to meaningfully contribute to the proceedings of the group, they can be replaced with first considering an appointment from the list of initial candidates to join the group. The decision will be made as for the selection of candidates (see above). If no one from this list is suitable then another expert could be solicited and co-opted without resourcing to an open call for nomination.

The size of the Working Group should not exceed 10-12 members and will be adjusted based on the need for expertise and representation.

On rare occasions joint reviews of evidence by SAGE and another area WHO advisory committee (focusing on another area than immunization but with expertise and relevance to the topic being considered) may have to be organized. As a result a SAGE Working Group may be formed in conjunction with this other solicited advisory committee. In this instance members of the solicited advisory committee might also be co-opted on the Working Group and a Working Group co-Chair may be appointed from among members of this other advisory committee. In this case, the selection of Working Group members will

equally involve the Chair and secretariat of the solicited advisory committee.

Working Group members will not be remunerated for their participation in the Working Group; however, reasonable expenses such as travel expenses incurred by attendance at Working Group meetings, SAGE meetings or related meetings will be compensated by WHO.

Working Group Process

Working Groups, with support of the WHO Secretariat will perform or coordinate, systematic assessment of the evidence such as analysis of data addressing efficacy, effectiveness, safety, feasibility, and economic aspects of immunization policy to address questions developed by the Working Group in order to propose appropriate vaccine policy recommendations. This is done in accordance with the process for evidence –review and development of recommendations by SAGE as available at http://www.who.int/immunization/sage/Guidelines_development_recommendations.pdf?ua=1. SAGE uses the Grading of Recommendations Assessment, Development and Evaluation (GRADE) process for the review of evidence. The Working Group will be expected to define the questions to inform the recommendations. It should identify critical questions for which an in-depth review/systematic review of the evidence is needed and determine important outcomes. In developing proposed recommendations the Working Group should complete an evidence-to-recommendation table and systematically consider the following criteria: balance of benefits and harms of the intervention, resource use and value for money, equity impacts, feasibility, acceptability, values and preferences, and other relevant considerations.
Recommendations should be based on GRADing of evidence. Only when not appropriate (and as per criteria stated in the Guidance for the development of evidence-based vaccine related recommendations) the group may opt to develop Good Practice Statements.

All proposed recommendation and comprehensive evidence in support of recommendations including GRADE tables and evidence to decision tables should be presented to SAGE.

SAGE Working Groups are not allowed to render consensus advice or recommendations directly to the WHO Director-General. SAGE Working Group Chairs, other Working Group representatives, or the Working Groups per se are not empowered to speak on behalf of SAGE. Rather, they are utilized by SAGE to gather and organize information upon which SAGE can deliberate and act. Thus, while SAGE Working Groups can and should examine an area in detail and define the issues, including developing options for recommendations, the actual processes of group deliberation terminating in development of group consensus and recommendations must occur in the public forum of SAGE meetings by SAGE. If the Working Group cannot reach consensus then the diverging views will be reflected in the background document or Working Group report presented to SAGE. Such documents will be publicly posted on the SAGE website as soon as the SAGE meeting is over.

Effective communication and a strong working collaboration between the Working Group Chair, Lead WHO staff and the Working Group members are significant determinants of the effectiveness of a Working Group. Draft minutes of Working Group in person meetings or conference calls are produced. As soon as the minutes are approved by the Working Group, they are made available to SAGE members on a protected web workspace. Depending on the Working Group, minutes may be produced by the Secretariat or a Working Group member may be asked to serve as rapporteur. Minutes are not publicly available and are only publicly shared in the context of a SAGE session when included in the background documents.

With the lead WHO Staff, the Chair of the Working Group develops a plan for routine operations of the group. Working Groups accomplish most of their work through teleconferences. A set day and time for routine monthly teleconferences may be established, in order to allow standing teleconferences to be arranged and Working Group members to anticipate and reserve time for these teleconferences. The frequency of Working Group teleconferences may be changed depending on the urgency of issues being considered by the group and the amount of preparatory work needed prior to a topic being brought up for plenary discussion and decision making at SAGE. Some Working Groups may more effectively achieve their purpose through exchange of e-mail communications with intermittent teleconferences. WHO establishes the telephone bridge for teleconferences and ensures free access that telephone charges are not impacted to Working Group members.

In-person meetings of Working Groups may facilitate the proceedings of the group and Working Groups are expected to have at least one face-to-face meeting. If a Working Group is planning to conclude its proceedings at a given face-to-face meeting, this meeting should be held at least one month in advance of the SAGE meeting during which the Working Group is expected to report to SAGE to allow for sufficient time to draft the background materials and proposed recommendations. These face-to-face meetings are normally held in Geneva but they may also be held in different locations if this minimizes cost and facilitates participation of Working Group members and necessary experts.

Individuals other than Working Group members and the Secretariat may participate in Working Group meetings only if their contribution is required by the Working Group. These may include organization representatives, industry representatives/experts, public health officials, faculty staff of academic institutions or other experts. These experts are excluded from any discussions and deliberations within the Working Group and are solely invited to provide specific requested information on a predefined topic. Observers are not allowed to attend Working Group proceedings.

Working Groups are terminated after completion of the TOR and reporting to SAGE unless SAGE asks for additional work. Working Group focused on the development of recommendations on vaccine use may only be closed after the WHO position paper is published following the issuance of recommendations by SAGE. Working Group members will be asked to contribute to the peer-review of the document prior to publication and might be asked to help address reviewer's comments.

Working Groups are encouraged to submit publications of the reviews of the scientific evidence to peer-review journals. This

could be done before or after the SAGE meetings. If published before the SAGE meeting, the publications should reflect the scientific evidence only and not pre-empt the view of SAGE with stating the proposed recommendations and if published after the SAGE meeting should reference the SAGE report.

Management of Conflict of Interest

The value and impact of SAGE recommendations and WHO policy recommendations are critically dependent upon public trust in the integrity of the process. Reported interests are assessed and managed according to SAGE procedures. A summary of the declared interests is publicly posted on the SAGE website in conjunction with the Working Group's TORs and composition (http://www.who.int/immunization/sage/working_mechanisms/en/). Members are expected to proactively inform WHO on any change in relevant interests. These will then be thoroughly assessed by the Working Group Chair, the SAGE Executive secretary as well as the Chair of SAGE. In case of a constituted conflict of interest, the selection panel will meet (see above) to determine a replacement. Should the declared change not result in a conflict of interest, the Working Group member will be able to remain on the Working Group. In both cases, the posted summary will be updated accordingly.

World Health Organization

CURRENT SAGE WORKING GROUPS

Disclaimer: this list includes the current working groups and their active members. These working groups are listed in the order in which they were established. For the complete history of current and previous working groups and their membership from inception, please visit the SAGE website (http://www.who.int/immunization/sage/working_mechanisms/en/).

1. SAGE working group on polio (established August 2008)

Terms of Reference

1. Prepare SAGE for the development of comprehensive policy guidance on the use of IPV in the post-eradication era in low and middle income settings, including by:
    - Reviewing long-term Polio Risks & Risk Management Strategies: reviewing the long-term risks associated with live polioviruses after wild polio transmission globally, and reviewing the range of strategies for mitigating those risks in low-income settings (e.g. coordinated OPV cessation, mOPV stockpiles and response mechanism).
    - Assessing Current & Future IPV Products: reviewing the existing range of IPV products, in terms of supply capacity, production cost, price, presentations, etc, and their appropriateness and suitability for low-income settings, particularly sub-Saharan Africa; and studying the IPV 'pipeline' and its implications for post-eradication IPV use in terms of potential new products (e.g. Sabin-IPV, adjuvanted-IPV, fractional dose IPV), production costs, and prices.
    - Establishing Potential IPV Policies & Implications: establishing the range of IPV vaccination schedule options that could be utilized in a post-eradication world, given the difference in polio immunization objectives and polio risks compared with a polio-endemic world; and identifying and characterizing the programmatic implications, economics and opportunity costs of those policy options, for both IPV stand-alone and combination formulations, in low-income settings and particularly sub-Saharan Africa;
    - Identifying and prioritizing knowledge gaps that should be addressed to facilitate SAGE decision-making on the role(s) and options for IPV use in the post-eradication era in low-income settings.
2. Propose key recommendations to SAGE for updating the 2003 position paper on IPV and consolidating it with other relevant documents (including the 2006 supplement to the IPV position paper) into one vaccine position paper on routine polio immunization covering both IPV and OPV and giving consideration to the ongoing polio eradication efforts.
3. Advise SAGE on technical guidance to WHO and the GPEI for the development and finalization of the overall polio eradication 'endgame strategy' to reduce long-term risks associated with OPV and to accelerate wild poliovirus eradication, including:
    - Policy and programmatic options for the use of different OPV formulations and IPV delivery options, and
    - Strategy and priorities in the related areas of outbreak response, surveillance, containment, risk assessment (esp. Vaccine Derived Polio Viruses - VDPVs), research and product development, and vaccine supply.

Composition

SAGE Members

- Dr Ilesh Jani, (Co-Chair of the Working Group), National Institute of Health, Mozambique
- Ezzeddine Mohsni, Senior Technical Adviser in Global Health Development/ Eastern Mediterranean Public Health Network (Working Group member from February 2019)

Experts

- Yagob Al-Mazrou, Secretary General - Health Services Council of the Kingdom of Saudi Arabia, Saudi Arabia
- Guillaume Chabot-Couture, Director of research, global development, Institute for Disease Modeling , Seattle, WA, USA
- Shelley Deeks, Chief, Communicable Diseases, Emergency Preparedness and Response, Public Health Ontario, Toronto, Canada
- Peter Figueroa University of the West Indies, Jamaica (Co-Chair of Working Group and SAGE member until April 2015)
- Nick Grassly, Imperial College, UK
- Jeffrey Mphahlele, Vice President for Research, South African Medical Research Council, Pretoria, South Africa
- Jean-Marc Olivé, Chair of the Technical Advisory Group (TAG), Pakistan, Afghanistan, Horn of Africa and Lake Chad
- Walter Orenstein, Emory University, USA
- Jacob John Thekkekara, Advisor, Christian Medical College Hospital, Vellore, India Kimberley Thompson, Kids Risk Project, Harvard School of Public Health, USA
- Khalequ Zaman, Scientist and Epidemiologist, International Centre for Diarrhoeal Disease Research, Dhaka, Bangladesh

2. SAGE working group on measles and rubella vaccines (established November 2011)

Terms of Reference

- Review progress towards global measles control targets and regional measles and rubella elimination goals and highlight key obstacles.
- Prepare for regular updates and review by SAGE on progress and challenges in achieving existing measles and rubella control targets and propose necessary updating of current WHO recommendations on vaccines (including outbreak response immunization) and surveillance strategies.
- Identify gaps in essential evidence and programme barriers to achieving measles and rubella/CRS elimination targets and present SAGE with proposed areas for operational or basic science research. The working group will liaise with other relevant technical advisory committees (e.g. Immunization and vaccines related implementation research advisory committee (IVIR-AC), and the Immunization Practice Advisory Committee (IPAC)) to address relevant quantitative issues as well as those related to immunization practices.
- Explore the potential use of new technologies that could help improve coverage and thereby expedite elimination of measles/rubella.
- Advise SAGE, no later than 2020, whether a formal global goal for measles eradication and/or rubella eradication should be set with timeframes for its achievement.

Composition

SAGE Members

- Nikki Turner, University of Auckland, New Zealand. (Chair of the Working Group from October 2016)
- Jaleela Sayed Jawad, Ministry of Health, Kingdom of Bahrain (Member of the Working Group since January 2017, SAGE Member since 2015).
- Youngmee Jee, Centre for Pathology and Immunology, National Institute of Health, Korean Centre for Disease Control and Prevention, Republic of Korea (Member of the Working Group since January 2019, SAGE Member since 2017)

Experts

- Narendra Arora, International Clinical Epidemiology Network, India (Member of the Working Group since November 2011, SAGE Member 2010 - 2016);
- Ma Chao, Chinese Center for Disease Control and Prevention, China (Member of the Working Group since June 2019)
- David Durrheim, Hunter New England Area Health Service, Public Health Medicine, University of Newcastle, Australia (Member of the Working Group since November 2011, SAGE Member 2009 - 2012);
- Deepa Gamage, Epidemiology Unit, Ministry of Health, Sri Lanka (Member of the Working Group since June 2019)
- Olubukola (Bukky) T. Idoko, Medical Research Council Unit, The Gambia at London School of Hygiene and Tropical Medicine (Member of the Working Group since June 2019)
- Mark Jit, London School of Hygiene and Tropical Medicine, UK (Member of the Working Group since January 2017);
- Walter Orenstein, Emory University School of Medicine, USA (Member of the Working Group since January 2017);
- Nkengafac Villyen Motaze, National Institute for Communicable Diseases, South Africa (Member of the Working Group since January 2018);
- Paul Rota, Division of Viral Diseases, Centers for Disease Control and Prevention, USA (Member of the Working Group since January 2018);
- William Schluter, Global Immunization Division, Centers for Disease Control and Prevention, USA (Member of the Working Group since January 2018).

3. SAGE Working Group on the Decade of Vaccines (established March 2013)

Terms of Reference

The SAGE Working Group (WG) will facilitate a yearly SAGE independent review of the implementation of the Decade of Vaccines' Global Vaccine Action Plan (GVAP) and assessment of progress. Specifically, the WG will:

1. Review the quality of the data on the GVAP indicators and make recommendations on changes to the formulation of the indicators, operational definitions and/or the processes for data collection;
2. Independently evaluate and document progress towards each of the 6 GVAP Strategic Objectives and towards the achievement of the Decade of Vaccines Goals (2011-2020), using the GVAP Monitoring & Evaluation / Accountability Framework;
3. Identify successes, challenges and areas where additional efforts or corrective actions by countries, regions, partners, donor agencies or other parties, are needed;
4. Identify and document best practices;

5. Prepare the GVAP implementation annual report to be presented to the SAGE, and thereafter, with SAGE inputs, be submitted for discussion to the WHO January EB meeting, to the WHA and the independent Expert Review Group (iERG) for the UN Secretary General's Global Strategy for Women's and Children's Health.

In its review the WG should take a broad perspective, encompassing the general environment, including the health system context.

Composition

SAGE Members

- Noni MacDonald, Dalhousie University, IWK Health Centre, Canada. (Chair of the Working Group of June 2017 to replace Narendra Arora)
- Ezzeddine Mohsni (joining SAGE in January 2019), Senior Technical Adviser in GHD/EMPHNET (Global Health Development / Eastern Mediterranean Public Health Network)

Experts

- Oleru Huda Abason, Parliament of Uganda, Uganda. (Member of the Working Group from May 2016)
- Mahmoud Mustafa Amani, The Carter Center, Sudan.
- Jon Kim Andrus, Sabin Vaccine Institute, United States of America. (Member of the Working Group from May 2016)
- Yagob Al-Mazrou, Health Services Council, Saudi Arabia.(Former SAGE member 2012-2017)
- Narendra Arora, International Clinical Epidemiology Network, India. (Chair of the Working Group until May 2017 and SAGE member until April 2016)
- Susan Elden, Department for International Development, United Kingdom. (Member of the Working Group from May 2016)
- Marie-Yvette Madrid, Independent Consultant, Switzerland.
- Rebecca Martin, Centers for Disease Control and Prevention, United States of America.
- Helen Rees, University of Witwatersrand, South Africa. (former SAGE Chair 2010 - 2013)
- David Salisbury, Centre on Global Health Security, United Kingdom. (former SAGE Chair 2005 - 2010)
- Qinjian Zhao, Xiamen University, China. (Member of the Working Group from May 2016)

4. SAGE Working Group on Ebola Vaccines and Vaccination (established November 2014)

Terms of Reference

The Strategic Advisory Group of Experts (SAGE) on Immunization Working Group is exceptionally established with an urgent program of work to facilitate a SAGE review of available evidence and advice to WHO on the potential post-licensure use of the Ebola vaccines in order to mitigate the public health impact of the disease and possibly curtail the ongoing epidemic, as well as to prevent or reduce the risk of spread of disease in the future. The Working Group will consult with the Task Force for Immunization for the African region to get their inputs into the operationalization of immunization delivery and consolidate the feedback into a report to SAGE with recommendations on potential strategies for the deployment of vaccines.

In order to facilitate the review, the Working Group will provide technical advice and support to the WHO secretariat by:

1. Reviewing the essential evidence required for making policy recommendations and on strategies for deployment of vaccines.
2. Reviewing the available epidemiological data to define the risk of disease and mortality in different population groups in order to allow prioritization of vaccination.
3. Reviewing the evidence, as it becomes available, on the safety, and efficacy of candidate vaccines, including the optimal vaccination schedules to be used for each vaccine.
4. Reviewing the data on the projected impact of different vaccination strategies generated by mathematical models.
5. Reviewing the synthesis of the above data for presentation to SAGE and in drafting recommendations for consideration by SAGE.
6. Reviewing the projections of vaccine supply to inform recommendations on the deployment of vaccines.

Composition

SAGE Members

- Fred Were, University of Nairobi, Kenya. (Co-Chair of the Working Group from April 2016)
- Shabir Mahdi, Professor of Vaccinology at the University of the Witwatersrand, Johannesburg, South Africa. (Serves as SAGE member on the Working Group as of January 2019)

Experts

- Nick Andrews, Public Health England, United Kingdom.
- George Bonsu, Ministry of Health, Ghana.
- David Durrheim, Hunter New England Area Health Service, Australia. (SAGE member until April 2012)
- Jean-Paul Jemmy, Médecins Sans Frontières, Belgium.
- Ann Kelly, University of Exeter, United Kingdom.
- Keymanthri Moodley, Stellenbosch University, South Africa.
- Diop Ndack, University Cheikh Anta Diop, Senegal.
- Cesar Velasco Muñoz, Hospital Clínico Lozano Blesa, Spain.
- Chris Ockenhouse, PATH, United States of America.
- Helen Rees, University of Witwatersrand, South Africa. (Co-Chair of the Working Group and former SAGE Chair 2010 - 2013)
- Oyewale Tomori, Redeemer's University, Nigeria. (Co-Chair of the Working Group until March 2016 and SAGE member until April 2015)

5. SAGE Working Group on pneumococcal conjugate vaccine (established December 2016)

Terms of Reference

1. Review and summarize the measured and modelled evidence on PCV immunogenicity and impact (direct and indirect) on carriage, disease, and mortality with respect to the following questions/issues:
    a. Effectiveness and/or impact of different schedules and strategies for PCV use in industrialized and developing countries;
    b. Preference of 2p+1 or 3p+0 schedule for current or future impact
    c. Choice of PCV products;
    d. Catch-up vaccination of infants and/or older age groups during PCV introduction;
    e. Maximize herd protection;
    f. Optimize duration of protection.
2. Propose to SAGE recommendations on optimal PCV use related to the above listed questions and issues in order to revisit the 2012 WHO PCV position paper.
3. Identify and prioritize knowledge gaps and critical questions to prepare a concrete scope of work with a proposed timeline for future PCV working group activities. The following questions/issues will likely be included:
    a. Serotype replacement in the era of extended valency conjugate vaccines;
    b. Options for optimal PCV use in the future, including in settings of near-elimination levels of vaccine serotype disease;
    c. PCV use in adults, including the elderly;
    d. Incremental benefit of the polysaccharide vaccine in adults in era of PCV use.
4. Provide SAGE with summaries and analyses needed to support its discussion and recommendation process.

Composition

SAGE Members

- Andrew J. Pollard, University of Oxford, United Kingdom (Chair of the Working Group)
- Peter McIntyre, University of Sydney, Australia

Experts

- Narendra Arora, The INCLEN Trust International, New Delhi
- Stefan Flasche, London School of Hygiene & Tropical Medicine, United Kingdom
- Kyung-Hyo Kim, Ewha Womans University School of Medicine, Republic of Korea
- David Goldblatt, University College London, United Kingdom
- Elisabeth Lieke Sanders, National Institute for Public Health and the Environment, The Netherlands
- Dafrossa Lyimo, Ministry of Health, Tanzania
- Elizabeth Miller, Public Health England, United Kingdom
- Edward Kim Mulholland, Murdoch Childrens Research Institute, Australia
- Tamara Pilishvili, Centers for Disease Control and Prevention, United States of America
- Betuel Sigauque, Manhiça Health Research Centre, Mozambique
- Cristiana Toscano, Federal University of Goiás, Brazil
- Kate O'Brien, Johns Hopkins Bloomberg School of Public Health, United States of America (resigned from the Working Group in January 2019)

6. SAGE Working Group on Quality and Use of Global Immunization and Surveillance Data (established August 2017)

Terms of Reference

The Working Group will be requested to review the current global immunization and surveillance data collection, its use and impact as well as limitations and needs and propose recommendations to improve quality, access to, and use of immunization data for enhancing immunization programme performance at national and subnational levels. These recommendations will then be presented for review by SAGE.

1. Take stock of data availability and determine if there are unmet immunization monitoring and evaluation data needs at global level, and guide reporting processes;
2. Review existing and new draft standards and guidance on immunization monitoring and vaccine-preventable disease (VPD) surveillance data to identify gaps, revisions, and areas that require updates;
3. Review and assess the current 'state' of immunization and VPD-surveillance data quality at country and global level;
4. Review evidence on:
    1) factors that may cause and/or limit access to quality and use of immunization and VPD-surveillance data for decision-making at different levels;
    2) the effectiveness (including where possible, cost-effectiveness) of interventions for improving access to, improving quality of, or promoting the use of data at national and subnational levels;
5. Review the status of information systems that collect immunization and VPD-surveillance data, the availability of modern information technologies, and their current and potential future role in supporting the collection, management, analysis and use of immunization and surveillance data;
6. Identify knowledge gaps and create a prioritized research agenda.

Composition

SAGE Members

- Jaleela Jawad, Ministry of Health, Bahrain (Chair of the Working Group)
- Noni MacDonald, Dalhousie University, IWK Health Centre, Canada

Experts

- George Bonsu, Ghana Health Service, Ghana
- Michael Edelstein, Public Health England, United Kingdom
- Hashim Ali Elzein Elmousaad, Independent Consultant, Sudan
- Pradeep Haldar, Ministry of Health and Family Welfare, India
- Claudio Lanata, Instituto de Investigacion Nutricional, Peru
- Ana Morice, Independent Consultant, Costa Rica
- Mimi Mynak, Jigme Dorji Wangchuk National Referral Hospital, Ministry of Health, Bhutan
- Edward Nicole, South African Medical Research Council; Stellenbosch University, South Africa
- Su Qiru, Chinese CDC, China (resigned from Working Group in April 2018)
- Nargis Rahimi, Shifo Foundation, Sweden
- Heather Scobie, Centers for Disease Control and Prevention, United States of America

7. SAGE Working Group on Influenza (established December 2017)

Terms of Reference

The Working Group will be requested to review the scientific evidence and relevant programmatic considerations to assess whether there is sufficient evidence to inform a revision of the global policy on the use of influenza vaccines, and for subsequent updating of the WHO position paper on influenza vaccines.

Specifically the Working Group will be asked to review the following elements:

1. the evidence on the effect of prior immunization on the efficacy and effectiveness of seasonal influenza vaccines, and whether a change in policy would result in improved public health outcomes
2. the evidence on the effectiveness of adjuvanted seasonal influenza vaccines in pediatric populations
3. the evidence on the effectiveness of improved formulations for influenza vaccines for older adults and other risk groups
4. the evidence on the effectiveness of live attenuated influenza vaccines.

Composition

SAGE members

- Rakesh Aggarwal: Institute of Medical Sciences, Lucknow, India
- Andrew J. Pollard: University of Oxford, United Kingdom (Chair of the Working Group)

Experts

- Jon Abramson, Wake Forest Baptist Health, USA;
- Joseph Bresee, Centers for Disease Control and Prevention, USA;
- Cheryl Cohen, National Institute of Communicable Diseases, South Africa;
- Rebecca J. Cox, University of Bergen, Norway;

- Luzhao Feng, Chinese Center for Disease Control and Prevention, China;
- Kawsar Talaat, Johns Hopkins Bloomberg School of Public Health, USA;
- Hanna Nohynek, National Institute for Health and Welfare, Finland;
- Richard Pebody, Public Health England, United Kingdom;
- Sheena Sullivan, WHO Collaborating Centre for Reference and Research on Influenza, Australia;
- Bryna Warshawsky, Public Health Ontario; Ontario Agency for Health Protection and Promotion, Canada;
- Maria Zambon, Public Health England, United Kingdom.

8. SAGE Working Group on HPV (established June 2018)

Terms of Reference

- To critically appraise the evidence and potential effect and cost effectiveness of various vaccination strategies towards the achievement of cervical cancer elimination.
- To review the potential contribution of HPV vaccination towards cervical cancer elimination.
- To develop and propose interim goals that can be achieved through immunization as part of the efforts towards cancer elimination.
- To develop and propose indicators to monitor the accomplishment of these interim goals.
- To discuss and propose additional research related to vaccines and immunization needed to attain these goals and outline potential innovations that may help enhance the achievement of these goals.

Composition
SAGE members
- Rakesh Aggarwal, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India (Chair of the Working Group, SAGE member since 2017);
- Andrew J. Pollard, University of Oxford, United Kingdom (SAGE member since 2016)

Experts
- Neerja Bhatla, All India Institute of Medical Sciences, India;
- Shereen Bhutta, Independent Expert, Pakistan;
- Eduardo Franco, McGill University, Canada;
- Silvia Franceschi, CRO Aviano National Cancer Institute IRCCS, Italy;
- Deepa Gamage, Ministry of Health, Sri Lanka;
- Suzanne Garland, University of Melbourne, Australia;
- Lauri Markowitz, U.S. Centers for Disease Control and Prevention, USA;
- You-Lin Qiao, Cancer Hospital, Chinese Academy of Medical Sciences, China;
- Helen Rees, University of the Witwatersrand, South Africa (SAGE member 2005-2013);
- John Schiller, Laboratory of Cellular Oncology, National Cancer Institute, NIH, USA;
- Margaret Stanley, University of Cambridge, UK

9. SAGE Working Group on meningococcal vaccines and vaccination (established May 2019)

Terms of Reference

The Working Group is established to prepare a SAGE review of new evidence and advice to WHO on the use of meningococcal vaccines in order to mitigate the public health impact of the disease, including to reduce the risk of epidemics and to prevent health emergencies. Specifically, this will include updating recommendations for the optimal use of meningococcal conjugate vaccines in the meningitis belt and globally; as well developing recommendations for the use of meningococcal B vaccines.

The Working Group will also prepare a SAGE review of the plan and advice to WHO on the global roadmap to defeat meningitis by 2030, focusing on bacterial meningitis and equitable and sustainable access to vaccines, diagnosis and treatment. In order to prepare for the review, the Working Group will provide technical advice and support to the WHO secretariat through reviews of:

- The essential evidence required for updating or developing policy recommendations for meningococcal vaccines, including on strategies for use of vaccines to respond to epidemics;
- The updated epidemiological data on meningococcal carriage, disease, mortality and epidemics, globally and in different regions and population groups;

- The evidence on the use of meningococcal vaccines, globally and in different regions and population groups, including in outbreak response settings, with a particular focus on protein based vaccines against group B meningococcus and conjugate vaccines against all other meningococci;
- The evidence on the safety, immunogenicity and efficacy of candidate vaccines, in various target age groups and using different schedules.
- The results from modelling studies on the impact of different vaccination strategies.
- The summary of the above data for presentation to SAGE and the draft recommendations for consideration by SAGE. These recommendations will be used to update the WHO position paper on meningococcal vaccines.
- The draft Defeating meningitis by 2030 global roadmap and the draft advice for consideration by SAGE.

Composition

SAGE members

- Firdausi Qadri (Chair of the WG): International Centre for Diarrhoeal Disease and Research, Bangladesh
- Nicola Turner: University of Auckland, New Zealand

Experts

- Ray Borrow: Public Health England, UK
- Dominique Caugant: Norwegian Institute of Public Health, Norway
- Matthew Coldiron: Epicentre, France
- Abdulrazaq Garba Habib: Bayero University Kano, Nigeria
- Ziad Memish: Saudi Ministry of Health, Saudi
- Judith Mueller: Ecole des Hautes Etudes en Santé Publique, France
- Rasmata Ouedraogo: Centre Hospitalier Pédiatrique Charles de Gaulle, Burkina Faso
- Marco Sáfadi: Santa Casa de São Paulo School of Medical Sciences, Brazil
- Manish Sadarangani: University of British Columbia and British Columbia Children's Hopsital, Canada
- David Stephens: Emory University School of Medicine, USA
- Caroline Trotter: University of Cambridge, UK
- Ann von Gottberg: National Health Laboratory Service, South Africa
- Shao Zhujun: Chinese Center for Disease Control and Prevention, China

World Health Organization

Strategic Advisory Group of Experts (SAGE) on Immunization
8-10 October 2019
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Meeting of the Strategic Advisory Group of Experts on immunization, April 2019 – conclusions and recommendations

The Strategic Advisory Group of Experts (SAGE) on Immunization[1] met on 2–4 April 2019. This report summarizes their discussions, conclusions and recommendations.[2]

Report from the WHO Department of Immunization, Vaccines and Biologicals

The report entitled, "Paradoxes of the Present and a Focus for the Future of Vaccines and Immunization," presented by the Director of the WHO Department of Immunization, Vaccines and Biologicals reviewed four key aspects: (1) over the last decades, the world has improved in nearly all dimensions of development, population control, and health; (2) the world in 2019 is increasingly uncertain and volatile; (3) the vaccine and immunization agenda is being reshaped to deliver on equity, security and prosperity; and (4) vaccines and immunization are central to achieving the Sustainable Development Goals (SDGs) and WHO's "triple billion" goal as part of its 13th Programme of Work.[3]

Much progress has been made, with 116 million infants in 2017 protected with 3 doses of diphtheria-tetanus-pertussis vaccine, measles vaccination having averted an estimated 21.1 million deaths during 2000–2017 and more countries adding new life-saving vaccines to their national immunization programmes. Yet, the report of the Global Vaccine Action

[1] See www.who.int/immunization/sage/en/index.html, accessed April 2019.

[2] Presentations and background materials used at the SAGE meeting, a list of SAGE members and their declarations of interests are available at https://www.who.int/immunization/sage/meetings/2019/april/en/, accessed April 2019.

[3] See https://www.who.int/about/what-we-do/thirteenth-general-programme-of-work-2019-2023, accessed April 2019.

Réunion du Groupe stratégique consultatif d'experts sur la vaccination, avril 2019 – conclusions et recommandations

Le Groupe stratégique consultatif d'experts (SAGE) sur la vaccination[1] s'est réuni du 2 au 4 avril 2019. Le présent rapport résume les discussions, conclusions et recommandations auxquelles il est parvenu.[2]

Rapport du Département Vaccination, vaccins et produits biologiques de l'OMS

Le rapport intitulé «Paradoxes of the Present and a Focus for the Future of Vaccines and Immunization», présenté par le Directeur du Département Vaccination, vaccins et produits biologiques de l'OMS, a abordé 4 principaux thèmes: 1) au cours des dernières décennies, le monde s'est amélioré dans presque toutes les dimensions du développement, du contrôle de la population et de la santé; 2) le monde en 2019 est de plus en plus incertain et instable; 3) le programme pour les vaccins et la vaccination est remodelé pour assurer l'équité, la sécurité et la prospérité; et 4) les vaccins et la vaccination sont essentiels pour atteindre les objectifs du développement durable (ODD) et l'objectif du «triple milliard» de l'OMS dans le cadre du 13e programme de travail.[3]

Les progrès accomplis sont nombreux: en 2017, 116 millions de nourrissons ont été protégés avec 3 doses de vaccin antidiphtérique-antitétanique-anticoquelucheux, la vaccination contre la rougeole a permis d'éviter environ 21,1 millions de décès entre 2000 et 2017 et davantage de pays ont ajouté de nouveaux vaccins vitaux à leurs programmes nationaux de vaccination. Pourtant, le rapport 2018 du

[1] Voir www.who.int/immunization/sage/en/index.html, consulté en avril 2019.

[2] Les communications et les documents de travail utilisés pour la réunion du SAGE, ainsi que la liste des membres du SAGE et leurs déclarations d'intérêts sont disponibles à l'adresse: https://www.who.int/immunization/sage/meetings/2019/april/en, consulté en avril 2019.

[3] Voir https://www.who.int/about/what-we-do/thirteenth-general-programme-of-work-2019-2023, consulté en avril 2019.

Plan (GVAP) in 2018 noted that 9 of the 10 goals set at the beginning of the decade will not be achieved by 2020. Three countries are still endemic for circulating wild poliovirus (Afghanistan, Nigeria and Pakistan), no region has achieved and sustained measles elimination, coverage with a first dose of measles vaccine is stagnating at 85%, and 19.9 million children are under- or unvaccinated.

Throughout the world, more populations face conflict and migration, climate change, infectious disease outbreaks and substantial inequities in wealth, health and security. Meanwhile, there is increasing circulation of misinformation and misrepresentation on various topics, including vaccines, which lead to distrust, less vaccination and a greater risk of outbreaks of previously controlled, vaccine-preventable diseases. Outbreaks of measles are a sign of populations with low vaccine coverage; all the WHO regions have experienced larger and more frequent measles outbreaks in the past 12 months.

The next decade is an opportunity to reshape the vaccines and immunization agenda to deliver on equity, security and prosperity. Partners and stakeholders should address priorities and find new solutions, while contributing to the broader global health agenda, including the SDGs, primary health care[4] and universal health coverage.[5]

To ensure equity, the estimated 19.9 million children who are under- or unvaccinated should be vaccinated; introduction of pneumococcal and rotavirus vaccines should be accelerated; more girls should be vaccinated with human papillomavirus vaccine; and tactics should be found to vaccinate children living in fragile, conflict or humanitarian crisis settings. Several long-awaited new vaccines against respiratory syncytial virus, malaria, tuberculosis and HIV could improve health and ensure equity in the future.

Vaccines and immunization safeguard health security by preventing disease outbreaks. Examples include deployment of cholera vaccine in the aftermath of the tropical cyclone Idai that hit Mozambique on 15 March 2019, use of a vaccine against Ebola virus disease in the Democratic Republic of the Congo (DRC) and use of pneumococcal and typhoid vaccines in areas of high antimicrobial resistance.

Outbreaks of vaccine-preventable diseases cause morbidity and mortality and also have a significant economic impact. Estimates in the business case for the WHO African Region indicate that preventing outbreaks and sustaining vaccination against 4 vaccine-preventable diseases – measles, rubella, rotavirus and pneumococcal disease – could result in savings of US$ 60 billion by 2030. This gain and the numbers of deaths and medical

Plan d'action mondial pour les vaccins (GVAP) indiquait que 9 des 10 objectifs fixés au début de la décennie ne seraient pas atteints en 2020. Dans 3 pays (Afghanistan, Nigéria et Pakistan), le poliovirus sauvage circule encore de manière endémique, aucune région n'a réussi et maintenu l'élimination de la rougeole, la couverture par la première dose du vaccin antirougeoleux stagne à 85% et 19,9 millions d'enfants sont sous-vaccinés ou non vaccinés.

Partout dans le monde, de plus en plus de populations sont confrontées à des conflits et à des migrations, à des changements climatiques, à des épidémies de maladies infectieuses et à des inégalités considérables en matière de richesse, de santé et de sécurité. Dans le même temps, on assiste à une diffusion croissante de fausses informations et de fausses déclarations sur divers sujets, notamment les vaccins, qui suscitent la méfiance, réduisent le nombre de personnes vaccinées et augmentent le risque de flambées épidémiques de maladies évitables par la vaccination auparavant contrôlées. Les flambées épidémiques de rougeole révèlent une faible couverture vaccinale dans les populations; toutes les Régions de l'OMS ont connu des flambées de rougeole plus importantes et plus fréquentes au cours des 12 derniers mois.

La prochaine décennie est l'occasion de remodeler le programme pour les vaccins et la vaccination afin d'assurer l'équité, la sécurité et la prospérité. Les partenaires et les parties prenantes doivent s'attaquer aux priorités et trouver de nouvelles solutions, tout en contribuant au vaste programme d'action mondial en faveur de la santé, notamment les ODD, les soins de santé primaires[4] et la couverture santé universelle.[5]

Pour assurer l'équité, les 19,9 millions d'enfants estimés sous-vaccinés ou non vaccinés doivent être vaccinés; l'introduction des vaccins antipneumococciques et antirotavirus doit être accélérée; davantage de filles doivent être vaccinées contre le papillomavirus humain; et l'on doit élaborer des tactiques pour vacciner les enfants vivant dans des situations précaires, de conflit ou de crises humanitaires. Plusieurs nouveaux vaccins tant attendus contre le virus respiratoire syncytial, le paludisme, la tuberculose et le VIH pourraient améliorer la santé et assurer l'équité dans le futur.

Les vaccins et la vaccination préservent la sécurité sanitaire en prévenant les flambées de maladies. Citons par exemple le déploiement du vaccin anticholérique à la suite du cyclone tropical Idai qui a frappé le Mozambique le 15 mars 2019, l'utilisation d'un vaccin contre la maladie à virus Ebola en République démocratique du Congo (RDC) et l'utilisation des vaccins contre le pneumocoque et la fièvre typhoïde dans les zones à forte résistance antimicrobienne.

Les flambées épidémiques de maladies évitables par la vaccination entraînent morbidité et mortalité, et ont également un impact économique important. Selon les estimations de l'analyse de rentabilité de la Région africaine de l'OMS, la prévention des épidémies et le maintien de la vaccination contre 4 maladies évitables par la vaccination – rougeole, rubéole, rotavirus et pneumocoques – pourraient permettre d'économiser US$ 60 milliards d'ici 2030. Ce gain et le nombre de décès et la

[4] See https://www.who.int/news-room/fact-sheets/detail/primary-health-care, accessed April 2019

[5] See https://www.who.int/news-room/fact-sheets/detail/universal-health-coverage-(uhc), accessed April 2019

[4] Voir https://www.who.int/news-room/fact-sheets/detail/primary-health-care, consulté en avril 2019.

[5] Voir https://www.who.int/news-room/fact-sheets/detail/universal-health-coverage-(uhc), consulté en avril 2019.

impoverishment averted by vaccines show that vaccines contribute to development and prosperity. Of all the basic health services, vaccination has the highest coverage and reaches more households than other health interventions. Vaccination is a platform for primary health care and underpins universal health coverage. The 2030 vision places vaccines as a human right and part of a healthy life, with tailored approaches for country programmes. Vaccination is linked to 14 of the 17 SDGs, thus providing a compelling argument for the value of vaccines.

paupérisation médicale évités par les vaccins montrent que ces derniers contribuent au développement et à la prospérité. De tous les services de santé de base, la vaccination a la couverture la plus élevée et touche plus de ménages que les autres interventions sanitaires. La vaccination est une plateforme pour les soins de santé primaires et elle est à la base de la couverture santé universelle. La vision 2030 envisage les vaccins comme un droit humain et un élément constitutif d'une vie en bonne santé, avec des approches adaptées pour les programmes nationaux. La vaccination est liée à 14 des 17 ODD, ce qui constitue un argument convaincant en faveur de la valeur de la vaccination.

Reports from WHO Regional Offices

The WHO Regional Office for Africa reported on the measles outbreak in Madagascar in 2018–2019, which has resulted in almost 120 000 cases and about 1000 deaths. Although the country has taken action to halt the outbreak, it is clear that its national immunization programme requires revision. Similar revisions are needed in other African countries to ensure that their programmes are adequate for the next decade. The outbreak of Ebola virus disease that began 8 months ago in North Kivu province in the DRC has become the country's most severe. In areas of conflict and under highly challenging conditions, front-line responders have continued to work to ensure that people have the necessary information, care, treatment and vaccination. Since cyclone Idai, Mozambique has experienced increased numbers of cholera cases, and WHO and other stakeholders are helping to restore health services and to prevent, detect, verify and respond to disease outbreaks through strengthened surveillance. The technical support of WHO to the DRC and Nigeria illustrates the tailored approaches that are being used to address public health challenges and strengthen immunization systems.

The WHO Regional Office for the Americas also reported on progress and challenges in immunization programmes. Sustaining high levels of vaccine coverage in all districts is a major concern, and a comprehensive analysis is planned. The Region experienced outbreaks of diphtheria, measles and yellow fever, and Haiti is continuing to tackle outbreaks of diphtheria. Measles cases were reported in 10 countries, and endemic transmission of measles has been re-established in Brazil and the Bolivarian Republic of Venezuela. The Region is preparing an action plan and a public health response to ensure future re-verification of measles elimination.

In the WHO Eastern Mediterranean Region, a large proportion of children live in 2 of the 3 countries endemic for wild poliovirus, in conflict areas or in humanitarian emergencies. Several countries in the Region, such as Sudan, have nevertheless maintained strong immunization programmes. The commitment of the governments of many middle-income countries to fully finance new vaccines is essential. Nevertheless, lower- to middle-income countries continue to have difficulty in introducing new vaccines because of their high cost and inadequate allocation of domestic resources. The Region and the world must prepare appropriately for mass gatherings such as the Hajj and

Rapports des bureaux régionaux de l'OMS

Le Bureau régional OMS de l'Afrique a rendu compte de la flambée épidémique de rougeole à Madagascar en 2018-2019, qui a provoqué près de 120 000 cas et environ 1000 décès. Bien que le pays ait pris des mesures pour enrayer l'épidémie, il est clair que son programme national de vaccination doit être révisé. Des révisions similaires sont nécessaires dans d'autres pays africains afin de s'assurer que leurs programmes sont adéquats pour la prochaine décennie. L'épidémie de maladie à virus Ebola qui a commencé il y a 8 mois dans la province du Nord-Kivu en RDC est devenue la plus grave que le pays ait connue. Dans les zones de conflit et dans des conditions très difficiles, les intervenants de première ligne ont continué de veiller à ce que la population dispose des informations, des soins, des traitements et des vaccins nécessaires. Depuis le cyclone Idai, le nombre de cas de choléra a augmenté au Mozambique et l'OMS et d'autres parties prenantes aident à rétablir les services de santé et à prévenir, détecter, vérifier et combattre les flambées épidémiques grâce à une surveillance renforcée. L'appui technique de l'OMS à la RDC et au Nigéria illustre les approches «sur mesure» employées pour résoudre les problèmes de santé publique et renforcer les systèmes de vaccination.

Le Bureau régional OMS des Amériques a également rendu compte des progrès et des difficultés des programmes de vaccination. Le maintien d'une couverture vaccinale élevée dans tous les districts est une préoccupation majeure, et une analyse complète est prévue. La Région a connu des flambées épidémiques de diphtérie, de rougeole et de fièvre jaune, et Haïti continue de combattre des flambées de diphtérie. Des cas de rougeole ont été notifiés dans 10 pays, et la transmission endémique de la rougeole s'est rétablie au Brésil et en République bolivarienne du Venezuela. La Région prépare actuellement un plan d'action et une action de santé publique pour vérifier à nouveau prochainement l'élimination de la rougeole.

Dans la Région OMS de la Méditerranée orientale, une vaste proportion d'enfants vivent dans 2 des 3 pays d'endémie du poliovirus sauvage, dans des zones de conflit ou en situation d'urgence humanitaire. Plusieurs pays de la Région, comme le Soudan, ont néanmoins maintenu de solides programmes de vaccination. L'engagement des gouvernements de nombreux pays à revenu intermédiaire à financer intégralement les nouveaux vaccins est essentiel. Cependant, les pays à revenu faible ou intermédiaire continuent d'éprouver des difficultés à introduire de nouveaux vaccins en raison de leur coût élevé et de l'insuffisance des ressources nationales allouées. La Région et le monde doivent se préparer de manière appropriée aux rassemblements de masse tels que le Hadj et l'Umrah, qui

Umrah, which bring millions of pilgrims to Mecca. The number could reach 30 million by 2030.

The WHO European Region reported on the work of the European Technical Advisory Group of Experts on immunization (ETAGE) for ensuring application of SAGE recommendations, such as school entry vaccination checks and vaccination of health care workers and pregnant women, through national technical advisory groups. Although more children are being vaccinated against measles than before, progress between and within countries has been uneven, and increasing numbers of clusters of unprotected individuals resulted in a record number of cases in 2018. The Regional Office is preparing a strategy and a plan to assist countries in monitoring and addressing inequity. Concern remains about the ability of some middle-income countries to adequately finance their immunization programmes. Progress was reported in Ukraine, where the Ministry of Health recently invited partners to identify support to address these challenges, and a multi-year domestic funding plan has been established for intensified vaccination activities.

The WHO Regional Office for South-East Asia reported that the Region is maintaining its polio-free status and its maternal and neonatal tetanus elimination status. Four countries (Bhutan, Maldives, the Democratic People's Republic of Korea and Timor-Leste) have been verified as having eliminated endemic measles, and 6 countries have been certified as having controlled rubella and congenital rubella syndrome. Myanmar, however, experienced a measles outbreak. It will be important to follow the recommendations of the national technical advisory group on use of vaccines such as inactivated polio vaccine (IPV), vaccines against human papillomavirus and Japanese encephalitis and pneumococcal conjugate vaccines. All partners should support countries in following up on reviews of their Expanded Programmes on Immunization and of evaluations after vaccine introduction. Countries in the Region are using tailored approaches to improve coverage and equity, especially among high-risk populations and in under-served areas. Since the influx of migrant refugees into the Cox's Bazar area of Bangladesh, campaigns have been conducted with bivalent oral polio vaccine (OPV), measles–rubella vaccine, pentavalent vaccine, vaccines against tetanus, diphtheria and pertussis, pneumococcal conjugate vaccine and oral cholera vaccine. Since June 2018, routine immunization services have also been established to ensure vaccination of new cohorts.

The WHO Regional Office for the Western Pacific reported progress in achieving the goals in the regional framework for implementation of the GVAP. A regional strategic framework is being prepared for endorsement by the Regional Committee in 2020 to ensure alignment with global health and immunization strategies. The Region has maintained its polio-free status since certification in 2000. As of September 2018, 8 countries and areas [Australia, Brunei Darussalam, Cambodia, Hong Kong SAR (China), Japan, Macao SAR (China), New Zealand and Republic of Korea] have been verified as

amènent des millions de pèlerins à la Mecque. Le nombre de pèlerins pourrait atteindre 30 millions en 2030.

La Région OMS de l'Europe a rendu compte des travaux du Groupe consultatif technique européen d'experts sur la vaccination (ETAGE) pour veiller à l'application des recommandations du SAGE – par le biais de groupes consultatifs techniques nationaux – telles que les contrôles de vaccination à l'entrée à l'école et la vaccination des agents de santé et des femmes enceintes. Bien qu'un plus grand nombre d'enfants soient vaccinés contre la rougeole qu'auparavant, les progrès ont été inégaux d'un pays à l'autre et à l'intérieur d'un même pays, et le nombre croissant de groupes de personnes non protégées a entraîné un nombre record de cas en 2018. Le Bureau régional prépare actuellement une stratégie et un plan pour aider les pays à surveiller et à corriger les inégalités. La capacité de certains pays à revenu intermédiaire à financer convenablement leurs programmes de vaccination demeure une préoccupation. Des progrès ont été rapportés en Ukraine, où le Ministère de la santé a récemment invité les partenaires à identifier un soutien pour surmonter ces difficultés, et un plan de financement national pluriannuel a été établi pour intensifier les activités de vaccination.

Le Bureau régional OMS de l'Asie du Sud-Est a indiqué que la Région maintenait son statut de région exempte de poliomyélite et son statut région ayant éliminé le tétanos maternel et néonatal. L'élimination de la rougeole endémique a été vérifiée dans 4 pays (Bhoutan, Maldives, République populaire démocratique de Corée et Timor-Leste) et le contrôle de la rubéole et du syndrome de rubéole congénitale a été certifié dans 6 pays. Le Myanmar a toutefois connu une flambée épidémique de rougeole. Il sera important de suivre les recommandations du groupe consultatif technique national sur l'utilisation de vaccins tels que le vaccin antipoliomyélitique inactivé (VPI), les vaccins contre le papillomavirus humain et l'encéphalite japonaise et les vaccins conjugués antipneumococcique. Tous les partenaires doivent aider les pays à assurer le suivi des révisions de leurs programmes élargis de vaccination et des évaluations après l'introduction d'un vaccin. Les pays de la Région utilisent des approches sur mesure pour améliorer la couverture et l'équité, en particulier parmi les populations à haut risque et dans les zones mal desservies. Depuis l'afflux de réfugiés migrants dans la région de Cox's Bazar au Bangladesh, des campagnes ont été menées avec le vaccin antipoliomyélitique oral (VPO) bivalent, le vaccin antirougeoleux-antirubéoleux, le vaccin pentavalent, les vaccins contre le tétanos, la diphtérie et la coqueluche, le vaccin conjugué antipneumococcique et le vaccin anticholérique oral. Depuis juin 2018, des services de vaccination systématique ont également été mis en place pour assurer la vaccination des nouvelles cohortes.

La Région OMS du Pacifique occidental a rapporté les progrès accomplis vers la réalisation des objectifs du Cadre régional de mise en œuvre du GVAP. Elle prépare actuellement un cadre stratégique régional à soumettre à l'approbation du Comité régional en 2020 afin d'assurer son alignement sur les stratégies mondiales de santé et de vaccination. La Région a maintenu son statut de région exempte de poliomyélite depuis sa certification en 2000. En septembre 2018, l'élimination ou l'interruption de la transmission endémique de la rougeole ont été vérifiés dans 8 pays et territoires (Australie, Brunéi Darussalam, Cambodge, Japon, Nouvelle-Zélande, RAS de Hong Kong [Chine],

having eliminated or interrupted endemic transmission of measles. Four countries (Cambodia, Fiji, Lao People's Democratic Republic and Papua New Guinea) conducted supplementary vaccination with measles–rubella vaccine with WHO support. Measles is, however, returning, with outbreaks in the Philippines. In June 2018, an outbreak of circulating vaccine-derived poliovirus type 1 was identified in Papua New Guinea; however, the outbreak was contained within 4 months.

Report from the GAVI Alliance

SAGE is the main advisory board and provides policy and technical guidance for the work of the GAVI Alliance. Several current and former SAGE members are involved in making decisions within the Alliance, including on the Programme and Policy Committee and in the 2018 Vaccine Investment Strategy and the Vaccine Innovation Prioritization Strategy.

At its Board meeting in December 2018, 9 new and expanded vaccine programmes were approved,[6] including a training programme for health care workers in influenza vaccination for pandemic preparedness. The approvals reflect a shift from infant vaccination to a life-course approach, which is aligned with the priorities of the 13th WHO Programme of Work. The GAVI Board also approved support to accelerate development of yellow fever diagnostics to increase early, specific detection in order to initiate and target vaccination.

The GAVI Board at a retreat in March 2019 on the "GAVI 5.0 strategy" discussed how the Alliance could contribute to the SDG vision of leaving no one behind. The 4 areas discussed were: introduction of vaccines, reaching under-immunized populations, ensuring financial and programme sustainability and healthy markets and innovation. The participants agreed on the comparative advantage of GAVI in shaping the market. The discussion on its role in middle-income countries that have not been eligible for GAVI support will continue at its Board meeting in June.

GAVI faces several challenges. To ensure vaccine coverage and equity, ways must be found to accelerate progress, better identify and localize under-immunized groups and find ways to reach them. It must ensure use of policies for effective programming, such as translating global policy on the use of typhoid conjugate vaccine into national contexts. It should find ways to better use vaccines in outbreaks and emergencies and determine whether the training programme in influenza vaccination for health care workers can protect them in future epidemics and pandemics. The emerging challenges include achieving elimination goals for diseases such as measles and cervical cancer, improving the quality of vaccination campaigns, strengthening routine

RAS de Macao [Chine] et République de Corée). Quatre pays (Cambodge, Fidji, Papouasie-Nouvelle-Guinée et République démocratique populaire lao) ont mené des activités de vaccination supplémentaire contre la rougeole et la rubéole avec le soutien de l'OMS. La rougeole est toutefois de retour, avec des flambées épidémiques qui touchent les Philippines. En juin 2018, une flambée épidémique de poliovirus circulant de type 1 dérivé d'une souche vaccinale a été identifiée en Papouasie-Nouvelle-Guinée; cette flambée a néanmoins pu être maîtrisée en 4 mois.

Rapport de l'Alliance GAVI

Le SAGE est le principal conseil consultatif et fournit des orientations politiques et techniques pour les travaux de l'Alliance GAVI. Plusieurs membres actuels et passés du SAGE participent aux décisions prises par l'Alliance GAVI, notamment concernant le Comité des programmes et des politiques, la Stratégie d'investissement en faveur de la vaccination de 2018 et la Stratégie d'établissement des priorités en matière d'innovation vaccinale.

Lors de la réunion de son conseil d'administration en décembre 2018, l'Alliance GAVI a approuvé 9 programmes de vaccination nouveaux et élargis,[6] comprenant un programme de formation des agents de santé à la vaccination antigrippale pour se préparer à une pandémie. L'approbation de ces programmes reflètent le passage d'une vaccination des nourrissons à une approche de vaccination tout au long de la vie, qui est alignée sur les priorités du 13e programme général de travail de l'OMS. Le conseil d'administration de l'Alliance GAVI a également approuvé un soutien pour accélérer le développement du diagnostic de la fièvre jaune afin de favoriser une détection précoce et spécifique pour mettre en route et cibler la vaccination.

Le conseil d'administration de l'Alliance GAVI, lors d'une retraite en mars 2019 sur la «GAVI 5.0 strategy», a discuté de la manière dont l'Alliance pourrait contribuer au principe des ODD de ne laisser personne de côté. Les 4 domaines abordés étaient les suivants: introduction de vaccins, vaccination des populations sous-immunisées, garantie de la viabilité financière et programmatique, marchés et innovation en santé. Les participants sont convenus de l'avantage comparatif de l'Alliance GAVI dans le façonnage du marché. Les discussions sur son rôle dans les pays à revenu intermédiaire qui n'ont pas rempli les critères pour recevoir le soutien de l'Alliance GAVI se poursuivront lors de la réunion de son conseil d'administration en juin.

L'Alliance GAVI est confrontée à plusieurs difficultés. Pour assurer la couverture vaccinale et l'équité, il est nécessaire de trouver des façons d'accélérer les progrès, de mieux identifier et localiser les groupes sous-immunisés et de trouver des moyens de les atteindre. Elle doit assurer l'application des politiques nécessaires à une programmation efficace, par exemple en traduisant la politique mondiale sur l'utilisation du vaccin conjugué contre la typhoïde dans les contextes nationaux. Elle doit trouver des moyens de mieux utiliser les vaccins lors de flambées épidémiques et de situations d'urgence, et déterminer si le programme de formation à la vaccination antigrippale destiné aux agents de santé peut les protéger lors de futures épidémies et pandémies. Parmi les nouveaux défis à relever figurent la réalisation des objectifs d'élimination de maladies

[6] See: https://www.gavi.org/about/governance/gavi-board/minutes/2018/28-nov/, accessed April 2019.

[6] Voir https://www.gavi.org/about/governance/gavi-board/minutes/2018/28-nov/, consulté en avril 2019.

immunization and ensuring global synergy in elimination campaigns, from leprosy and malaria to meningitis and cholera. In the context of an increasing choice of vaccines, more attention should be paid to country prioritization and decision-making about the introduction of vaccines and vaccination strategies to increase country ownership.

Beyond the 2018 Vaccine Investment Strategy, future evidence and policy gaps in addressing disease burdens should be anticipated and resolved, including delivery of novel vaccines, such as the RTS,S malaria, second-generation tuberculosis, group B streptococcus and HIV vaccines.

In 2019–2020, GAVI will update its policies, including on country eligibility and transition, co-financing, health system investment and gender. The policies will take a more differentiated approach to ensure equitable vaccination coverage and evolving support to further unlock domestic resources.

Quality and use of data on immunization and surveillance

SAGE was presented with a comprehensive review of data availability, unmet data needs, existing standards and guidance on data and information on the barriers and enablers related to the quality and use of immunization and vaccine-preventable diseases VPD surveillance data. SAGE noted that, although activities to improve data quality have been under way for the past 20 years, the annual GVAP reports regularly note that poor data are impeding improvement of immunization programmes and recommend that data quality and use of data be priorities.

The definition of data quality was discussed. A possible description of quality data is "data that are accurate, precise, relevant, complete and timely enough for the intended purpose" (or "fit-for-purpose"), which is to monitor the performance of immunization programmes, ensure efficient programme management or provide evidence for decisions.

Although considerable amounts of data on immunization and on surveillance of vaccine-preventable diseases are collected routinely and are available sub-nationally, nationally, regionally and globally, their quality, access to and use of the data often remain suboptimal. Global and regional guidance and standards for monitoring, assessment and data quality and use have been issued, but access to these documents should be improved.

Evidence suggests that data use results in improved data quality. Strong policies and mechanisms for governing data generation, management and use, including data-sharing while maintaining confidentiality at all levels, are essential. Strong leadership in national governments and political will are critical to

telles que la rougeole et le cancer du col de l'utérus, l'amélioration de la qualité des campagnes de vaccination, le renforcement de la vaccination systématique et une synergie mondiale des campagnes d'élimination, de la lèpre et du paludisme à la méningite et au choléra. Dans le contexte d'un choix croissant de vaccins, il convient d'accorder davantage d'attention à la définition des pays prioritaires et à la prise de décisions concernant l'introduction de vaccins et les stratégies de vaccination afin d'accroître l'appropriation nationale de ces décisions.

Au-delà de la Stratégie d'investissement en faveur de la vaccination de 2018, il faut anticiper et combler les lacunes futures en matière de données scientifiques et de politiques pour réduire la charge des maladies, notamment en ce qui concerne la fourniture de nouveaux vaccins, tels que le vaccin antipaludique RTS,S, le vaccin antituberculeux de deuxième génération, le vaccin contre le streptocoque du groupe B et le vaccin contre le VIH.

En 2019-2020, l'Alliance GAVI actualisera ses politiques, notamment en matière de critères de sélection des pays et de transition, de cofinancement, d'investissement dans les systèmes de santé et de genre. Ces politiques adopteront une approche plus différenciée pour assurer une couverture vaccinale équitable et un soutien évolutif afin de débloquer davantage les ressources nationales.

Qualité et utilisation des données sur la vaccination et la surveillance

Il a été présenté au SAGE un examen exhaustif de la disponibilité des données, des besoins non satisfaits en matière de données, des normes et des orientations existantes sur les données et des informations sur les obstacles et les catalyseurs liés à la qualité et à l'utilisation des données sur la vaccination et la surveillance des maladies évitables par la vaccination. Le SAGE a noté que, bien que des mesures visant à améliorer la qualité des données soient mises en place depuis 20 ans, les rapports annuels du GVAP constatent régulièrement que la mauvaise qualité des données entrave l'amélioration des programmes de vaccination et recommandent que la qualité des données et leur utilisation soient prioritaires.

La définition de la qualité des données a fait l'objet d'un débat. Les données de qualité peuvent être décrites comme «des données qui sont exactes, précises, pertinentes, complètes et produites en temps utile pour servir l'objectif recherché» (ou «adaptées à l'objectif visé»), qui est de surveiller la performance des programmes de vaccination, d'assurer une gestion programmatique efficace ou de fournir des éléments probants pour la prise de décisions.

Malgré les quantités considérables de données sur la vaccination et la surveillance des maladies évitables par la vaccination soient régulièrement collectées et disponibles aux niveaux infranational, national, régional et mondial, leur qualité, leur accessibilité et leur utilisation demeurent souvent sous-optimaux. Des orientations et des normes mondiales et régionales en matière de surveillance, d'évaluation et de qualité et d'utilisation des données ont été publiées, mais il est nécessaire d'améliorer l'accès à ces documents.

Les données probantes suggèrent que l'utilisation des données entraîne une amélioration de la qualité des données. Il est essentiel de disposer de politiques et de mécanismes robustes pour encadrer la production, la gestion et l'utilisation des données, y compris le partage des données, tout en assurant leur confidentialité à tous les niveaux. Un leadership solide au

ensure that sufficient resources, policies and regulations are in place.

Data quality and use ultimately rely on the skill, knowledge and attitudes of frontline workers and the existence of a "data use culture". Thus, interventions should enable and empower health workers, as data-related activities often compete with time for clinical duties. The situation requires a multi-faceted approach, including pre- and in-service training, supportive supervision, feedback and dedicated time for data-related tasks.

Recent advances in information and communication technology have resulted in innovative tools for immunization activities, including digital information systems for aggregated data or electronic registries, decision-support tools, mobile and geospatial technologies and predictive analytics to improve estimates of coverage and populations. While there is evidence that some of these tools improve data quality and use, most have not been widely used or thoroughly evaluated. The success of innovations requires other elements, including adequate infrastructure, sustainable financing, political will and a skilled, motivated workforce.

Improving data quality and use will require a shift from periodic data quality assessments, often driven by global partners, to country-driven routine monitoring of data quality as part of a Continuous Quality Improvement (CQI) approach. Beyond optimizing the use of existing data, new measures, tools and indicators will be required to improve the equity of services provided to populations in various geographical areas and move towards a life-course vaccination approach, with global improvements in vaccination coverage. In particular, programmes require methods for improving estimates of target populations, including migrant and mobile populations.

The SAGE Working Group on the Quality and Use of Global Immunization and Surveillance Data will further discuss and review its findings through a health systems lens to support SAGE in making specific, implementable recommendations.

Report from the Global Advisory Committee on Vaccine Safety: Development of a Manual on Immunization Stress-Related Responses (ISRR)

Reports of clusters of anxiety-related reactions following vaccination, which affected immunization programmes because of negative attention from the media and the public, were first discussed by the Global Advisory Committee on Vaccine Safety in December 2015. An expert working group assessed the causes of such events and their characteristics and drafted guidance for vaccinators and programme managers. After an extensive review of the evidence, it became clear that

sein des gouvernements nationaux et une volonté politique forte sont indispensables pour garantir la mise en place de ressources, de politiques et de réglementations suffisantes.

La qualité et l'utilisation des données reposent en fin de compte sur les compétences, les connaissances et les attitudes des intervenants de première ligne et sur l'existence d'une «culture de l'utilisation des données». Ainsi, les interventions doivent donner aux agents de santé la possibilité et les moyens d'agir, car le temps consacré aux activités liées aux données entrent souvent en concurrence avec celui dédié aux activités cliniques. La situation exige une approche à multiples facettes, y compris une formation préalable et en cours d'emploi, une supervision de soutien, une rétroinformation et du temps consacré aux tâches liées aux données.

Les progrès récents des technologies de l'information et de la communication ont conduit à la mise au point d'outils novateurs pour les activités de vaccination, notamment des systèmes d'information numériques pour les données agrégées ou des registres électroniques, des outils d'aide à la décision, des technologies mobiles et géospatiales et des analyses prédictives pour améliorer les estimations de la couverture et des populations. Bien qu'il soit prouvé que certains de ces outils améliorent la qualité et l'utilisation des données, la plupart d'entre eux n'ont pas été utilisés à grande échelle ou évalués de manière approfondie. Le succès des innovations requiert aussi d'autres éléments, notamment des infrastructures adéquates, un financement durable, une volonté politique et du personnel qualifié et motivé.

L'amélioration de la qualité et de l'utilisation des données exigera de passer d'évaluations périodiques de la qualité des données, souvent menées par des partenaires mondiaux, à un suivi régulier de la qualité des données à l'initiative des pays dans le cadre d'une approche d'amélioration continue de la qualité. Au-delà de l'optimisation de l'utilisation des données existantes, de nouvelles mesures, outils et indicateurs seront nécessaires pour améliorer l'équité des services fournis aux populations dans diverses zones géographiques et évoluer vers une approche de vaccination tout au long de la vie, avec une amélioration de la couverture vaccinale à l'échelle mondiale. En particulier, les programmes doivent disposer de méthodes pour améliorer les estimations des populations cibles, y compris les populations migrantes et mobiles.

Le Groupe de travail du SAGE sur la qualité et l'utilisation des données mondiales sur la vaccination et la surveillance poursuivra l'examen de ses conclusions sous l'angle des systèmes de santé pour aider le SAGE à formuler des recommandations précises et applicables.

Rapport du Comité consultatif mondial pour la sécurité des vaccins: élaboration d'un manuel sur les réponses liées au stress après la vaccination

Le Comité consultatif mondial pour la sécurité des vaccins a examiné pour la première fois en décembre 2015 des rapports faisant état de grappes de réactions liées à l'anxiété après la vaccination, qui ont affecté les programmes de vaccination en raison de l'attention négative portée par les médias et le public. Un groupe de travail composé d'experts a évalué les causes de ces manifestations et leurs caractéristiques et a rédigé des orientations provisoires à l'intention des vaccinateurs et des administrateurs de programmes. Après un examen approfondi

a term such as "immunization anxiety-related reaction" did not cover the spectrum of manifestations and that a broader term was required; the term "immunization stress-related response (ISRR)" was proposed, which encompasses the broad range of responses that may be experienced after vaccination, without implying that they are causally related. Once an ISRR is suspected, the WHO process for assessing causality should be followed to determine whether there is a causal relation between vaccination and the event.

A draft manual was prepared for immunization programme managers and health care providers on the prevention and management of clusters and individuals with such reactions. The draft, which was endorsed by the Global Advisory Committee on Vaccine Safety in December 2018, explains ISRR and the context of the occurrence of such reactions, provides guidance on prevention, diagnosis, management and communication when such events occur and describes research gaps and strategies for moving forward.

SAGE discussed the importance of correctly identifying and responding to such events and the difficulties for immunization programmes and health care providers, including identification of such events and the repercussions of incorrect diagnosis and mismanagement. Aspects that require attention include distinguishing anaphylaxis from conditions such as a vasovagal response, indirect injuries due to falls during vasovagal responses and correct communication approaches for patients, caregivers and, when appropriate, the community and the public when ISRRs occur.

SAGE agreed that the finalized manual should be a core tool for vaccine safety. Incorporation of ISRR into national guidelines for "adverse events following immunization" will ensure that ISRR is included in regular surveillance of such events, when they are identified, reported and investigated. SAGE recommended that a short synopsis for translation into local languages be made available for frontline vaccinators.

Lessons learnt from the Global Vaccine Action Plan and update on the development of a Post-2020 Immunization Strategy

GVAP review and lessons learnt

The GVAP is scheduled to be completed in 2020, and the next global immunization strategy is currently in development. To inform the post 2020 immunization strategy development, the GVAP reporting process for 2019 has been substantially adapted. The focus this year will be on developing an overall GVAP review and lessons learnt report, which will replace this year's SAGE GVAP assessment report.

SAGE was given the preliminary findings of the GVAP review, which was based on a desk review, stakeholder surveys and interviews. The final document will be presented to SAGE for endorsement in October 2019. The report has also been submitted as a background

des données probantes, il est devenu évident qu'un terme comme «réaction liée à l'anxiété après la vaccination» ne couvrait pas l'ensemble des manifestations observées et qu'un terme couvrant un champ plus étendu s'imposait; le terme «réponse liée au stress après la vaccination (RLSV)» a été proposé; ce dernier englobe le large éventail des réponses susceptibles de survenir après la vaccination, sans laisser entendre que celles-ci ont un lien causal. Lorsqu'on suspecte la présence d'une RLSV, il convient de suivre la procédure de l'OMS pour évaluer la causalité afin de déterminer s'il y a une relation causale entre la vaccination et la manifestation constatée.

Un manuel provisoire sur la prévention et la prise en charge de ces réactions en grappe ou individuelles a été élaboré à l'intention des administrateurs de programmes de vaccination et des prestataires de soins de santé. Ce manuel, qui a été approuvé par le Comité consultatif mondial pour la sécurité des vaccins en décembre 2018, explique la RLSV et le contexte dans lequel ces réactions se produisent, fournit des orientations sur la prévention, le diagnostic, la prise en charge et la communication lorsque de telles manifestations se produisent et décrit les lacunes de la recherche et les stratégies pour l'avenir.

Le SAGE a discuté de l'importance d'identifier et de répondre correctement à ces manifestions et des difficultés y afférentes pour les programmes de vaccination et les prestataires de soins de santé, notamment l'identification de ces manifestions et les répercussions d'un diagnostic erroné et d'une prise en charge inadéquate. Les points qui nécessitent une attention particulière sont notamment la distinction à opérer entre l'anaphylaxie et, par exemple, un épisode vasovagal ou des blessures indirectes causées par une chute pendant un épisode vasovagal, et les bonnes approches de communication auprès des patients, des soignants et, le cas échéant, de la communauté et du public lorsque des RLSV surviennent.

Le SAGE est convenu que le manuel finalisé devra être un outil central dans le cadre de la sécurité des vaccins. L'intégration des RLSV dans les lignes directrices nationales relatives aux «manifestations postvaccinales indésirables» garantira que les RLSV feront l'objet d'une surveillance régulière lorsqu'elles sont identifiées, signalées et examinées. Le SAGE a recommandé qu'un bref synopsis à traduire dans les langues locales soit mis à la disposition des vaccinateurs de première ligne.

Enseignements tirés du Plan d'action mondial pour les vaccins et point sur l'élaboration d'une stratégie de vaccination pour l'après 2020

Examen du GVAP et enseignements tirés

Le GVAP devrait être achevé en 2020, et la prochaine stratégie mondiale de vaccination est en préparation. Afin d'éclairer l'élaboration de la stratégie de vaccination pour l'après 2020, la procédure d'établissement des rapports sur le GVAP pour 2019 a été notablement remaniée. Cette année, l'accent sera mis sur l'élaboration d'un rapport global sur l'examen du GVAP et les enseignements tirés, qui remplacera le rapport d'évaluation du GVAP du SAGE.

Le SAGE a reçu les résultats préliminaires de l'examen du GVAP fondé sur une étude documentaire, des sondages auprès des parties prenantes et des entretiens. Le document final sera présenté au SAGE pour approbation en octobre 2019. Ce rapport a également été soumis comme document d'information pour

document for the post 2020 "co-creation forum", which took place in Geneva on 19–21 March 2019. The review covers 5 work streams: evaluation of the GVAP partnership and collaboration; evaluation of the added value of GVAP; evaluation of the monitoring and evaluation framework; overall assessment of progress in immunization during the decade; and an analysis of changes in global immunization in 2010–2018.

The interim report indicated that GVAP has been a powerful means for aligning global immunization actors, including in research and development; for ensuring comprehensive immunization strategies in all regions; for a strong monitoring and evaluation framework; for better data quality; and for a significant increase in the number of functioning national immunization technical advisory groups globally. Although most goals and objectives were not met globally, progress in most indicators was notable. Weaknesses that were identified included the perception of GVAP as a top–down strategy, with insufficient engagement in countries; the absence of strong leadership and accountability of GVAP partners, particularly at regional and country levels; lack of clear guidance and means to address specific challenges in countries, such as coverage of underserved populations; the fact that progress (i.e. introduction of new vaccines) depended on the availability of funding; and insufficient attention to communication and advocacy.

To put GVAP into perspective, the interim review also included a brief description of significant changes in global immunization since 2010. These include the global change from the Millennium Development Goals to the SDGs; demographic, political and social changes; humanitarian crises and population movements; increased numbers of recommended vaccines and target groups; increased recognition of "vaccine hesitancy"; and the progressive phasing out of support from the GAVI and the Global Polio Eradication Initiative (GPEI) in a number of countries.

SAGE welcomed the review of lessons learnt from the GVAP and its contribution to development of the new global strategy. SAGE took note of the interim findings and encouraged the GVAP Secretariat and the Decade of Vaccines Working Group to extend the report to draw all possible lessons from GVAP.

Development of the post-2020 immunization strategy

The second part of the session addressed the vision and strategy for vaccines and immunization in the coming decade. The Director of IVB described a vision based on the outcome of the "co-creation forum" held on 19–21 March and attended by over 110 participants representing over 50 organizations and more than 30 countries. The forum agreed on a 3-level strategy: an overall vision for 2030, with high-level strategic priorities in a brief format intended for a general audience; a slightly longer second-level framework for

le «forum de la co-création» pour l'après 2020, qui s'est tenu à Genève du 19 au 21 mars 2019. L'examen porte sur 5 axes de travail: évaluation du partenariat et de la collaboration dans le cadre du GVAP; évaluation de la valeur ajoutée du GVAP; évaluation du cadre de suivi et d'évaluation; évaluation globale des progrès de la vaccination au cours de la décennie; et analyse de l'évolution de la vaccination mondiale sur la période 2010-2018.

Le rapport intérimaire indiquait que le GVAP était un moyen efficace d'aligner les acteurs mondiaux de la vaccination, notamment dans le domaine de la recherche-développement, pour assurer des stratégies intégrales de vaccination dans toutes les régions, pour établir un cadre solide de suivi et d'évaluation, pour améliorer la qualité des données et pour accroître sensiblement le nombre de groupes consultatifs techniques nationaux pour la vaccination opérationnels dans le monde. Bien que la majorité des buts et objectifs n'aient pas été atteints à l'échelle mondiale, des progrès notables ont été réalisés pour la plupart des indicateurs. Les faiblesses identifiées comprenaient la perception que le GVAP était une stratégie descendante et l'engagement dans les pays insuffisant; l'absence d'un leadership fort et d'une responsabilisation des partenaires du GVAP, en particulier aux niveaux régional et national; le manque d'orientations claires et de moyens pour remédier à des difficultés particulières dans les pays, comme la couverture des populations mal desservies; le fait que les progrès (c.-à-d. l'introduction de nouveaux vaccins) dépendent de la disponibilité des fonds; l'attention insuffisante portée à la communication et la sensibilisation.

Pour mettre le GVAP en perspective, l'examen intérimaire comprenait également une brève description des changements importants survenus dans le domaine de la vaccination mondiale depuis 2010. Parmi ceux-ci, le passage des objectifs du Millénaire pour le développement aux objectifs de développement durable à l'échelle mondiale; les changements démographiques, politiques et sociaux; les crises humanitaires et les mouvements de population; l'augmentation du nombre de vaccins recommandés et de groupes cibles; l'augmentation du phénomène d'«hésitation à se faire vacciner»; la suppression progressive du soutien de l'Alliance GAVI et l'Initiative mondiale pour l'éradication de la poliomyélite (IMEP) dans un certain nombre de pays.

Le SAGE s'est félicité de l'examen des enseignements tirés du GVAP et de sa contribution à l'élaboration de la nouvelle stratégie mondiale. Il a pris note des conclusions intérimaires et a encouragé le Secrétariat du GVAP et le Groupe de travail sur la Décennie de la vaccination à étoffer ce rapport afin de tirer toutes les leçons possibles du GVAP.

Élaboration de la stratégie de vaccination pour l'après 2020

La deuxième partie de la session a porté sur la vision et la stratégie en matière de vaccins et de vaccination pour la prochaine décennie. Le Directeur du Département Vaccination, vaccins et produits biologiques a décrit une vision fondée sur les résultats du «forum de co-création» qui s'est tenu du 19 au 21 mars dernier et qui a réuni plus de 110 participants représentant plus de 50 organisations et plus de 30 pays. Le forum s'est mis d'accord sur une stratégie à 3 niveaux: une vision globale pour 2030, avec des priorités stratégiques de haut niveau dans un format court destinée au grand public; un cadre de

immunization stakeholders; and a third level that consists of a repository of regional and country plans, disease strategies and partners' strategies. Co-creation of the new strategy with all partners was emphasized. The participants agreed to prepare an initial draft of the vision and the strategic framework and to circulate it widely in the coming months to partners in countries, regions and globally to elicit comments. After this review, a new draft will be presented to SAGE in October 2019, before finalization and submission to the WHO Executive Board and the World Health Assembly (WHA) in 2020.

The suggested approach, which accounts for changes in immunization programmes and global health and builds on lessons from GVAP, is a framework to explain why the world needs a new strategy, the strategic priorities for achieving the vision for 2030 and how the identified priorities will be translated into action. The vision and strategy to be adopted by WHA in 2020 will subsequently be complemented by other components, such as a monitoring and evaluation framework and an advocacy plan.

SAGE welcomed the accelerated agenda for developing the new strategy. It recommended that the authors incorporate resilience to account for turnover of current decisionmakers and political leaders. The engagement of communities was considered to be the key to success, including new groups, such as younger people. SAGE emphasized the importance of maintaining a focus on the ultimate targets – vaccine recipients and frontline workers who deliver vaccines – and recommended that this be reflected in the language used in the new strategy.

Report from international immunization partners – Coalition for Epidemic Preparedness Innovations

The session continued a series of presentations initiated in 2015 on the immunization-related activities of international partner organizations. During the current meeting, the Coalition for Epidemic Preparedness Innovations (CEPI) was invited to present its activities to SAGE.

The Coalition described its history, mission, resources and functioning, including its role in financing and coordinating vaccine development for emerging high-threat infectious diseases, such as Middle-East respiratory syndrome, Lassa fever, Nipah virus disease, chikungunya, Rift Valley fever and also "disease X", an unknown emerging disease. The Coalition facilitates the development of candidate vaccines, from late preclinical studies to clinical trials, before epidemics begin. It is also coordinating use of candidate vaccines against Ebola virus. Its aim is to ensure equitable access to products for affected populations during outbreaks. Mechanisms are being sought for stockpiling unlicensed products in late clinical development. CEPI identifies gaps in funding or research and acts

deuxième niveau légèrement plus long pour les acteurs de la vaccination; et un troisième niveau qui consiste en un répertoire des plans régionaux et nationaux, des stratégies sanitaires et des stratégies des partenaires. L'accent a été mis sur la co-création de la nouvelle stratégie avec tous les partenaires. Les participants sont convenus de préparer un avant-projet de vision et de cadre stratégique et de le diffuser largement dans les mois à venir auprès des partenaires dans les pays, les régions et à l'échelle mondiale pour recueillir leurs commentaires. Après cet examen, un nouveau projet provisoire sera présenté au SAGE en octobre 2019, avant d'être finalisé et soumis au Conseil exécutif de l'OMS et à l'Assemblée mondiale de la Santé en 2020.

L'approche suggérée, qui tient compte des changements dans les programmes de vaccination et la santé mondiale et s'appuie sur les enseignements tirés du GVAP, est un cadre visant à expliquer pourquoi le monde a besoin d'une nouvelle stratégie, les priorités stratégiques pour réaliser la vision à l'horizon 2030 et comment les priorités identifiées seront traduites en actions. La vision et la stratégie qui seront adoptées par l'Assemblée mondiale de la Santé en 2020 seront ensuite complétées avec d'autres éléments, tels qu'un cadre de suivi et d'évaluation et un plan de sensibilisation.

Le SAGE s'est félicité du programme accéléré pour l'élaboration de la nouvelle stratégie. Il a recommandé que les auteurs intègrent une certaine élasticité pour tenir compte du roulement des décideurs et des dirigeants politiques actuels. Il a été considéré que la clé du succès résidait dans l'engagement des communautés, y compris de nouveaux groupes, comme les jeunes. Le SAGE a souligné l'importance de maintenir l'accent sur les cibles premières – les bénéficiaires de la vaccination et les intervenants de première ligne qui administrent les vaccins – et a recommandé que cela soit reflété dans le langage utilisé dans cette nouvelle stratégie.

Rapport des partenaires internationaux dans le domaine de la vaccination – Coalition pour les innovations en matière de préparation aux épidémies

Cette session s'inscrivait dans la continuité d'une série de présentations, lancée en 2015, sur les activités relatives à la vaccination des organisations internationales partenaires. Au cours de la réunion, la Coalition for Epidemic Preparedness Innovations a été invitée à présenter ses activités au SAGE.

La Coalition a décrit son histoire, sa mission, ses ressources et son fonctionnement, y compris son rôle dans le financement et la coordination du développement de vaccins contre des maladies infectieuses émergentes à haut risque, telles que le syndrome respiratoire du Moyen-Orient, la fièvre de Lassa, la maladie à virus Nipah, le chikungunya, la fièvre de la vallée du Rift et aussi la «maladie X», une nouvelle maladie inconnue. La Coalition facilite la mise au point de vaccins candidats – à partir des études précliniques tardives jusqu'aux essais cliniques – avant le début des épidémies. Elle coordonne également l'utilisation de vaccins candidats contre le virus Ebola. Son objectif est d'assurer un accès équitable à ces produits pour les populations touchées pendant les flambées épidémiques. Des mécanismes sont à l'étude pour stocker les produits non homologués dans le cadre d'un développement clinique tardif. La Coalition

when market forces fail. Its strategic objectives are preparedness, response and sustainability.

SAGE expressed interest in CEPI's initiative to use lessons learnt during outbreaks of Ebola virus disease in future vaccine development for the greatest impact. SAGE expressed appreciation for the work of CEPI and welcomed dialogue between SAGE and CEPI on emerging public health issues.

Malaria vaccine and the framework for policy decision on use of RTS,S/AS01 malaria vaccine

SAGE was given an update on the RTS,S/AS01 malaria vaccine implementation programme (MVIP), a synopsis of the vaccine development pathway, the main results of the phase 3 clinical trial and the considerations that led to the WHO recommendation in 2016 for pilot-testing of RTS,S/AS01.[7] The MVIP was established by WHO to coordinate and support national immunization programmes in Ghana, Kenya and Malawi in introducing the vaccine in selected areas and to ensure rigorous evaluation of the programmatic feasibility of administering the required 4 doses, the impact on mortality and the safety of the vaccine. The main aim of the programme is to answer the questions identified in 2015 by SAGE and the Malaria Policy Advisory Committee (MPAC) as a basis for WHO recommendations on wider use of the vaccine. SAGE acknowledged the progress made at global, regional and country levels in preparing for introduction of the first malaria vaccine and shared its excitement about the imminent launch.

SAGE reviewed the proposed framework for policy decision on use of the RTS,S/AS01 vaccine, which is designed to anticipate how and when data collected in the MVIP can be used in future WHO recommendations.

The data and considerations on which the proposed framework is based were presented. The new data included the results of a 7-year follow-up of children enrolled at 3 of the 11 sites in the phase 3 trial, which showed significant protection against clinical malaria throughout the period in children who received 3 or 4 doses of the vaccine and significant protection against severe malaria in children who received 4 doses.[8] There was no evidence that children who received only 3 doses were at greater risk of severe malaria overall. These findings allayed previous concern, expressed in the SAGE/MPAC review in 2015, about a potential excess risk for severe malaria in children who did not receive the fourth vaccine dose. The analysis also showed very few cases of severe malaria after the first 4 years of follow-up, in keeping with the natural age pattern of malaria, and no additional imbalance in meningitis,

identifie les lacunes dans le financement ou la recherche et agit lorsque les forces du marché échouent. Ses objectifs stratégiques sont la préparation, la riposte et la pérennité.

Le SAGE a exprimé son intérêt pour l'initiative de la Coalition d'utiliser les enseignements tirés des épidémies de maladie à virus Ebola dans le développement de futurs vaccins afin d'obtenir le plus grand impact possible. Le SAGE a salué les travaux de la Coalition et s'est félicité du dialogue entre le SAGE et la Coalition sur les questions de santé publique émergentes.

Vaccin antipaludique et cadre pour la prise de décision politique sur l'utilisation du vaccin antipaludique RTS,S/AS01

Il a été présenté au SAGE un point de la situation sur le programme de mise en œuvre de la vaccination antipaludique (MVIP) avec le RTS,S/AS01, un résumé de la démarche adoptée pour le développement du vaccin, les principaux résultats de l'essai clinique de phase 3 et les considérations qui ont conduit l'OMS à recommander en 2016 des essais pilotes avec le RTS,S/AS01.[7] Le MVIP a été créé par l'OMS pour coordonner et soutenir les programmes nationaux de vaccination au Ghana, au Kenya et au Malawi en vue de l'introduction du vaccin dans des zones choisies et pour assurer une évaluation rigoureuse de la faisabilité programmatique de l'administration des 4 doses requises, de l'impact sur la mortalité et de l'innocuité du vaccin. L'objectif principal du programme est de répondre aux questions identifiées en 2015 par le SAGE et le Comité de pilotage de la politique de lutte antipaludique (MPAC) pour servir de base aux recommandations de l'OMS sur une utilisation plus large du vaccin. Le SAGE a reconnu les progrès réalisés aux niveaux mondial, régional et national dans la préparation de l'introduction du premier vaccin antipaludique et a fait part de son enthousiasme quant à son lancement imminent.

Le SAGE a examiné le cadre proposé pour la prise de décision politique sur l'utilisation du vaccin RTS,S/AS01, conçu pour prévoir comment et quand les données collectées dans le cadre du MVIP pourront être utilisées dans les futures recommandations de l'OMS.

Les données et considérations sur lesquelles repose le cadre proposé ont été présentées. Les nouvelles données comprenaient les résultats d'un suivi de 7 ans d'enfants recrutés dans 3 des 11 sites de l'essai de phase 3, qui ont mis en évidence une protection significative contre le paludisme clinique tout au long de cette période chez les enfants qui avaient reçu 3 ou 4 doses du vaccin et une protection significative contre le paludisme grave chez les enfants qui avaient reçu 4 doses.[8] Rien n'indiquait une augmentation globale du risque de paludisme grave chez les enfants ayant reçu seulement 3 doses. Ce constat dissipe les préoccupations exprimées par le SAGE et le MPAC en 2015 quant à la possibilité d'un risque excédentaire de paludisme grave parmi les enfants n'ayant pas reçu la quatrième dose de vaccin. L'analyse a également révélé qu'après les 4 premières années de suivi, le nombre de cas de paludisme grave était très faible, correspondant au profil naturel de la maladie selon l'âge; aucun autre déséquilibre du nombre de cas

[7] Malaria vaccine: WHO position paper – January 2016 (http://www.who.int/wer/2016/wer9104.pdf?ua=1, accessed April 2019).

[8] Article on MAL-076 study results in press, to be published shortly in The Lancet Infectious Diseases.

[7] Note de synthèse: position de l'OMS à propos du vaccin antipaludique – janvier 2016 (http://www.who.int/wer/2016/wer9104.pdf?ua=1, consulté en avril 2019).

[8] Article sur les résultats de l'étude MAL-076 sous presse, qui sera publié sous peu dans The Lancet Infectious Diseases.

cerebral malaria or deaths. This information, which was not available at the time of the recommendations in October 2015, provides reassurance that children who receive only 3 doses also benefit from reduced clinical malaria as compared with children who do not receive the vaccine.[9]

With due consideration of the findings, SAGE endorsed a stepwise approach for MVIP data review and for future recommendations on use of the RTS,S/AS01 vaccine.

Step 1: It may be possible to update WHO recommendations for broader use of RTS,S/AS01 vaccine if and when:

- concerns regarding safety signals observed in the phase 3 trial (related to meningitis, cerebral malaria, and sex-specific mortality) are satisfactorily resolved, by demonstrating either a lack of a risk of an important size during RTS,S/AS01 pilot implementation or an assessment of a positive risk-benefit profile; and
- either severe malaria or mortality data trends are assessed as consistent with a beneficial impact of the vaccine;

Based on current assumptions across the 3 MVIP countries related to the expected rate of accumulating events and vaccine introduction timings, the required data on safety and impact trends could be available approximately 24 months after the beginning of RTS,S/AS01 vaccination. SAGE was reassured that MVIP is planning statistical analysis, and the timing will be confirmed once preliminary data on the rates of actual events are available.

Step 2: Adjustments or refinements to the policy recommendation may be made based on the final MVIP data set expected to be available approximately 50 months after the start of vaccination in the third MVIP country. The pilots are designed to establish the public health value of the fourth vaccine dose, including assessment of the vaccine's impact on mortality.

SAGE agreed that a malaria vaccine recommendation could be made in the absence of data showing vaccine impact on mortality. Impact on severe malaria is an acceptable surrogate indicator for impact on mortality and thus could support a recommendation if assessed as consistent with a beneficial impact.

SAGE confirmed that a policy recommendation for broader use of RTS,S/AS01 need not be predicated on attainment of high coverage (including with a fourth dose).

SAGE did not expect that the impact of RTS,S/AS01 introduction on the coverage of other vaccines or malaria control interventions will be major factors

de méningite, de neuropaludisme ou de décès n'a été mis en évidence. Ces informations, qui n'étaient pas disponibles lorsque les recommandations d'octobre 2015 ont été formulées, rassurent sur le fait que les enfants qui reçoivent seulement 3 doses bénéficient aussi d'une réduction du risque de paludisme clinique par rapport aux enfants n'ayant pas été vaccinés.[9]

En tenant dûment compte de ces résultats, le SAGE a approuvé l'adoption d'une approche par étapes pour l'examen des données du MVIP et la formulation des futures recommandations sur l'utilisation du vaccin RTS,S/AS01.

Étape 1: L'actualisation des recommandations de l'OMS pour une utilisation plus large du vaccin RTS,S/AS01 pourra être envisagée lorsque les conditions suivantes seront réunies:

- les préoccupations liées aux signaux de sécurité observés dans l'essai de phase 3 (relatifs à la méningite, au neuropaludisme et à la mortalité selon le sexe) auront été réglées de manière satisfaisante, soit parce que les projets pilotes de mise en œuvre de la vaccination par le RTS,S/AS01 auront démontré l'absence de risque majeur, soit parce que le profil risque-bénéfice aura été évalué comme positif; et
- l'évolution des données sur le paludisme sévère ou sur la mortalité sera jugée compatible avec un effet bénéfique du vaccin;

Compte tenu des hypothèses actuelles sur le taux escompté d'accumulation des événements et le calendrier d'introduction du vaccin dans les 3 pays du MVIP, les données requises concernant les tendances d'innocuité et d'impact pourraient être disponibles environ 24 mois après le début de la vaccination par le RTS,S/AS01. Le SAGE a noté avec satisfaction que le MVIP prévoit d'effectuer une analyse statistique, selon un calendrier qui sera confirmé une fois que les données préliminaires sur les taux effectifs de survenue des événements seront disponibles.

Étape 2: La recommandation politique pourrait faire l'objet d'ajustements ou d'améliorations sur la base des données finales du MVIP, qui devraient être disponibles environ 50 mois après le début de la vaccination dans le troisième pays du MVIP. Les projets pilotes sont conçus pour déterminer l'utilité de la quatrième dose de vaccin pour la santé publique, et notamment évaluer l'impact du vaccin sur la mortalité.

Le SAGE a convenu qu'une recommandation sur le vaccin antipaludique pourrait être formulée en l'absence de données démontrant un impact du vaccin sur la mortalité. L'impact sur le paludisme grave est un indicateur de substitution acceptable de l'impact sur la mortalité et pourrait donc servir de base à une recommandation s'il est jugé compatible avec un impact bénéfique.

Le SAGE a confirmé que l'émission d'une recommandation politique pour une utilisation plus large du RTS,S/AS01 n'était pas tributaire de l'obtention d'une couverture élevée (y compris par la quatrième dose).

Le SAGE ne pense pas que l'incidence de l'introduction du RTS,S/AS01 sur la couverture d'autres vaccins ou sur les interventions de lutte contre le paludisme sera un facteur important

[9] Joint Technical Expert Group on Malaria Vaccines (JTEG) and the WHO Secretariat. Background paper on the RTS,S/AS01 Malaria Vaccine, 2015 (https://www.who.int/immunization/sage/meetings/2015/october/1_Final_malaria_vaccine_background_paper_v2015_09_30.pdf, accessed April 2019).

[9] Joint Technical Expert Group on Malaria Vaccines (JTEG) and the WHO Secretariat. Background paper on the RTS,S/AS01 Malaria Vaccine, 2015 (https://www.who.int/immunization/sage/meetings/2015/october/1_Final_malaria_vaccine_background_paper_v2015_09_30.pdf, consulté en avril 2019).

influencing a vaccine recommendation. Rather, these indicators should inform strategies for implementation, including opportunities for improvement.

SAGE confirmed that regional and national consultations should be held before revision of the WHO recommendations on use of RTS,S/AS01 vaccine.

The value of the framework relies on shared understanding and alignment of expectations among immunization and malaria experts. The Chair of MPAC was present, and several members participated in person or by telephone in the SAGE session. MPAC has endorsed the framework formally during its meeting on 10–12 April 2019.[10]

Polio – the last mile

SAGE noted the work and progress of the GPEI but expressed concern that more cases of paralytic polio due to wild poliovirus were reported in 2018 than in 2017: 33 cases due to wild poliovirus type 1 (WPV1) were reported worldwide in 2018 (21 in Afghanistan, 12 in Pakistan) and 22 in 2017 (14 in Afghanistan, 8 in Pakistan). In addition, WPV1 continues to be detected through environmental surveillance in the northern, central and southern corridors of transmission in Afghanistan and Pakistan.

In 2018, 104 cases of polio due to circulating vaccine-derived polioviruses (cVDPV) were reported: 20 due to cVDPV2 in the DRC, 34 due to cVDPV2 in Nigeria, 26 due to cVDPV1 in Papua New Guinea, 12 due to cVDPVs in Somalia (5 cVDPV2, 6 cVDPV3 and 1 co-infection), 10 due to cVDPV2 in Niger, 1 due to cVDPV2 in Mozambique and 1 due to cVDPV1 in Indonesia.

SAGE observed that, although the circulation of endemic WPV1 and cVDPVs has not been interrupted, much has been achieved in the past year. Nigeria has been free of WPV for over 2 years, and the response to cVDPV outbreaks was successful, except in Nigeria, where cases continue to be reported.

SAGE expressed concern about reaching children in inaccessible areas, specifically in Afghanistan, parts of Pakistan, Nigeria, the Horn of Africa and DRC. SAGE urged the polio programme to work closely with national immunization programmes to strengthen the overall expanded programme on immunization in the framework of primary health care.

As of April 2019, 31 of the 33 countries that still did not include IPV in routine immunization programmes had introduced at least one dose; Mongolia and Zimbabwe are planning introduction later in the month. SAGE noted that supply projections indicate there will be sufficient IPV to cover routine vaccination and sufficient IPV by 2022 for introduction of a 2-dose IPV

[10] Malaria Policy Advisory Committee meeting report (April 2019) (https://www.who.int/malaria/publications/atoz/mpac-report-april-2019/en/, accessed May 2019).

susceptible d'influer sur la formulation d'une recommandation. Il s'agira plutôt d'un indicateur à prendre en compte dans l'élaboration des stratégies de mise en œuvre, y compris dans l'identification des possibilités d'amélioration.

Le SAGE a confirmé que des consultations régionales et nationales devraient avoir lieu avant toute révision des recommandations de l'OMS sur l'utilisation du vaccin RTS,S/AS01.

La valeur de ce cadre repose sur une compréhension commune et une harmonisation des attentes parmi les experts de la vaccination et de la lutte antipaludique. Le Président du MPAC était présent et plusieurs membres ont participé en personne ou par téléphone à cette session du SAGE. Le MPAC a officiellement approuvé le cadre lors de sa réunion du 10 au 12 avril 2019.[10]

Poliomyélite: la dernière ligne droite

Le SAGE a pris connaissance des travaux accomplis par l'IMEP et des progrès qu'elle a réalisés, s'inquiétant néanmoins du fait que davantage de cas de poliomyélite paralytique dus au poliovirus sauvage ont été signalés en 2018 qu'en 2017: 33 cas dus au poliovirus sauvage de type 1 (PVS1) ont été notifiés dans le monde en 2018 (21 en Afghanistan, 12 au Pakistan) contre 22 en 2017 (14 en Afghanistan, 8 au Pakistan). En outre, le PVS1 continue d'être détecté par la surveillance environnementale dans les corridors de transmission nord, central et sud en Afghanistan et au Pakistan.

En 2018, 104 cas de poliomyélite dus à des poliovirus circulants dérivés d'une souche vaccinale (PVDVc) ont été signalés: 20 dus au PVDVc2 en RDC, 34 dus au PVDVc2 au Nigéria, 26 dus au PVDVc1 en Papouasie Nouvelle-Guinée, 12 dus à des PVDVc en Somalie (5 PVDVc2, 6 PVDVc3 et 1 co-infection), 10 dus au PVDVc2 au Niger, 1 dû au PVDVc2 au Mozambique et 1 dû au PVDVc1 en Indonésie.

Le SAGE a observé que, même si la circulation du PVS1 endémique et des PVDVc n'a pas été interrompue, de grandes avancées ont été réalisées au cours de l'année écoulée. Le Nigéria est exempt de PVS depuis plus de 2 ans, et la riposte aux flambées épidémiques de PVDVc a été efficace, sauf au Nigéria, où des cas continuent d'être notifiés.

Le SAGE a fait part de son inquiétude quant aux difficultés rencontrées pour atteindre les enfants dans les zones inaccessibles, en particulier en Afghanistan, dans certaines régions du Pakistan, au Nigéria, dans la Corne de l'Afrique et en RDC. Il a insisté pour que le programme de lutte contre la poliomyélite travaille en étroite collaboration avec les programmes de vaccination nationaux en vue de renforcer le Programme élargi de vaccination dans le cadre des soins de santé primaires.

D'après les données disponibles en avril 2019, sur 33 pays n'ayant toujours pas intégré le VPI aux programmes de vaccination systématique, 31 avaient introduit au moins une dose; la Mongolie et le Zimbabwe prévoient de l'introduire d'ici à la fin du mois. Le SAGE a relevé que, d'après les prévisions, les stocks de VPI seront suffisants pour assurer la vaccination systématique et pour mettre en place, d'ici à 2022, un calendrier

[10] Malaria Policy Advisory Committee meeting report (April 2019) (https://www.who.int/malaria/publications/atoz/mpac-report-april-2019/en/, consulté en mai 2019).

schedule[11] in all countries that procure vaccines through UNICEF and sufficient IPV by the end of 2020 or 2021 for catch-up vaccination of children (requiring 43 million doses) who were missed because the shortage.

SAGE expressed concern that many children have not received IPV, not only because of the shortage but also because of poor performance of routine vaccination, especially in Africa. SAGE suggested that polio programmes and expanded programmes on immunization address the issue jointly and report possible solutions to SAGE.

Persistent transmission of cVDPV2 has stimulated multiple campaigns with monovalent OPV type 2 vaccine to control outbreaks. SAGE proposed that the GPEI determine the criteria for requesting that OPV2-containing vaccine production be resumed. SAGE agreed that discussions on the criteria are important and should be further explored during future working group meetings. Criteria for assessing readiness for withdrawal of bivalent OPV were discussed previously, and SAGE agreed that certification of WPV eradication is the most critical. Other criteria should be refined. The currently proposed criteria, in addition to sensitive surveillance, a stockpile of vaccines and containment, are:

- adequate population immunity, especially in high-risk communities;
- no persistent circulation of cVDPV1 or cVDPV3 (beyond 6 months after first notification);
- sufficient supplies of IPV so that all countries can adopt a 2-dose IPV schedule (intramuscular or intradermal);
- established surveillance of primary immunodeficiency disorders; and
- therapeutic options are available for clearing infections in people who excrete iVDPV.

SAGE noted that the Global Certification Commission is likely to certify eradication of WPV3 in the near future. Subsequently, SAGE will have to decide whether to remove type 3 poliovirus from bivalent OPV. One advantage would be the prevention of vaccine-associated paralytic poliomyelitis (VAPP), which is caused by this vaccine virus. SAGE recognized, however, that a switch from bivalent OPV to monovalent OPV1 would be an enormous programmatic and regulatory task. SAGE agreed that the current priorities for GPEI are to stop transmission of WPV1 in endemic countries and to stop persistent cVDPV2 outbreaks. Removal of OPV3 might distract GPEI from its primary task of eradicating WPV. SAGE will make a formal recommendation on OPV3 removal when the Global Certification Commission has decided to certify WPV3 eradication.

As recommended by SAGE in October 2016, GPEI prepared guidelines for surveillance of poliovirus

[11] For schedule recommendations see: https://www.who.int/immunization/policy/Immunization_routine_table1.pdf?ua=1, accessed April 2019.

de vaccination par le VPI à 2 doses[11] dans tous les pays qui s'approvisionnent en vaccins par l'intermédiaire de l'UNICEF. Ils seront également suffisants pour effectuer, d'ici à la fin de 2020 ou de 2021, une vaccination de rattrapage des enfants qui ont été omis en raison de la pénurie (opération nécessitant 43 millions de doses).

Le SAGE s'est dit préoccupé par le fait que de nombreux enfants n'ont toujours pas reçu le VPI, en raison non seulement de la pénurie, mais aussi des déficiences de la vaccination systématique, en particulier en Afrique. Le SAGE a suggéré que les programmes de lutte contre la poliomyélite et les programmes élargis de vaccination s'attellent conjointement au problème et lui présentent les solutions possibles.

La persistance de la transmission du PVDVc2 a conduit à plusieurs campagnes visant à combattre les flambées épidémiques par le recours au VPO monovalent de type 2. Le SAGE a proposé que l'IMEP détermine les critères à employer pour demander la reprise de la production de vaccins contenant le VPO2. Le SAGE a convenu que les discussions sur les critères sont importantes et devraient être approfondies lors de futures réunions de groupes de travail. Les critères pour évaluer l'état de préparation au retrait du VPO bivalent ont déjà fait l'objet de discussions, et le SAGE a convenu que la certification de l'éradication du PVS est le critère le plus important. Les autres critères devraient être affinés. Ceux actuellement proposés, outre une surveillance sensible, un stock de vaccins et le confinement, sont les suivants:

- immunité adéquate de la population, en particulier dans les communautés à haut risque;
- aucune circulation persistante (c'est-à-dire plus de 6 mois après la première notification) de PVDVc1 ou de PVDVc3;
- approvisionnement suffisant en VPI pour la mise en place d'un schéma vaccinal à 2 doses (intramusculaire ou intradermique) dans tous les pays;
- surveillance bien établie du déficit immunitaire primaire; et
- disponibilité d'options thérapeutiques pour éliminer l'infection chez les sujets qui excrètent des PVDV associés à une immunodéficience (PVDVi).

Le SAGE a noté que la Commission mondiale de certification certifiera vraisemblablement l'éradication du PVS3 dans un futur proche. Par la suite, le SAGE devra décider s'il faut retirer le poliovirus de type 3 du VPO bivalent. Un avantage en découlant serait la prévention de la poliomyélite paralytique associée au vaccin, laquelle est causée par ce virus vaccinal. Le SAGE a reconnu, cependant, qu'un passage du VPO bivalent au VPO1 monovalent constituerait une tâche immense du point de vue programmatique et réglementaire. Le SAGE a convenu que les priorités actuelles de l'IMEP sont d'interrompre la transmission du PVS1 dans les pays d'endémie et d'enrayer les flambées épidémiques persistantes de PVDVc2. Le retrait du VPO3 pourrait détourner l'IMEP de sa tâche principale qui est d'éradiquer le PVS. Le SAGE fera une recommandation officielle sur le retrait du VPO3 quand la Commission mondiale de certification aura décidé de certifier l'éradication du PVS3.

Comme le SAGE l'a recommandé en octobre 2016, l'IMEP a établi des lignes directrices pour la surveillance du poliovirus chez les

[11] Pour les calendriers recommandés, voir: https://www.who.int/immunization/policy/Immunization_routine_table1.pdf?ua=1, consulté en avril 2019.

among patients with primary immunodeficiency. SAGE reviewed the guidelines and endorsed them for implementation. As the capacity to identify excreters among primary immunodeficient is lacking in many countries, SAGE recommended the establishment of respective surveillance systems.

Global roadmap for defeating meningitis

SAGE members were informed of the status of the WHO global roadmap for defeating meningitis by 2030, which will be submitted for recommendation by SAGE in October 2019. The roadmap is supported by 5 pillars: (1) prevention and epidemic control, (2) diagnosis and treatment, (3) surveillance, (4) support and after-care for families and survivors and (5) advocacy and information. WHO estimated in 2015 that 300 000 deaths were due to bacterial meningitis in people of all ages but particularly infants and children. Furthermore, survivors of bacterial meningitis have many disabling sequelae. The roadmap focuses on organisms that are responsible for most cases of acute bacterial meningitis (*Neisseria meningitidis, Streptococcus pneumoniae, Haemophilus influenzae* and *Streptococcus agalactiae* [group B streptococcus]), but it is anticipated that other organisms causing meningitis will be included as appropriate.

SAGE welcomed the ambitious initiative, noting that it will support renewed commitment to use of existing vaccines and provide a framework for use of vaccines in clinical development; however, it cautioned against overconfidence in achieving elimination goals. Not all cases of meningitis and not all the organisms that cause meningitis can be eliminated or controlled with vaccines and vaccination. One limitation with regard to vaccine-preventable meningitis other than serogroup A is the perception in many countries that the disease is rare and that vaccination is therefore not an economic priority. Although vaccines against group B streptococcus show promise in terms of immunogenicity, the path to licensing presents challenges. Meningitis due to *Mycobacterium tuberculosis*, *Cryptococcus* and other pathogens should not be forgotten in the initiative.

SAGE concluded that the proposed strategic structure and pillars are promising and commended inclusion of disability due to meningitis jointly for patients and their families. The level of awareness reflects the constituency that initiated the work, which comprises families that have lost or have disabled children. As meningitis will probably not be eliminated in the near future, a global roadmap will maintain awareness and motivate progress in this field. SAGE provided advice on the next steps and on striking a balance between aspirations, nurtured by the energy of a strong community eager to see change, and the necessity for comprehensive goals and milestones. Previous successes, such as the disappearance of meningococcal A disease in the "meningitis belt" in less than 10 years of vaccinations after a century of epidemics, are important examples, which show what is possible. The next iterations of the roadmap will be based on consultations on all the

patients présentant une immunodéficience primaire. Le SAGE a examiné ces lignes directrices et les a adoptées en vue de leur mise en œuvre. Comme de nombreux pays n'ont pas la capacité d'identifier les sujets excrétant le virus parmi les individus présentant une immunodéficience primaire, le SAGE a recommandé que les pays concernés mettent en place des systèmes de surveillance.

Feuille de route mondiale pour vaincre la méningite

Les membres du SAGE ont été informés de l'état d'avancement de la feuille de route mondiale de l'OMS pour vaincre la méningite d'ici à 2030, qui sera présenté au SAGE en octobre 2019 pour recommandation. La feuille de route repose sur 5 piliers: 1) prévention et lutte contre l'épidémie, 2) diagnostic et traitement, 3) surveillance, 4) soutien et suivi post-soins pour les familles et les survivants et 5) sensibilisation et information. D'après les estimations de l'OMS, la méningite bactérienne a tué 300 000 personnes en 2015; ces décès ont été enregistrés dans toutes les classes d'âge, mais plus particulièrement chez les nourrissons et les enfants. En outre, les survivants de la méningite bactérienne présentent de nombreuses séquelles invalidantes. La feuille de route se concentre sur les micro-organismes responsables de la plupart des cas de méningite bactérienne aiguë (*Neisseria meningitidis, Streptococcus pneumoniae, Haemophilus influenzae* et *Streptococcus agalactiae* [streptocoque du groupe B]), mais d'autres organismes causant cette maladie devraient être inclus le cas échéant.

Le SAGE s'est félicité de cette initiative ambitieuse, notant qu'elle favorisera un engagement renouvelé en faveur de l'utilisation des vaccins existants et fixera un cadre pour l'emploi des vaccins en cours de développement clinique; il a toutefois averti qu'il fallait se garder de tout excès de confiance quant à la possibilité d'atteindre les objectifs d'élimination. Les vaccins et la vaccination ne permettent ni d'éliminer, ni de juguler tous les cas de méningite et tous les micro-organismes responsables de cette maladie. Une des limitations concernant la méningite évitable par la vaccination (hors-sérogroupe A) est la conception qui prévaut dans de nombreux pays selon laquelle la maladie est rare et la vaccination ne constitue donc pas une priorité économique. Bien que les vaccins contre le streptocoque du groupe B soient prometteurs en termes d'immunogénicité, des difficultés se présentent pour l'homologation. L'initiative devrait aussi tenir compte de la méningite due à *Mycobacterium tuberculosis*, à *Cryptococcus* et à d'autres agents pathogènes.

Le SAGE a conclu que la structure stratégique proposée et ses piliers sont prometteurs et s'est félicité de constater qu'ils intègrent le problème du handicap dû à la méningite et de son incidence sur les patients et sur les familles. La prise en compte de ces enjeux est à mettre au crédit des parties à l'origine de l'initiative, parmi lesquelles des familles ayant perdu des enfants ou ayant des enfants handicapés. La méningite n'allant probablement pas être éliminée dans un avenir proche, une feuille de route mondiale permettra de maintenir le niveau de sensibilisation et d'encourager les avancées dans ce domaine. Le SAGE a formulé des recommandations sur les prochaines étapes et sur l'équilibre à trouver entre les aspirations, nourries par l'énergie insufflée par une communauté solide et avide de changement, et la nécessité de fixer des objectifs globaux et des étapes intermédiaires. Les succès déjà obtenus, comme la disparition de la maladie à méningocoque A dans la ceinture de la méningite après moins de 10 ans de campagnes de vaccination et après un siècle d'épidémies, sont des exemples majeurs qui

elements of the strategy, and they will be refined to ensure that they contribute to achieving the goals. The work of SAGE addresses the first and third pillars of the roadmap. Meningitis is relevant not only to the SAGE Working Group on Meningococcal Vaccines and Vaccination but also to the SAGE Working Group on Pneumococcal Vaccines and others.

Ebola virus vaccines

The WHO Health Emergencies Response team presented the epidemiology of the outbreak of Ebola virus disease in the DRC and the status of the response in North Kivu. They highlighted the important contribution of vaccination in the response, which reduced transmission, and praised the heroic work of the ground staff in this difficult task. As of 2 April 2019, there were 1100 cases of Ebola virus disease (1034 laboratory confirmed, 66 probable) and 690 deaths, giving a case fatality ratio of 63%. Health care workers represented 81 of the cases. Also as of 2 April, more than 65 800 contacts had been registered, and 7674 were under surveillance in 15 health zones; 83–87% of the contacts had been followed up during the previous 7 days. Since 8 August 2018, the rVSV-ZEBOV-GP vaccine has been used in the response to the outbreak in North Kivu and Ituri in the context of "compassionate use/expanded access" in a clinical trial protocol with informed consent. As of 2 April 2019, teams had vaccinated 94 357 people, including 25 603 children aged 1–17 years and 29 265 health care and frontline workers.

SAGE expressed admiration and gratitude for the courage and determination of the Guinean led Congolese vaccination teams, noting their accomplishments and their continuing activities in the face of difficult terrain and other challenges.

In considering the interim recommendations of 20 February 2019,[12] SAGE reviewed possible vaccination strategies on the basis of recent epidemiological data, impact modelling and information from the DRC vaccination response team. SAGE discussed whether, with an unlimited supply of vaccine, geographical targeting instead of ring vaccination might more rapidly control the DRC outbreak. The transmission dynamics of the DRC outbreak reflect a highly mobile population where contacts who are not captured by the rings seed new areas (which can be geographically distant), often followed by amplified transmission in health facilities and propagation within family and community networks. In modelling studies, geographically targeted mass vaccination and ring plus[13] were less efficient in terms of cases averted, doses of vaccine required and cases prevented per 100 vaccine doses than ring vaccination.

[12] See https://www.who.int/immunization/interim_ebola_recommendations_feb_2019.pdf?ua=1, accessed April 2019.

[13] "Ring plus vaccination" is a strategy in which only about 40% of contacts and contacts of contacts are identified and vaccinated and vaccination also includes population a few blocks around health facilities visited by symptomatic patients, as nosocomial transmission contributes to the occurrence of cases among unknown contacts. This corresponds to overall identification of 10–35% of contacts.

Vaccins contre le virus Ebola

L'équipe OMS chargée de la riposte aux situations d'urgence sanitaire a fait le point sur l'épidémiologie de la flambée de maladie à virus Ebola en RDC et la riposte au Nord-Kivu. Elle a souligné que la vaccination joue un rôle majeur dans la riposte, contribuant à réduire la transmission, et a loué le travail héroïque accompli par le personnel sur le terrain, qui est confronté à une tâche difficile. Au 2 avril 2019, on comptait 1100 cas de maladie à virus Ebola (dont 1034 confirmés en laboratoire et 66 probables) et 690 décès, soit un taux de létalité de 63%. Parmi ces cas, 81 étaient des agents de santé. Plus de 65 800 contacts avaient été enregistrés au 2 avril, et 7674 avaient été placés sous surveillance dans 15 zones de santé; 83-87% des contacts avaient fait l'objet d'un suivi au cours des 7 jours précédents. Depuis le 8 août 2018, le vaccin rVSV-ZEBOV-GP est utilisé en riposte à la flambée dans les provinces du Nord-Kivu et de l'Ituri au titre d'un «protocole d'usage compassionnel et d'accès élargi» dans le cadre d'un essai clinique avec consentement éclairé. Au 2 avril 2019, les équipes avaient vacciné 94 357 personnes, dont 25 603 enfants âgés de 1 à 17 ans et 29 265 agents de santé et agents de première ligne.

Le SAGE a exprimé son admiration et sa reconnaissance pour le courage et la détermination des équipes de vaccination congolaises sous supervision guinéenne et a salué leurs réalisations et leur persévérance face à un terrain difficile et à divers autres obstacles.

Dans le cadre de l'examen des recommandations provisoires du 20 février 2019,[12] le SAGE a passé en revue les stratégies de vaccination possibles à la lumière des données épidémiologiques les plus récentes, d'études de modélisation de l'impact et d'informations transmises par l'équipe de riposte vaccinale de la RDC. Le SAGE s'est demandé si, dans un contexte d'approvisionnement non limité en vaccins, la vaccination géographique ciblée permettrait de juguler la flambée plus rapidement que la vaccination en anneau en RDC. La dynamique de transmission de cette flambée en RDC est le reflet d'une population très mobile, dans laquelle des contacts qui ne sont pas identifiés dans de nouvelles zones des anneaux (pouvant être éloignées sur le plan géographique) sont souvent à l'origine d'une transmission amplifiée dans les établissements de santé et d'une propagation de la maladie au sein des réseaux familiaux et communautaires. Dans les études de modélisation, la vaccination de masse géographiquement ciblée et la vaccination en anneau «plus»[13] étaient moins

[12] Voir https://www.who.int/immunization/interim_ebola_recommendations_feb_2019_FR.pdf, consulté en avril 2019.

[13] La vaccination en anneau «plus» est une stratégie dans laquelle seuls environ 40% des contacts et des contacts de contacts sont identifiés et vaccinés et où le vaccin est également administré à la population résidant dans les quelques rues qui entourent les établissements de santé fréquentés par des patients symptomatiques. Elle se justifie par la présence d'une transmission nosocomiale contribuant à la survenue de cas parmi des contacts non identifiés. Cela correspond à un taux global d'identification de 10 à 35% des contacts.

In addition, other strategies require that teams remain longer in areas of civil conflict. Because of the continuing security problems in the area, vaccination teams require security escorts and have to move into and out of the field as quickly as possible, sometimes after negotiation with armed groups or over difficult terrain. The DRC ring vaccination response team reported ongoing vigorous and repeat efforts to locate the ring around every case (overall, rings have been defined around nearly 90% of the identified cases). The innovative approaches used in the field, with the highly mobile target population, favour continuation of the ring vaccination approach. SAGE concluded that ring vaccination is currently the most effective strategy in this outbreak of Ebola virus disease in the DRC.[14] Targeting broader geographical areas should remain a fallback strategy if contact tracing is not feasible and vaccine supplies are sufficient.

SAGE reviewed the risk–benefit analysis of vaccinating lactating women and infants <1 year of age with rVSV-ZEBOV-GP as part of the ring vaccination strategy in North Kivu. The "compassionate use/expanded access protocol" for use of the vaccine in the DRC currently excludes these 2 groups, although the DRC Ethics Review Committee authorized their inclusion. The rVSV-ZEBOV-GP is a live, attenuated, replication-competent viral vector vaccine. There is a lack of clinical safety data and potential safety concerns associated with rVSV vaccines related to the potential shedding of vaccine virus in breast milk and the immature immune system in children below 12 months of age. However, the known high attack rates and case fatality rates (CFRs) among women and young infants outweigh these potential risks in favor of the use of the vaccine in these groups. An examination of EVD cases in North Kivu found an attack rate of 1.3 cases per 100,000 persons in lactating women with a CFR of 63%, an attack rate of 23.5 cases per 100,000 in women of childbearing age (15–49 years old) with a CFR of 55%, and an attack rate of 30 cases per 100,000 persons in children under 1 year of age with a CFR of 70%. SAGE considered that the high rates of attack and fatality in these groups and the accumulating data on vaccine safety and efficacy for other groups justify inclusion in the ongoing ring vaccination in North Kivu of infants aged 6–12 months and lactating women. As data on the safety of the vaccine in infants aged 6–12 months accumulate, inclusion of infants from 6 weeks of age should be considered. Despite possible difficulties in follow-up, every effort should be made to monitor the safety of vaccination of lactating women, their infants and vaccinated children. A protocol for the collection of body fluids such as breast milk and urine

[14] In the interval between the SAGE meeting and the publication of this report, the situation in DRC deteriorated with a large increase in number of cases. This led SAGE on 7 May 2019 to revisit its recommendations and issue interim recommendations on the vaccination strategy and adjusted dosage (https://www.who.int/immunization/policy/position_papers/interim_ebola_recommendations_may_2019.pdf?ua=1, accessed May 2019).

efficaces que la vaccination en anneau, en termes de cas évités, de doses de vaccin requises et de cas prévenus pour 100 doses de vaccin. En outre, les autres stratégies exigent une présence prolongée des équipes dans des zones de conflit civil. En raison de l'insécurité persistance dans cette région, les équipes de vaccination doivent être accompagnées d'escortes de sécurité et doivent arriver sur le terrain et repartir le plus rapidement plus possible, parfois après négociation avec des groupes armés ou sur un terrain difficile. L'équipe de vaccination de la RDC a rendu compte des efforts énergiques et répétés déployés pour localiser l'anneau autour de chaque cas; de manière générale, ces anneaux ont été déterminés pour près de 90% des cas identifiés. Les approches innovantes employées sur le terrain, en présence d'une population cible très mobile, plaident en faveur d'une poursuite de la stratégie de vaccination en anneau. Le SAGE a conclu que la vaccination en anneau constitue actuellement la stratégie la plus efficace pour combattre cette flambée de maladie à virus Ebola en RDC.[14] La stratégie consistant à cibler des zones géographiques plus étendues devrait rester une solution de repli à mettre en œuvre si la recherche des contacts n'est pas réalisable et si l'approvisionnement en vaccin est suffisant.

Le SAGE a étudié l'analyse risque-bénéfice de la vaccination par le rVSV-ZEBOV-GP chez les femmes allaitantes et les nourrissons de <1 an dans le cadre de la stratégie de vaccination en anneau au Nord-Kivu. Ces 2 groupes sont actuellement exclus du «protocole d'usage compassionnel et d'accès élargi» du vaccin en RDC, bien que le Comité d'examen éthique de la RDC ait autorisé leur inclusion. Le rVSV-ZEBOV-GP est un vecteur viral vivant atténué apte à la réplication. L'excrétion potentielle du virus vaccinal dans le lait maternel et l'immaturité du système immunitaire des enfants de moins de 12 mois suscitent des préoccupations quant à l'innocuité des vaccins rVSV dans ces groupes, pour lesquels on ne dispose pas de données d'innocuité cliniques suffisantes. Cependant, on sait que les femmes et les jeunes nourrissons présentent des taux d'atteinte et de létalité élevés, qui l'emportent sur les risques potentiels et plaident en faveur d'une utilisation du vaccin dans ces groupes. Une analyse des cas de MVE au Nord-Kivu a mis en évidence un taux d'atteinte de 1,3 cas pour 100 000 personnes et un taux de létalité de 63% chez les femmes allaitantes, un taux d'atteinte de 23,5 cas pour 100 000 et un taux de létalité de 55% chez les femmes en âge de procréer (15 à 49 ans), et un taux d'atteinte de 30 cas pour 100 000 et un taux de létalité de 70% chez les enfants de moins de 1 an. Le SAGE a jugé que l'importance des taux d'atteinte et de létalité dans ces groupes et le volume croissant de données d'innocuité et d'efficacité disponibles pour d'autres groupes justifient d'inclure les nourrissons âgés de 6 à 12 mois et les femmes allaitantes dans la vaccination en anneau actuellement mise en œuvre au Nord-Kivu. À mesure que de nouvelles données deviendront disponibles concernant l'innocuité du vaccin chez les nourrissons âgés de 6 à 12 mois, l'inclusion des nourrissons dès l'âge de 6 semaines pourra être envisagée. Bien que le suivi puisse s'avérer difficile, il convient de déployer tous les efforts nécessaires pour surveiller l'innocuité de la vaccination parmi les femmes allaitantes, leurs nourris-

[14] Pendant la période écoulée entre la réunion du SAGE et la publication du présent rapport, la situation s'est détériorée en RDC et le nombre de cas a fortement progressé. C'est pourquoi le 7 mai 2019, le SAGE a formulé de nouvelles recommandations provisoires sur la stratégie de vaccination et l'ajustement de la dose vaccinale (https://www.who.int/immunization/policy/position_papers/interim_ebola_recommendations_may_2019.pdf?ua=1, consulté en mai 2019).

to be tested for vaccine virus would be desirable, to extend the currently limited information on safety in these population groups.

SAGE previously recommended that consideration be given to urgent evaluation of new candidate vaccines. This recommendation remains to be implemented. Relevant partners are again urged to conduct studies to evaluate additional candidate vaccines. The studies should be scientifically and epidemiologically justified, have appropriate approval, including from all relevant African and other regulatory and ethics authorities, and have defined endpoints suitable for licensing. As the next candidate vaccines are based on non-replicating viruses, pregnant and lactating women should be included in the trial protocols. In addition, SAGE recommends that manufacturers of candidate vaccines against Ebola virus disease prioritize strategies to generate data on safety, immunogenicity and possibly efficacy in pregnant women, lactating women and infants <1 year as early as possible during vaccine development.

Update on the evaluation of SAGE

SAGE was given the results of an evaluation of SAGE that was begun in April 2018 and will be completed in May 2019. The reasons for an evaluation at the time included: a call for immunization to contribute to broader public health initiatives; shifts in organizational priorities; an evolving agenda in global immunization, particularly after 2020; increasing expectations of efficiency, relevance, transparency, timeliness and the highest scientific excellence in normative work; and good practice since the previous evaluation was conducted a decade ago. The evaluation also responds to an initiative to redesign WHO norms and standards to ensure that they are fitfor-purpose and include early assessment of their relevance for the Organization's needs and priorities and their impact in countries.

The evaluation was conducted under the guidance and oversight of an 8-member Expert Advisory Group of Experts on SAGE Evaluation. Facts and information were collected during August–December 2018 through a desk review, 2 online anonymized surveys of stakeholders and in-depth interviews of a subset of stakeholders. Areas for improvement and recommendations were then listed.

The main findings and preliminary recommendations were reviewed. Stakeholders considered that SAGE is extremely valuable, well respected and plays a critical role in global immunization. In view of the evolving area of global immunization, SAGE's scope and mission should be revised and its modus operandi might have

sons et les enfants vaccinés. Si les informations limitées dont on dispose actuellement concernant l'innocuité du vaccin dans ces groupes de population peuvent être étendues, il serait souhaitable d'élaborer un protocole pour le prélèvement de liquides biologiques tels que le lait maternel et l'urine à des fins de détection du virus vaccinal.

Le SAGE avait précédemment recommandé de procéder à une évaluation urgente des nouveaux vaccins candidats. Cette recommandation n'a pas encore été mise en œuvre. Le SAGE a de nouveau vivement encouragé les partenaires concernés à mener des études d'évaluation de vaccins candidats supplémentaires. Ces études doivent être justifiées sur le plan scientifique et épidémiologique, avoir fait l'objet d'une approbation adéquate, y compris de la part de toutes les autorités africaines compétentes et d'autres autorités de réglementation et d'éthique, et avoir défini des critères de jugement adaptés aux conditions d'homologation. Étant donné que les prochains vaccins candidats contiennent des virus non aptes à la réplication, les femmes enceintes et allaitantes devraient être incluses dans les protocoles d'essai. En outre, le SAGE a recommandé aux fabricants de vaccins candidats contre la maladie à virus Ebola d'accorder une attention prioritaire, dès les premiers stades du processus de développement, aux stratégies susceptibles de générer des données sur l'innocuité, l'immunogénicité et l'efficacité potentielle des vaccins chez les femmes enceintes, les femmes allaitantes et les nourrissons de <1 an.

Informations actualisées concernant l'évaluation du SAGE

Le SAGE a pris connaissance des résultats d'une évaluation de ses activités qui a débuté en avril 2018 et sera totalement achevée en mai 2019. Plusieurs raisons avaient mené à lancer ce projet: un appel en faveur d'une meilleure contribution de la vaccination aux initiatives plus larges de santé publique; les changements de priorités institutionnelles; l'évolution du programme de vaccination mondial (en particulier après 2020); les attentes toujours plus élevées en matière d'efficience, de pertinence, de transparence, de respect des délais et d'excellence scientifique des travaux normatifs; et les bonnes pratiques adoptées depuis la précédente évaluation, menée il y a 10 ans. L'évaluation s'inscrit également dans le cadre d'une initiative visant à refondre les normes et les critères de l'OMS pour garantir qu'ils sont adaptés et intègrent une évaluation précoce de leur utilité (au regard des besoins et priorités de l'Organisation) et de leur impact dans les pays.

L'évaluation a été menée sous l'égide d'un groupe consultatif d'experts de l'évaluation du SAGE, composé de 8 membres. Les données factuelles et d'autres informations ont été recueillies entre août et décembre 2018 dans le cadre d'un examen sur dossier, de 2 enquêtes en ligne menées auprès de parties intéressées (en préservant leur anonymat) et d'entretiens approfondis auprès d'un sous-ensemble de parties prenantes. Cela a ensuite permis de recenser les améliorations à apporter et d'établir des recommandations.

Les principaux résultats et les recommandations préliminaires ont été examinés. Les parties prenantes estiment que le SAGE apporte une contribution très utile, est très respecté et joue un rôle déterminant dans les activités de vaccination au plan mondial. Compte tenu des évolutions observées dans ce domaine, la portée et la mission du SAGE devraient être révisés

to be adapted in order to address emerging needs and trends. While SAGE does not advise on vaccine research or development, it could establish more formal mechanisms for identifying areas that require further vaccine and operational research. Stakeholders considered that the mandates and functions of other WHO immunization advisory bodies should be examined to avoid overlaps and optimize synergy. SAGE should consider regional and country needs more systematically by strengthening channels or developing new ones in collaboration with the regional offices. Countries will increasingly require detailed guidance for decision-making rather than sweeping recommendations. The "implementability" of recommendations should be considered through feedback from countries. Relations among SAGE and regional and national immunization technical advisory groups could be made more functional to increase engagement. Relations with global stakeholders could be based on rules of engagement and regular dialogue. The fundamental areas of expertise required are well represented in the current SAGE membership, but SAGE should ensure access to all relevant expertise when they require additional competence and skills. Agendas could be set with a more transparent, systematic approach to prioritization. Greater clarity in decision-making, in the establishment and use of working groups, in updating position papers and in preparation of meetings is advised, with use of more modern communication and information technology. Conflicts of interest other than simple financial interest should be defined. Better dissemination of SAGE outputs could be explored. Importantly, resources for the SAGE Secretariat should be assessed so that proposed recommendations can be implemented. A final report of the evaluation, with recommendations, will be provided to WHO in May 2019.

et il faudra peut-être adapter ses modes opératoires à la lumière des nouveaux besoins et tendances. Même si le SAGE ne formule pas de recommandations en matière de recherche et développement sur les vaccins, il pourrait établir des mécanismes plus formels pour identifier les domaines dans lesquels des recherches supplémentaires sur les vaccins, ou une recherche opérationnelle plus poussée, sont nécessaires. Les parties prenantes ont jugé que les mandats et les fonctions des autres organes consultatifs de l'OMS sur la vaccination devraient être examinés afin d'éviter les doubles emplois et d'optimiser les synergies. Le SAGE devrait examiner les besoins régionaux et nationaux de façon plus systématique en renforçant les canaux existants ou en en établissant de nouveaux en collaboration avec les bureaux régionaux. Les pays auront de plus en plus besoin de d'orientations détaillées aux fins de la prise de décisions, plutôt que de recommandations globales. La faisabilité des recommandations doit être examinée en fonction des observations communiquées par les pays. Les relations entre le SAGE et les groupes consultatifs techniques régionaux et nationaux sur la vaccination pourraient être rendues plus efficaces afin de renforcer la collaboration. De même, les rapports avec les parties prenantes mondiales pourraient s'appuyer sur des règles de collaboration et un dialogue régulier. Les domaines de compétence majeurs sont bien représentés parmi les membres du SAGE, mais celui-ci doit veiller à pouvoir accéder facilement à d'autres compétences et savoir-faire, lorsque nécessaire. Les programmes de travail pourraient être fixés en adoptant une approche plus transparente et systématique de la détermination des priorités. Il est recommandé de faire preuve d'une plus grande clarté dans la prise de décisions, la création et l'utilisation des groupes de travail, l'actualisation des notes de synthèse et la préparation des réunions, en employant des technologies de l'information et de la communication plus modernes. Il convient également de définir les conflits d'intérêt ne relevant pas de simples intérêts financiers. Les moyens de mieux diffuser les travaux du SAGE pourraient également être étudiés. Fait important, les ressources dont dispose le secrétariat du SAGE devraient être évaluées de sorte que les recommandations proposées puissent être mises en œuvre. Un rapport d'évaluation final assorti de recommandations sera communiqué à l'OMS en mai 2019.

SAGE noted that evaluation is healthy and useful. SAGE welcomed the advice to increase connections with regions and to increase the relevance of its recommendations to countries. With regard to broader public health agendas with non-immunization stakeholders or led by non-immunization partners that may be broadly cross-cutting (e.g. including maternal and child health, adolescent health and cancer control), SAGE asked how work that is relevant to its mandate should be managed and coordinated. SAGE has experience in cross-cutting agendas, as at the current meeting, when the session on malaria included MPAC, an advisory committee for another department. SAGE recognized, however, that more attention should be paid to coordination now and after 2020 when there will be greater emphasis on health systems and broader agendas. ■

Le SAGE a noté qu'il est à la fois sain utile de procéder à une évaluation. Il a accueilli favorablement le conseil qui lui a été donné de renforcer ses liens avec les Régions et de formuler des recommandations plus pertinentes pour les pays. Il s'est demandé comment les travaux intéressant son mandat devraient être administrés et coordonnés dans le cas de programmes plus généraux de santé publique faisant intervenir des parties prenantes d'autres secteurs que la vaccination, ou dirigés par des partenaires d'autres secteurs, et dont la vocation est donc transversale (incluant par exemple la santé de la mère et de l'enfant, la santé de l'adolescent et la lutte contre le cancer). Le SAGE possède une expérience des programmes transversaux, comme en témoigne cette réunion, au cours de laquelle le Comité de pilotage de la politique de lutte antipaludique (MPAC), un comité consultatif d'un autre département, a participé à une séance sur le paludisme. Le SAGE a reconnu, cependant, qu'il faudrait accorder plus d'attention à la coordination, aujourd'hui et après 2020, quand l'accent sera davantage mis sur les systèmes de santé et les programmes plus globaux. ■

WHO web sites on infectious diseases – Sites internet de l'OMS sur les maladies infectieuses

Avian influenza	**http://www.who.int/csr/disease/avian_influenza/en/**	Grippe aviaire
Buruli ulcer	**http://www.who.int/buruli/en/**	Ulcère de Buruli
Child and adolescent health and development	**http://www.who.int/child_adolescent_health/en/**	Santé et développement des enfants et des adolescents
Cholera	**http://www.who.int/cholera/en/**	Choléra
Deliberate use of biological and chemical agents	**http://www.who.int/csr/delibepidemics/informationresources/en/**	Usage délibéré d'agents chimiques et biologiques
Dengue	**http://www.who.int/denguecontrol/en/**	Dengue
Epidemic and pandemic surveillance and response	**http://www.who.int/csr/en/**	Alerte et action en cas d'épidémie et de pandémie
Eradication/elimination programmes	**http://www.who.int/topics/infectious_diseases/en/**	Programmes d'éradication/élimination
Fact sheets on infectious diseases	**http://www.who.int/topics/infectious_diseases/factsheets/en/**	Aide-mémoires sur les maladies infectieuses
Filariasis	**http://www.filariasis.org**	Filariose
Geographical information systems (GIS)	**http://gamapserver.who.int/mapLibrary/**	Systèmes d'information géographique
Global atlas of infectious diseases	**http://apps.who.int/globalatlas/InteractiveMap/HowTo/HowTo.html**	Atlas mondial des maladies infectieuses
Global Outbreak Alert and Response Network (GOARN)	**http://www.who.int/csr/outbreaknetwork/en/**	Réseau mondial d'alerte et d'action en cas d'épidémie (GOARN)
Health topics	**http://www.who.int/topics/en**	La santé de A à Z
Human African trypanosomiasis	**http://www.who.int/trypanosomiasis_african/en/**	Trypanosomiase humaine africaine
Influenza	**http://www.who.int/csr/disease/influenza/en/**	Grippe
Influenza network (FluNet)	**http://who.int/flunet**	Réseau grippe (FluNet)
International Health Regulations	**http://www.who.int/ihr/en/**	Règlement sanitaire international
International travel and health	**http://www.who.int/ith/en/**	Voyages internationaux et santé
Leishmaniasis	**http://www.who.int/leishmaniasis/en**	Leishmaniose
Leprosy	**http://www.who.int/lep/en**	Lèpre
Lymphatic filariasis	**http://www.who.int/lymphatic_filariasis/en/**	Filariose lymphatique
Malaria	**http://www.who.int/malaria/en**	Paludisme
Neglected tropical diseases	**http://www.who.int/neglected_diseases/en/**	Maladies tropicales négligées
Onchocerciasis	**http://www.who.int/onchocerciasis/en/**	Onchocercose
Outbreak news	**http://www.who.int/csr/don/en**	Flambées d'épidémies
Poliomyelitis	**http://www.polioeradication.org**	Poliomyélite
Rabies	**http://www.who.int/rabies/en**	Rage
Global Foodborne Infections Network (GFN)	**http://www.who.int/gfn/en**	Réseau mondial d'infections d'origine alimentaire
Smallpox	**http://www.who.int/csr/disease/smallpox/en**	Variole
Schistosomiasis	**http://www.who.int/schistosomiasis/en/**	Schistosomiase
Soil-transmitted helminthiases	**http://www.who.int/intestinal_worms/en/**	Géohelminthiases
Trachoma	**http://www.who.int/trachoma/en/**	Trachome
Tropical disease research	**http://www.who.int/tdr/**	Recherche sur les maladies tropicales
Tuberculosis	**http://www.who.int/tb/en** and/et **http://www.stoptb.org**	Tuberculose
Immunization, Vaccines and Biologicals	**http://www.who.int/immunization/en/**	Vaccination, Vaccins et Biologiques
Weekly Epidemiological Record	**http://www.who.int/wer/**	Relevé épidémiologique hebdomadaire
WHO Lyon Office for National Epidemic Preparedness and Response	**http://www.who.int/ihr/lyon/en/index.html**	Bureau OMS de Lyon pour la préparation et la réponse des pays aux épidémies
WHO Pesticide Evaluation Scheme (WHOPES)	**https://www.who.int/whopes/resources/en/**	Schéma OMS d'évaluation des pesticides (WHOPES)
Yellow fever	**http://www.who.int/csr/disease/yellowfev/en/**	Fièvre jaune

SAGE TRACKING RECORD OF RECOMMENDATIONS AND ACTION POINTS

SAGE recommendations are reflected in the SAGE tracking sheet. The "Recommendations/Action item" column reflects the specific recommendation made by SAGE. The "Meeting Date" column displays the date of the SAGE meeting during which the recommendation was originally made. The "Status" column indicates whether the work is currently ongoing, pending or completed.

Each recommendation has an appointed WHO focal point (not displayed in SAGE Yellow Book). The focal points are requested to update their recommendation in advance of each SAGE meeting and report on progress towards the recommendation in the "Comments and Follow Up" column.

When the recommendation is finalized, it is displayed as "Completed" in the SAGE yellow book. This item is then included in the SAGE Yellow Book for one additional SAGE meeting. After, the completed item is archived. Archived recommendations are no longer displayed in the SAGE Yellow Book but may still be accessed upon request to the SAGE secretariat. Therefore, the online tracking sheet provides a historical record of all SAGE recommendations and the Yellow Book displays the current recommendations.

Topic	Recommendations/Action item	Meeting Date	Status	Comments and Follow up
General	SAGE recommended that ways to improve curricula for medical personnel should be explored.	Nov 2008	Ongoing	The Regional Office for Africa (AFRO) has published the pre-service curriculum and efforts are being made to disseminate the findings and ensure that medical and nursing schools change their outdated curriculum. This is a long process but few steps have started in that direction. AFRO continues to work with countries on updating their pre service curriculum.
General	SAGE stressed that additional disaggregation was needed in the analysis of the progress achieved on the ground, and in identifying bottlenecks for progress, and recommended that reports display disparities observed at sub-national levels.	Apr 2015	Ongoing	WHO headquarters (HQ) continues working closely with regional offices to obtain subnational level for coverage and measles/rubella and other VPD surveillance data. Currently this is happening in the African Region on monthly as well as annual basis; and in the South East Asian Region and the European Region it is done on annual basis. Since 2017, WHO-HQ is collecting district level coverage data (numerator, denominator and coverage from DTP1, DTP3 and MCV1) as part of annual data collection exercise. In 2019, for 2018 data, out of 194 member states, 150 countries reported subnational coverage, 135 at the 1st subnational level and 102 at the 2nd subnational administrative level (district or equivalent). The nearly 24,000 districts for which data were received are home to over 100 million children, 75% of the surviving infants worldwide. Large differences exist in the size of districts and the coverage they report. A large proportion (more than 25%) report coverage over 100% and many district report large changes from one year to the next, highlighting the challenges to accurately measure coverage at subnational level. Detailed analysis and reported data are available from http://www.who.int/immunization/monitoring_surveillance/data/subnational/en/
AEFI reporting	SAGE urged that efforts be pursued to enhance Adverse Events Following Immunization (AEFI) reporting worldwide.	Apr 2016	Ongoing	Progress with adverse events following immunization (AEFI) surveillance is sustained with 114 countries reporting at least 10 AEFI per 100,000 surviving infants during 2017 as compared to 45 in 2010 and 97 in 2016. In order to further analyze national capacity, more refined indicators related to serious AEFI, timeliness and completeness of reporting are now being developed and evaluated. As at 30 June 2019, 2018 data indicate 120 countries that meet the AEFI reporting indicator, with an increase from 20 to 27 AFR countries. For the first time more than half AFR countries have minimal AEFI reporting.
Analysis of national legal framework on immunization	Legal frameworks: A comprehensive global audit should be undertaken to document the ways in which legislation and regulation have been used to promote or undermine immunization at a national level, to identify how legal and regulatory instruments can be best applied in different contexts and for different purposes to strengthen immunization systems	Oct 2017	ongoing	The University of Dalhousie Canada conducted a study to assess the impact of legislative frameworks on immunization, particularly in the context of establishment and governance of national immunization technical advisory groups (NITAGs). Preliminary results were presented at Decade of Vaccines (DoV) Working Group meeting in Aug 2018 and at the meeting of the Global NITAG Network in December 2018. Additional analysis was carried out - report was finalized in Aug 2019. A manuscript has been submitted to a peer-reviewed journal. In parallel, Sabin Vaccine Institute conducted a landscape analysis of immunization legislation in the European region and developed case studies, results are available on the Sabin website. Potential follow up studies to assess the impact of the legislation in select countries is under discussion.
Data quality	SAGE requested the establishment of a Working Group on Quality and Use of Global Immunization and Surveillance Data.	Apr 2017	Ongoing	The Working Group was established in August 2017 and reported to SAGE in April 2019. All relevant material are available here: https://www.who.int/immunization/sage/meetings/2019/april/presentations_background_docs/en/. SAGE will revisit this topic in October 2019 to issue recommendations.

Topic	Recommendations/Action item	Meeting Date	Status	Comments and Follow up
Decade of vaccines/GVAP	The SAGE working group should continuously review the Progress on GVAP and the need for reformulation of the indicators or mechanisms for collection and reporting of data.	Nov 2012	Ongoing	The SAGE Decade of Vaccines (DoV) Working Group (WG) continues to review annually progress on the Global Vaccine Action Plan (GVAP) indicators. The SAGE report of progress with the Global Vaccine Action Plan (GVAP) for 2018 was published online and is available at: http://www.who.int/immunization/global_vaccine_action_plan/en/ This year the SAGE DoV WG is overseeing the development of the overall GVAP review and lessons learnt. A highlevel interim lessons learnt item was presented at SAGE in April 2019 (after the post 2020 Global immunization strategy development multistakeholder meeting in March 2019). The full GVAP report report will be prepared for the October 2019 SAGE meeting. The GVAP review will replace the formal annual GVAP secretariat report and SAGE assessment report.
Diphtheria	SAGE expressed concern with the shortage of Td vaccine (tetanus toxoid + reduced diphtheria toxoid content) for routine immunization of children and adolescents, catch-up vaccination of adults and tetanus prevention after injury, and recommended that the demand and supply scenarios for Td vaccines should be assessed.	Apr 2017	Ongoing	An assessment of global demand and supply for Diptheria and Tetanus containing vaccines was conductd in 2017 and updated early 2019 for SAGE members and wider public. The main objective of the assessment was to understand possible supply implications of global implementation of WHO recommended schedule for D&T containing vaccines. The assessment can also be useful to guide current supply access issues. The assessment was conducted with support from Linksbridge and MMGH consulting group. The methodology used is similar to other global market studies conducted under the Market Information for Access Initiative - and endorsed by IVIRAC in 2019. The conclusion of the 2019 assessment on D&T were: • WHO recommends for all countries: 1) a life course of 6 doses of Diphtheria and Tetanus containing vaccines and 2) use of Td in place of TT • 108 / 194 countries do not meet these recommendations, but due to conducive circumstances, they are now likely to implement WHO recommendations • Full implementation of the recommendations would increase global demand for all D&T containing vaccines by ~15% between now and 2030 • Sufficient supply is available to cover both current and future demand for wP / non-aP containing vaccines • Supply of aP-containing vaccines is currently sufficient to support demand from countries where the product is in use; access in additional countries may be problematic • Countries with only one locally-registered product are at risk of supply shortages, irrespective of the global supply-demand balance

Topic	Recommendations/Action item	Meeting Date	Status	Comments and Follow up
Diphtheria	SAGE advised that WHO collaborate closely with partners to establish and manage a global procurement mechanism and a physical or virtual DAT stockpile that would be available to all countries. SAGE further urged that regulatory pathways be established to ensure the rapid deployment of DAT. In the long term, SAGE advised WHO to identify mechanisms to support the development of a monoclonal antibody as an alternative to DAT of equine origin.	Apr 2017	Ongoing	WHO has established a DAT international working group to coordinate and allocate extremely limited DAT supplies. In 2018 WHO coordinated the procurement of DAT among different procurement agencies and partners. DAT was supplied to Yemen, Bangladesh, Indonesia, Venezuela and Haiti. Around 20,000 vials have been deployed between WHO, PAHO and MSF. DAT-WG is now looking for solutions to establish either procurement mechanism to make agreement in advance or a stockpile to meet the urgent or unexpected demand during outbreaks. WHO is now evaluating the quality of the available DAT WHO DAT-WG coordinates the group to look at the following areas of work: 1. Procurement strategy 2. Forecasting and Stockpiling 3. Decision making criteria and mechanism for DAT allocation 4. Quality, standardization and WHO prequalification 5. DAT production capacity and new products (mAbs) Members of the coordinating group: MSF, UNICEF, ECDC, CDC, PEI, MHRA, EC, FDA, EMA, PHE, NIBSC
Ebola	SAGE reiterated that WHO should support the national regulatory authorities of countries endemic for ebola virus disease (EVD) to reach consensus on pathways for the evaluation and marketing authorization of candidate EVD vaccines.	Oct 2018	Ongoing	Work is ongoing within WHO in order to ensure continous support to national regulatory authorities and to reach consensus on pathways for new candidate vaccines.
Ebola vaccines	Noting WHO's unique position to coordinate the development of Ebola vaccines, SAGE stressed the importance of transparent and prompt sharing of information on the trial protocols and data from the phase 3 clinical trials, and the need for a greater role for WHO in facilitating the sharing of information so that results between studies will generate the greatest benefit for policy decision-making.	Apr 2015	Ongoing	SAGE established an Ebola working group (WG) in Nov 2014 which met regularly via teleconference as well as during a face-to-face meeting on the 9-10 Mar 2015. The WG reviewed the epidemiological data on Ebola Virus Disease (EVD), the preliminary results of the phase 1 trials, the status of the phase 2 and 3 trials, and the preparations for the large scale deployment of vaccines. They also identified the scope of the recommendations and the key questions and data for formulating recommendations. The framework was presented to SAGE at the Apr 2015 meeting. The WG met again on 19-20 Aug 2015 to review the available information and to start framing recommendations, based on the framework approved by SAGE in Apr 2015. The WG input was presented to SAGE at the Oct 2015 meeting. Now, that the final results of the Ring trial have been published in the Lancet in Dec 2016, a WG meeting took place 14-15 Mar 2017 to discuss the results. Regulatory evaluation of the vaccine is currently ongoing. There is information regarding a Russian developed vaccine that was licensed in Russia, but despite WHO requests no detailed data are available. The emerging data and draft recommendations were discussed during the face to face meeting of the WG which took place Mar 2017. The evidence was presented during the April 2017 SAGE meeting. In October 2018, SAGE discussed a review of data submitted by developers of candidate vaccines and of published data.

Topic	Recommendations/Action item	Meeting Date	Status	Comments and Follow up
Full public health value of vaccines	SAGE requests update on progress and implementation of the concept, and on a more public health related terminology.	Apr 2018	Ongoing	On the recommendation of SAGE, the term value proposition has been removed and the new terminology for the concept is the 'Full public value of vaccines (FPVV)'. Efforts to socialize the concept are continuing, and the FPVV was discussed at the 2019 PDVAC meeting. Efforts and collaborations to develop components of FPHVVs are underway for several vaccines including Herpes Simplex Virus, Group B strep and Group A strep vaccines, and vaccine products, including the next generation rotavirus vaccine NRRV. WHO has proposed a generic template to evaluate the FPVV, but needs now to socialise this and develop a framework to provide guidance on which components should be developed relative to the stage of vaccine/product development, target stakeholders and problem statement.
Health Workers	Further work on the terms of reference of a potential Health Workers SAGE Working Group is needed and some initial work needs to be done before bringing the proposal to establish the group to SAGE.	Apr 2019	Ongoing	To inform the potential work of a SAGE Working Group on health worker (HW) vaccination, WHO's Initiative for Vaccine Research (IVR) has called an International Expert Advisory task force to develop guidance to inform the introduction HW vaccination with influenza vaccine. This manual is being piloted in multiple countries introducing influenza vaccine or with influenza HW vaccination policies in place. Furthermore, IVR is conducting a literature review to better understand linkage between vaccine uptake in HWs and pregnant women. Finally, a multi country study is underway to understand acceptance of HW vaccination against influenza and which interventions could help address uptake issues.
Hepatitis A	Long-term protection from single or 2-dose schedules should be regularly monitored by countries and reviewed by SAGE. In April 2019, SAGE requested next steps to be undertaken to inform consideration of a single dose vaccination strategy by SAGE which would lead to an update to the 2012 WHO position paper on hepatitis A vaccines. These next steps include the identification of a complete global list of inactivated and live attenuated HepA vaccines that are being used, review of efficacy, effectiveness, long-term protection, program implementability, and impact on HepA virus disease of single dose schedules for the available HepA vaccines and review of data on HepA virus outbreaks, disease burden, and surveillance.	Apr 2012	Ongoing	Post-market surveillance continues in Argentina and a detailed report on the recent epidemiological situation was provided to WHO in March 2017. The next active follow-up report will be requested ahead of the April 2018 SAGE meeting. In 2014, in the context of a localized outbreak in a border area, 8 potential breakthrough cases were identified. For 5 of them there is uncertainty about the vaccination status and/or conditions (cold chain) in which vaccination was administered. Seven of these cases are in the 5-9 age group (distributed throughout the period) and one in the 1-4 age group. This resulted in an enhanced vigilance in the country. As exemplified by the outbreak in San Martin, the risk persists in the population. 73% of of hepatitis A virus (HAV) acute infection cases reported occurred in individuals over >10 years. All cases reported occurred in unvaccinated individuals. After now 11 years of follow-up, there is currently still no evidence of waning immunity and the outbreak experienced in 2014 was compatible with very high vaccine effectiveness. Hepatitis A cases have remained low in 2014, 2015, and 2016. Although a reduction in hepatitis A rates was experienced in all age groups, there is an increasing proportion of the remaining cases occurring in persons > 14 years of age in the post vaccination period. Most of these represent non-vaccinated adolescents or adults that escaped HAV-infection in previous outbreaks. Both Colombia and Paraguay also introduced a single dose national immunization schedule for 1 year old children. Yearly review of the Argentinian surveillance data will continue as Argentina was the front runner country to introduce a 1 dose schedule with the inactivated vaccine. The results of the phase 2 study conducted in 2013 with a median post-vaccination interval of 7.7 years were quite reassuring with a prevalence of protective antibodies of 97.4% (95% CI: 96.3-98.3) still protected. More recent analysis (phase 3) indicates that the prevalence of protective antibodies in children > 9 years following a single dose of hepatitis A vaccine was still 87.6% but a decrease was observed in all centers with decreased GMCs. It is still unclear if different samples or differences in methodology or recall bias in seronegative individuals could actually account for the difference, but this requires continued follow up. For the time being epidemiologic surveillance continues to show very low infection rates in all regions and age groups with sporadic cases occurring mainly in frontier regions and non-vaccinated adolescents. Currently, a study is ongoing to assess the immunological response after ten years of vaccination. Results are anticipated by the end of 2019. Preparatory work to inform consideration of a single dose vaccination strategy by SAGE has been initiated.

Topic	Recommendations/Action item	Meeting Date	Status	Comments and Follow up
Hepatitis B	SAGE strongly urges all the pre-qualified vaccine manufacturers of monovalent hepatitis B vaccine to pursue regulatory approval for Controlled Temperature Chain (CTC) as soon as possible, given the available evidence of compatibility with CTC requirements.	Oct 2016	Ongoing	During the course of 2018, one Hepatitis B vaccine manufacturer had obtained licensure approval from the relevant NRA for a Hepatitis B injectable vaccine (single dose, thimerosal containing 0.5ml presentation) to be stored up to 37°C for 28 days and up to 45°C for 4 days. The latter parameters are compatible with Controlled Temperature Chain (CTC) requirements. However, in November 2018, this manufacturer made a business decision not to proceed with a CTC label variation and informed WHO PQT of their decision to withdraw their request for pre-qualification. The main reason for the latter concerned the low potency preferred by the manufacturer which was not meeting the approval of PQT. Two other manufacturers have expressed a willingness to seek licensed and WHO-Prequalified label variations on their respective birth-dose Hepatitis B vaccines permitting use in a CTC. The CTC Working Group under the Immunization Practices Advisory Committee (IPAC) has made available a landscape analysis and strategy to further promote the use of hepatitis B birth-dose in a CTC. This Working Group will be meeting again in Maputo, Mozambique in December 2019, during which further discussion will be had to assess progress and opportunities to advance the CTC agenda regarding Hepatitis B.
Hepatitis B	SAGE recommended that the timely delivery of a birth dose of hepatitis B vaccine (that is, within 24 hours of birth) should be used as a performance measure for all immunization programmes. Reporting and monitoring systems should be strengthened to improve the quality of data on the birth dose.	Apr 2009	Closed	WER on status of global introduction and implementation of hepatitis B birth dose has been published in Feb 2018. A new indicator for Hepatitis B birth dose has been added to the WHO /UNICEF Joint Reporting Form (JRF) 2017. This new indicator will allow the distinction between timely (24 hours) and late birth dose administration. In Jun 2019 the African Regional Office (AFRO) held a regional workshop on HepB birth dose introductions and strengthening already existing programmes. A total of 12 countries participated, approximately half had introduced and created plans for improvements. Uganda, South Africa and Cote D'Ivoire plan to introduce in 2019. Guidance for hepatitis B birth dose introduction was published on June 2016 ('Preventing Perinatal Hepatitis B Virus Transmission: A Guide for Introducing Hepatitis B Birth Dose Vaccination', available from: http://www.who.int/immunization/documents/general/ISBN9789241509831/en/ in English, French, Spanish and Arabic. The guidance includes a chapter on reporting and monitoring birth dose vaccination. In Jan 2015 the African Regional Office (AFRO), and in Mar 2015 WPRO, held Hepatitis B birth dose consultations to improve birth dose coverage. In February 2015, an AFRO workshop on birth dose introduction was conducted in Brazzaville; this workshop included guidance on birth dose monitoring. An assessment of birth dose implementation has taken place in Sao Tome Principe in July 2015 and Nigeria in September 2015 and in the Gambia in December 2015. Senegal held a Hepatitis B birth dose training workshop in Dec and introduced birth dose in Jan 2016.
Hepatitis E	SAGE members expressed their concerns about the limited use of Hepatitis E vaccine, in particular in pregnant women, and welcomed the generation of new data to increase its use. SAGE would appreciate to be kept informed on the issue.	Apr 2019	Ongoing	WHO and partners are currently assessing the use of the vaccine in Namibia, where an outbreak has been ongoing for 1.5 years. For this, a generic protocol has been developed by MSF to generate new evidence on the use of the vaccine.
Hexavalent IPV-based combination vaccines PQ and supply	Track progress on Hexavalent IPV-based combination vaccines prequalification and supply	Oct 2017	Ongoing	This work is ongoing through the Gavi market shaping team who is leading on collecting information on hexavalent supply as well as communication with manufacturers on potential future demand. Gavi is currently developing a market shaping roadmap with partners on Hexavalent vaccine.

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HIV	SAGE requested regular updates on the progress of HIV-vaccine research.	Apr 2010	Ongoing	Two HIV vaccine efficacy studies have started in Africa, late 2017. The HVTN702 phase 2b efficacy trial in Southern Africa, builds on analyses of correlates of protection in the RV144 Phase 3 trial in Thailand (which showed 31 % protection against new HIV infection during the 3.5 years after vaccination, 60 % during the first year), is testing an immunization regime based on a canarypox-based vaccine called ALVAC-HIV and a bivalent gp120 protein subunit vaccine. As compared to the Rv144 trial this regimen includes a new adjuvant, targets the HIV Clade C and includes the addition of booster doses. The HVTN 705 Phase 2b trial in several African countries will test for a regimen based on 4 mosaic recombinant Ad26 and the gp140 protein trimer in alum. Another important development relates to the testing of several monoclonal antibodies having broadly neutralizing antiretroviral properties. Two multicenter, multi-country studies, one of which in women in South Africa, will test for prevention of HIV infection after several VRC01 monoclonal antibody injections. Several other approaches are being tested in translational research. WHO IVR organized a consultation on HIV vaccine development in 2018 to discuss the status of HIV vaccine research and the need for the global health community to prepare for the outcome of ongoing efficacy trials in highly endemic countries. Building on the meeting proceedings and report, key considerations have been expressed (accepted for publication in the Lancet HIV). Partner discussions are ongoing for a formal assessment of the full public value of HIV vaccnes and mAbs for HIV prevention. An ethics consultation about prevention trial design in the context of PreP is planned for.
HPV	The secretariat is developing a pathway, milestones and indicators towards that goal that will require careful consideration of the role of HPV vaccination, besides screening and care components. To guide WHO on this, it was agreed that a SAGE working group would be needed, with an initial reporting back to SAGE in October 2018. SAGE should consider new data in terms of cost-effectiveness, defining long- and interim- goals, identifying indicators for the elimination strategy as related to vaccination.	Jun 2018	Ongoing	SAGE established a Working Group in 2018. In October 2018, SAGE reviewed the latest evidence on the immunogenicity, efficacy and effectiveness of HPV vaccines, their administration schedules, number of doses and intervals, and use in HIV-infected and in male populations. SAGE also reviewed the results of 3 models showing the impact and effectiveness of various HPV vaccination and screening strategies, and the potential for cervical cancer elimination. SAGE also expressed concern about the constrained HPV vaccination supply forecast until at least 2024. Work is being done by the SAGE Working Group to assess options for more equitable distribution of HPV vaccines. Different allocation strategy(ies)and their potential effect on HPV infection, diseases and access to HPV vaccine in the short and mid-term have been discussed. Recommendations will be discussed at the SAGE meeting in October 2019
HPV	SAGE urged that a globally more equitable distribution of the available HPV doses be encouraged to ensure optimal global public health access to vaccines.	Oct 2018	Ongoing	A workplan for the assessment of options to achieve more equitable allocation of HPV vaccine under supply constraints is currently ongoing. SAGE WG on HPV vaccines reviewed uring it's meeting of June 6-7, 2019, the latest evidence on the immunogenicity, efficacy and effectiveness of HPV vaccines, the vaccine allocation strategy(ies) to achieve more equitable access to HPV and reviewed the potential effect on HPV infection, disease and access to HPV vaccines in the short and mid-term of various schedule and vaccine allocation strategies. Recommendations will be discussed during the SAGE meeting in October 2019.
Influenza	SAGE issued the recommendation to establish a Working Group on influenza vaccines.	Apr 2017	Ongoing	A SAGE Working Group on Influenza Vaccines has been established in December 2017. http://www.who.int/immunization/policy/sage/sage_wg_influenza_dec2017/en/ The Working Group deliberations are ongoing in 2019.
IPV Supply	THE IPV supply situation is expected to improve in 2018; all countries are expected to have access to IPV for routine immunization from the end of Q1 2018. SAGE acknowledged WHO´s work with Imperial College, London, to grade risks in Tier 3 and 4 countries based on susceptibility, transmission, exposure, and primary immunodeficiency-associated vaccine-derived poliovirus (iVDPV) prevalence.	Oct 2017	ongoing	In Q1 2018, UNICEF issued an update on IPV supply which provides the current understnading of IPV supply. this is available upon request. UNICEF does not anticipate a market with multiple suppliers and sufficient supply capacity to fully meet programmatic requirements of at least 2 doses of IPV to materialize before 2023.

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Lower middle-income countries: sustainable adoption and financing for new vaccines	SAGE requested that WHO facilitate the establishment of a partnership among all relevant stakeholders to consider: pooled procurement; tiered pricing; greater transparency of pricing; and exploring the role that UNICEF, the Pan American Health Organization and foundations can have in assisting these countries with procuring and financing vaccines.	Nov 2010	Ongoing	WHO set up a Middle Income Countries (MIC) Task Force in June 2014 with main immunization stakeholders (WHO, UNICEF, World Bank, Gavi Secretariat, BMGF, AMP, Sabin, Task Force for Global Health), which led to the creation of the "MIC strategy", presented at SAGE in April 2015. The strategy aims at improving sustainability of immunization programmes and access to vaccines in non-Gavi MICs. The MIC strategy is based on four pillars : i) Strengthening evidence-based decision-making; ii) Enhancing political commitment and ensuring financial sustainability of immunization programmes; iii) Enhancing demand for and equitable delivery of immunization services; and iv) Improving access to timely and affordable supply. The timeline for the strategy is up to 2020 to align with the GVAP timeframe and up to 2025 for a longer term horizon. Following SAGE endorsement of the MIC Strategy in Apr 2015, the WHO-led MIC Task Force initiated a country engagement process: in collaboration with key immunization partners WHO started multi-partner dialogues with four countries struggling with raising or maintaining high immunization coverage and/or introducing new vaccines. Selected countries were Romania, Swaziland, Jordan and Philippines. AAlso, some efforts to support all MIC countries in the area of access to timely and affordable supply have been implemented. Notably, the creation of a mechanism for access to supply in humanitarian emergencies in MICs not supported by Gavi; set up of a peer platform and regional workshop to strengthen country procurement capacity; work on price transparency continues successfully with 85% of world (n. of countries) sharing vaccine product, price and procurement information since the beginning of WHO price transparency efforts and the recent launch of the Market Information for Access to Vaccine (MI4A) project. Despite these efforts, progress in implementation of the strategy accross its 4 pillars is very slow due to lack of funding. As discussed at the Apr 2015 SAGE meeting, the partners would require about US$20M per year to fully implement the strategy. In Oct 2016, a meeting of the MIC Task Force was held to review progress and discuss next steps. The TF determined having concluded its mandate through a review of the MIC issue and the development of a partner-shared MIC strategy. It was thus proposed that the TF comes to a close. Anticipating that considerable time may be needed for funding to become available, the TF proposed that partners focus on i) regular normative/guidance work benefiting all countries including non Gavi MICs and ii) access to affordable and timely supply (continuing working on implementation of ongoing activities and potentially new one as possible). Partners committed to continue information sharing and collaborative spirit in these efforts. At meeting in June 2019, and in the context of Gavi 5.0 strategy, the Board requested that the Gavi Secretariat explore approaches to engaging with self-financing lower middle-income countries in recognition of major challenges in those countries. WHO and partner are exploring opportunities of complementary, coordinated approach to support access to vaccines in MICs.

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Malaria Vaccine	SAGE requested continued review of the planning of the pilot implementations and to receive regular updates on the results.	Oct 2015	Ongoing	Vaccinations started in all three pilot countries: in Malawi on 23 April 2019, in Ghana on 30 April 2019, and in Kenya on 13 September 2019. This historic milestone generated extensive news interest in nearly every geography. Data and feedback received so far suggest good acceptance of the programme by health care workers, care givers and communities and generally high demand in areas where communication and sensitization efforts were good. Issues for improvement have been identified through early supervisory visits. Pilot evaluation: The first cross-sectional household surveys (baseline) have been completed. Data collection through sentinel hospitals and community mortality surveillance are underway with continued efforts to strengthen these surveillance systems. The qualitative longitudinal study to assess issues related to vaccine uptake, community perceptions, and service delivery, began. In April 2019, the Framework for Policy Decision on RTS,S/AS01 was endorsed by SAGE and MPAC. The two advisory bodies agree to consider a policy decision on the broader use of the vaccine as soon as the minimum required data are available, which might be prior to the end of the pilots. In a statement released on 26 August 2019, MPAC draw attention to the stalling progress with malaria control and indicated that if the results from the MVIP are promising, the RTS,S vaccine, in combination with ITNs and other control measures, is likely to be an important additional tool to change the course of malaria incidence and reduce malaria deaths in African children. Current funding commitments by GFATM, Gavi and Unitaid cover MVIP activities through 2020. WHO and partners have intensified efforts to not only secure funding for 2021-2023 to complete the MVIP, but also to brief stakeholders on the current evidence base of the vaccine and the vision for access should there be a policy recommendation.
Maternal Immunization	SAGE encouraged WHO to promote more implementation research to generate generalizable data on the best ways to integrate maternal immunization into routine antenatal care in low resource settings. SAGE requested WHO to follow-up with a broad based consultation on vaccination of pregnant and lactating women.	Apr 2015	Ongoing	WHO's Initiative for Vaccine Research (IVR) is (1) Finalizing a Maternal Tetanus Immunization and Antenatal Care Situation Analysis (MIACSA) in collaboration with the WHO Maternal Child and Adolescent Department which will shed light on how ANC service delivery is being implemented in a larger number of LMIC countries; (2) Organizing a high level stakeholder meeting in Dec 2019 to take stock of evidence on immunogenicity, safety and efficacy of vaccines in pregnant women and support the development of a WHO guidance on ethical considerations on the inclusion of pregnant and lactating women in vaccine research (3) Finalizing the piloting of the WHO Economic Analysis Value Chain of Seasonal Flu Vaccination Programme in South Africa to inform on costs of vaccinating pregnant women in a Middle Income Country context; (4) finalizing a literature review assessing possible links of vaccine confidence/hesitancy and uptake in pregnant women and/or health workers.
Measles	SAGE noted that there is a need to address the substantial information gap on the role of factors such blunting and maternal immunity in infants aged <6 months, and the impact of vaccination <6 months of age on subsequent MCV doses.	Oct 2017	ongoing	This is an information gap and research is needed. The SAGE WG is working to prioritize research areas in order to increase interest of donors to fund and of research institutions to carry out the needed research
Measles	SAGE requested feedback on the utility of the M&R immunity gap guidance.	Oct 2018	Ongoing	Assessments are ongoing and feedback to SAGE will be provided as soon as available.
Measles	SAGE recommended that the most expeditious clinical development and regulatory pathway to licensure of measles containing vaccines (MCV) micro-array patch (MAP) be determined, and that barriers to the development, licensure, and use of MAPs for measles and rubella vaccine delivery be identified and addressed urgently.	Oct 2016	Ongoing	A Measles and Rubella vaccine(MR) / micro-array patch (MAP) Working Group (WG) was set up and has had five conference calls. A face to face consultation with the MR-MAP WG, vaccine manufacturers, MAP developers and other stakeholders took place in April 2018 and the outcomes and recommendations will be shared with SAGE (report to be published in Q2 2019). The MR-MAP Target Product Profile (TPP) has been posted for public consultation until end of Jan 2019 and will be finalized shortly thereafter. A background paper on the applicability of MAPs to LMICs has been accepted by the journal Vaccine.

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Measles	SAGE stressed that the accumulation of susceptible persons at both the national and subnational level should continue to be monitored to identify and address immunity gaps. SAGE requested that the Measles and Rubella Working Group refine the recommendations as to when follow-up SIAs should be conducted.	Oct 2016	Ongoing	The updated measles position paper (published May 2017) stresses the importance of monitoring the accumulation of susceptible persons at both the national and subnational level to identify and address the immunity gaps. The SAGE MR Working Group is looking at refining recommendations as to when follow up supplementary immunization activities (SIAs) should be conducted. Initial modeling results and data analyses were discussed at the SAGE WG meeting in June 2017 and again additional findings discussed in July 2018. The results of this work were presented to the IVAR-AC. IVIR_AC have created a sub working group that would continue to review the modelling work and provide feedback to the whole of the IVIR-AC. Additional work is needed to validate the models and revise the recommendations. This work is ongoing and will be presented to SAGE in 2020.
Measles rubella investment case	SAGE requests update on measles rubella investment case as per recommendations from April 2018 meeting	Apr 2018	Ongoing	This is in response to a request in a WHA resolution 2017 to bring this back to WHA 2020. The draft concept paper of the feasibility of measles and rubella eradication was presented at the October 2018 SAGE. IVIR-AC raised a number of concerns with the model, therefore an alternative modeling consortium was convened to redo the work under a condensed timeline. The modeling proposal was presented at IVIR-AC in March 2019 and the work commenced thereafter. Preliminary results were presented to the MR WG in July and will be reviewed by IVIR-AC in September prior to presentation to SAGE in October 2019.
Measles - Transmission	SAGE noted that there is a need to address the substantial information gap on transmission drivers.	Oct 2017	ongoing	This work needs to be addressed through improved surveillance and outbreak investigations in country.
Meningococcal A conjugate vaccine	SAGE recommended that countries completing mass vaccination campaigns introduce meningococcal A conjugate vaccine into the routine childhood immunization programme within 1–5 years following campaign completion, along with a one-time catch-up campaign for birth cohorts born since the initial mass vaccination and which would not be within the age range targeted by the routine immunization programme.	Oct 2014	Ongoing	The recommendations from SAGE are reflected in an update to the WHO meningococcal vaccine position paper. The updated guidance has been published in the Weekly Epidemiological Record (WER) on 20 Feb 2015: http://www.who.int/wer/2015/wer9008/en/. Eleven of the 26 meningitis belt countries have received approval from Gavi, the Vaccine Alliance for introduction of the meningococcal A conjugate vaccine into their routine immunization programme, with a single dose at 9, 15 or 18 months of age concomitantly with the administration of the first or second dose of Measles/Rubella vaccine. Among them, 10 countries have launched their introduction at the age of 9 months (n= 7 countries: Sudan, July 2016; Mali, February 2017; Central African Republic, June 2017; Chad, July 2017; Niger, October 2017; Cote d'Ivoire, August 2018; Nigeria, August 2019); or at the age of 18 months (n= 2 country: Ghana, November 2016; Gambia, April 2019); or at the age of 15 months (n= 1 country: Burkina Faso, March 2017), respectively. The remaining country intends to do so in 2020 (Togo). Another 3 countries (Benin, Eritrea, and Guinea) have applied to Gavi for an introduction in 2020-21. Other meningitis belt countries intend to apply for the introduction of the vaccine into their routine programme at the next Gavi application windows in January and May 2020, except for 4 countries located in the east end of the meningitis belt who intend to wait for the availability of affordable multivalent vaccines to consider an introduction into their routine programme while enhancing surveillance in the meantime. Further, two additional country have conducted their initial mass vaccination campaign in 2018 (Burundi) and 2019 (Kenya) while Eritrea has planned to do so in Q4-2019.
Migrant Population	Existing knowledge on reaching displaced and mobile populations - including individuals escaping conflict zones or natural disaster, economic migrants, seasonal migrants, those moving to urban centers and traditional nomadic communities - and other neglected populations should be synthesized to identify good practice, innovative approaches and gaps in knowledge.	Oct 2017	ongoing	This important item has been highlighted in the 2018 GVAP assessment report and again in the GVAP review and lessons learned report. The opportunity and modalities to collect and analyse data on this subject by WHO in collaboration with partners needs to be discussed again with IVB management according to priorities of the department.

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Missed opportunities for vaccination (MOV)	WHO should discuss and develop guidelines on how to reduce missed opportunities to vaccinate.	Oct 2014	Ongoing	During the April 2016 SAGE meeting, SAGE members were updated on the ongoing work in AFRO, PAHO and SEARO on using the missed opportunities for vaccination (MOV) strategy to facilitate the integration of immunization with other health services. Following the SAGE session, WHO received multiple requests from countries for technical assistance to implement the MOV strategy. Based on pilot MOV assessments conducted in Chad and Malawi in 2015 (PLOS ONE, 2019) and Kenya in 2016 (manuscripts in preparation), WHO published a set of updated MOV guidance documents and field tools in Q3-2017. These include: a planning guide and the assessment methodology (including the MOV protocol, sample questionnaires and generic field tools). The intervention guidebook is currently under review and will be published in Q1-2019. WHO launched a MOV web page which contains links to all the available materials for easy access to countries and is regularly updated with country experiences, MOV related documents and publications. Having strengthened the capacity of AFRO to implement the MOV strategy (MOV assessments completed in: Chad, Malawi, Burkina Faso (led by partner AMP), Kenya, DRC, Nigeria, Mozambique (led by partner VillageReach), Zimbabwe and Uganda), collaboration is ongoing with SEARO (MOV assessment completed in Timor Leste 2016), EMRO (MOV assessment completed in Jordan (led by partner UNICEF) in 2017) and WPRO (MOV lite model completed in Cambodia (in collaboration with CDC) in 2017). Since March 2016, a network of partners engaged in MOV has been established to provide regular updates via teleconference on the process and outcomes of the recent country MOV assessments, share future plans and framework for implementation, exchange lessons learned, and achieve consensus on a coordination mechanism for all MOV work among all partners. The sixth partner coordination call took place in September, 2018. WHO priorities include supporting countries to implement and monitor actions to reduce MOV; evaluate and document the impact of these interventions on coverage and timeliness; and continue building capacity in regions and countries to support additional assessments and MOV reduction strategies. To date, WHO has provided support to AMP in Burkina Faso to implement MOV activities in 2018/2019 and are supporting a consultant in Malawi to assist the country office and MoH with MOV activities in 2018/2019. Through monitoring and evaluation, the impact of post-MOV assessment country intervention action plans will be assessed and reported back to SAGE at a future date. In December 2018 WHO published a resource guide on integration named "Working together: An integration resource guide for planning and strengthening immunization services throughout the life course". This document brings together a range of resources to provide an overview of the global policies, potential interventions and strategies related to the integration of immunization services. It also provides guidance and country examples on the integration of immunization with additional health interventions throughout the life course.
MNTE	Where feasible, the use of serosurveys to validate assessment of risk identified from other data sources should be considered to guide vaccination strategies, especially in high-risk districts. Close attention should be paid to sampling strategies and laboratory methods to ensure that results are valid and interpretable. WHO should provide guidance on: sampling methods; sample collection and testing; and analysis, interpretation and use of serosurvey data for monitoring. WHO should consider establishing reference laboratories and reference serum panels to support standardization and quality assurance of the laboratory methods used in serosurveys.	Oct 2016	Ongoing	WHO/HQ working closely with with the US CDC/Atlanta to integrate tetanus immunity assessment into the ongoing HIV serosurvey in some high-risk districts in Nigeria and in the Lymphatic Filariasis (LF) serosurvey in Cambodia. WHO/HQ is facilitating the collaboration work between CDC Offices and coutnry offices in Nigeria and Cambodia for the integration of the two aspects of serosurveys.

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MNTE	UNICEF, UNFPA, and WHO should make all efforts to secure timely supply of the available WHO prequalified TT vaccine in compact single-dose pre-filled auto-disable injection devices to facilitate vaccination of inaccessible populations by community workers. Should the supply of TT vaccine in this latter presentation be less than expected, a clear plan for prioritizing and allocating available doses should be established.	Oct 2016	Ongoing	Despite the rejection by the Gavi PPC of the proposal submitted to it to request for financial assistance to support the production and availability of compact pre-filled autodestructive device (cPAD) to increase access to the Tetanus Toxoid vaccine in remote parts of some selected countries, the use of the devises and costs were clearly included in the investment case and highlights presented to donors at the Nov 2018 recent conference in NY. BD indicated some interest in funding Uniject procurement for some of the countries. The initiative will continue to follow up with this and other donors for funds to support financing of the devise in the most difficult-to-reach parts of countries. WHO/HQ will continue to advocate with partners and donors to fund the procurement of cPAD for use to deliver TTCV in remote and hard-to-reach areas during SIAs.
MNTE	UNICEF, UNFPA, and WHO should urgently develop an MNTE investment case and resource mobilization strategy to secure predictable and timely funding support for the remaining 18 countries, if the 2020 elimination timeline is to be met.	Oct 2016	Ongoing	The investment case for the 14 countries that are yet to eliminate has been finalized, online link and hard copies shared with stakeholders. Highlights were presented to MNTE donors during a Donor conference in Nov 2018 in New York. Work is ongoing for the investment case for the countries that have eliminated, as there is the need to incorporate findings from the post-validation missions that were conducted in Algeria, Timor Leste, Cameroon and Djibouti during 2018.
MNTE	UNICEF, United Nations Population Fund (UNFPA), and WHO should support countries in securing the necessary resources to implement their national elimination plans, including procurement of Td vaccine and operational costs for SIAs.	Oct 2016	Ongoing	The first phase of the maternal and neonatal tetanus elimination (MNTE) investment case that focuses on the remaining countries yet to attain elimination (14 at the moment) has been completed and both online and hard copies disseminated to all levels. The investment case highlights the areas of resources' need, and is being used for resource mobilization, especially from partners and donors as well as domestically mobilized resources. In addition, WHO/HQ is working closely with UNICEF/HQ to ensure that country tetanus toxoid (TT) supplemental immunization activities (SIAs) plans submitted are timely and adequately funded. Country SIAs plans were recently received from Central Africa Republic, Guinee, Nigeria and South Sudan to conduct rounds of TT SIAs in 2019. Disbursement of funds by UNICEF/HQ has been done for Guinee, Nigeria and South Sudan, while plan for Central African Republic is being reviewed.
MNTE	UNICEF, UNFPA and WHO should work with countries to generate and sustain political commitment to maintaining elimination of MNT, in order to guard against complacency once a country has been declared to have achieved elimination.	Oct 2016	Ongoing	As part of efforts to generate and sustain political commitments to sustaining elimination, a regional workshop was conducted in Aug 2018 for 19 countries in the African region including those that have already eliminated maternal and neonatal tetanus (MNT), to develop their sustainability plan. Similar workshops will be conducted in other regions in 2019, immediately aftet the Global maternal and neonatal tetanus elimination (MNTE) sustainability guideline is finalized and disseminated to countries. Post-validation surveys, which were commenced in 2018 will continue in priority countries in 2019, as part of efforts to sustain MNTE. All opportunities including the Regional Immunization Technical Advisory Group (RITAG) meetings and Immunization Managers' meetings are being utilized to advocate for efforts by countries to sustain their MNTE status. Update on the status of implementation of the AFR RITAG recommendations were presented at the annual meeting of the AFR RITAG in January 2019. Official announcement of MNT elimination in Kenya was made in a high profile event involving key country stakeholder with wide media coverage. A joint WHO/UNICEF HQ assessment and planning mission to Papua New Guinea discussed MNTE progress and challenges in that country. Participants were updated on the status of MNTE in the Central & West Africa RWG meeting in March 2019. The WHO guidelines on sustaining MNTE was finalized and access link pasted on WHO website. Several countries have developed or are in the process of developing their MNTE sustainability plans, which will be mostly funded through domestic resources.

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National immunization programme management	SAGE welcomed the initiative and stressed the importance and urgency of developing guidance that can be tailored to each country's unique structure and needs. SAGE emphasized the importance of looking at functions and competencies from a health-system perspective whereby all the immunization functions are adequately addressed with competent staff, regardless of the country's health system structure. SAGE recommended sharing of experiences between countries and regions on immunization workforce planning. SAGE suggested creating tools to assist countries in different aspects of immunization human resources management including: staff turnover and rotation policies, performance evaluations, and design of training. SAGE recommended that this work be piloted in a range of countries.	Apr 2017	Ongoing	A joint meeting with the US CDC and other relevant partners (JSI, BMGF, GAVI) was conducted in November 2017, to review the competencies needed at different level of the programme. A final list of competencies needed at national level will be available by Mar, 2019. The US CDC had drafted an article on this topic for a peer-reviewed journal, which was published in February 2019 (Traicoff et al. Developing standardized competencies to strengthen immunization systems and workforce). A new menu option has been created on WHO website called 'Workforce' which will host all related document in this area of work including the framework document of staff functions and competencies.
National Immunization Technical Advisory Groups (NITAGs)	SAGE recommended that tailored guidance, tools, training, mentoring programmes and sharing of information are needed to assist NITAGs. Therefore, SAGE stressed that initiatives such as the Global NITAG Network and the NITAG Resource Centre are essential and that these would require dedicated financial and human resources. SAGE further noted that NITAG evaluations are important beyond the current process indicators and should be continued and supported by countries and partner institutions. NITAG evaluations need to focus on function, quality and integration.	Apr 2017	Ongoing	The third Global NITAG Network (GNN) meeting was successfully held from the 6th to 7th of December 2018 in Ottawa, Canada. The meeting was attended by 35 NITAG country representatives (NITAG Chair, member or secretariat) from a total of 26 countries. The next meeting is scheduled for February 24-25 2020 in Atlanta, back to back with the ACIP meeting and will be hosted by the US-CDC. A scoping exercise is on-going to revise and harmonize all training materials and develop new modules according to the gap analysis. The NITAG Resource Center is being revamped.
Non-specific effects of vaccines	SAGE requested to be updated on the finalization of statement and publication on non-specific effects (NSE) of vaccines as well as finalization of study protocols.	Oct 2018	Ongoing	Feedback received from the public consultation on the protocols has been collated. A meeting to discuss and finalize the protocols is envisaged in 2019.
PCV	SAGE proposed surveillance and research priorities to guide future policy revision, including further assessment of dosing schedules and pneumococcal outbreak epidemiology, particularly epidemics of ST1 disease.	Oct 2017	ongoing	SAGE PCV working group was convened in 2017 and presented results at October 2017 SAGE meeting. One component of this WG was to review available evidence on use of catch-up campaigns, including in the context of pneumococcal outbreaks. This will be written up in a revised WHO PCV position paper that was published in February 2019. The SAGE WG is continuing in 2019-20 to address recommendations for pneumococcal vaccine use in older children and adults. We have also launched activities to analyze available pneumococcal and meningitis surveillance data and a systematic literature review to describe known outbreaks. This and disease modeling will be used to devise a strategy for responding to pneumococcal outbreaks, since the existing data is sparse.
Polio	SAGE requested WHO to complete the guidance on identification of potentially infectious materials (including stool and respiratory specimens) into 3 groups based on likelihood of being contaminated with VDPV2 or WPV2.	Oct 2016	Ongoing	The 'Guidance to minimize risks for facilities collecting, handling or storing materials potentially infectious for polioviruses' (PIM Guidance) was published on the GPEI website in April 2018 and Global Commission for Certification of Poliomyelitis Eradication (GCC) recommended its implementation by April 2019. PIM Guidance implementation workshops were organized in all 6 Regions, and action continues to ensure the collection of facility data and compilation of national progress reports on preparations for poliovirus containment and completion of Phase I of GAPIII. (PIM surveys are complex and impact thousands of facilities globally.) The current PIM guidance addresses type 2 PV only. The Polio Containment team is currently updating the guidance to include type 3 and type 1.

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Polio	SAGE advised GPEI to accelerate implementation of the WHO Global Action Plan for containment (GAPIII) including: a) all countries completing phase I; b) regional focal points closely monitoring country activities and ensuring each country completes its inventories of facilities that hold or handle polioviruses, and destroys or commits to destroying WPV2 by end 2015 and any other type 2 containing materials including Sabin poliovirus by July 2016.	Oct 2015	Ongoing	26 countries have reported the intention to retain PV2 materials (WPV2 or OPV2/Sabin2) in 74 designated poliovirus-essential facilities (PEFs). 25 of these countries have nominated a national authority for containment (NAC). Surveys of facilities that may retain type 2 potentially infectious materials are ongoing. In addition, all countries are encouraged to include type 3 and type 1 material in their surveys in anticipation of certification of type 3 and 1 in the near future. Facilities in South Africa, Indonesia, Sweden, USA, Iran, Japan, and Republic of Korea have entered the CCS and have submitted to the Global Commission for Certification of Poliomyelitis Eradication (GCC) applications for certificates of participation (CP) in the containment certification activities. Currently, 7 CPs have been issued.
Polio	SAGE noted that the IPV supply situation is further deteriorating. Therefore, the programme should explore the possible use of devices facilitating intradermal administration (e.g. jet injectors, intradermal adapters). SAGE also requested reconsideration of terminology from fractional IPV to intradermal; explore if PEF safety monitoring can be linked to IH regulation (April 2018)	Oct 2016	Ongoing	IPV supply has further improved in Q2 2019 and all countries now have sufficient supply of IPV for routine immunization. Pre-qualification of Tropis jet needle-free injector was achieved in June 2018 and is now available for use in the polio program. First IPV campaign was carried out using Tropis in Karachi in February 2019. Discussions on change of terminology of fractional dose and IH procedures are ongoing.
Polio	SAGE urged WHO to facilitate discussions and decision-making by National Immunization Technical Advisory Groups (NITAGs) to introduce IPV intradermal fractional dose use by providing necessary technical information.	Oct 2016	Ongoing	WHO prepared the communication and technical materials to National Immunization Technical Advisory Groups (NITAGs). The WHO secretariat is advocating for the use of fractional dose IPV at both regional and country technical advisory group meetings (TAGs). In China, WHO supports sIPV manufacturers to carry out clinical trials with fsIPV for in-label use. To date, 4 countries in Asia and 2 countries in Latin America use fIPV in their routine immunization program.
Polio	The documentation for 'legacy planning' should include contributions from communities and front-line health workers on their experiences with the polio programme, what it has meant for them and how lessons learnt could further improve the routine vaccine and health programme.	Apr 2013	Ongoing	Documentation and dissemination of lessons learned from polio eradication is one of the three objectives of transition planning. Through different initiatives (e.g. GPEI History Project,Johns Hopkins Curriculum Project, Multimedia Project, documentation of polio lessons-learned at the country level) contributions of frontline workers involved in polio eradication efforts are being captured. These projects involve interviews with community leaders and front-line health workers, who made a difference in changing strategies, when stakes were high and there was need for a paradigm shift in the programme.
Polio	SAGE encouraged further engagement of WHO regional offices in regard to the polio legacy planningto ensure adequate technical support to countries.	Oct 2015	Ongoing	WHO Regional Offices from AFRO, EMRO and SEARO are an integral part of the polio transition planning exercise at the country level, providing guidance and technical support to the countries to develop their national transition plans. In many cases, Regional Offices have integrated polio transition planning into broader region-specific immunization initiatives and strategies (e.g. Addis Declaration for Immunization, Regional Immunization Technical Advisory Group recommendations, discussions at the Regional Committees). In addition, the "Strategic Action Plan on Polio Transition", which was presented to the World Health Assembly in May 2018 was prepared with substantive input from AFRO, EMRO and SEARO. The Strategic Action Plan focuses on functions that need to be sustained to keep the world polio-free, to strengthen immunization and to strengthen outbreak preparedness, detection and response capacity and the estimated costs of sustaining these functions. The Regional Offices will play an important role in the implementation of the Strategic Action Plan and its Monitoring and Evaluation Framework.
Polio	SAGE requested its Polio Working Group (WG) to provide urgent guidance on optimal management of IPV supply and mitigation of other risks in case the IPV supply is further reduced.	Oct 2015	Ongoing	The IPV supply situation is being closely monitored. An update from the August 2019 Polio Working Group meeting, will be provided during the October 2019 SAGE meeting.

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Polio	SAGE advised GPEI to develop a targeted advocacy and communication plan to engage key countries and stakeholders to ensure completion of phase I and implementation of phase II, including establishment of national containment authority and national regulation for containment of poliovirus in designated essential poliovirus facilities.	Oct 2015	Ongoing	Active, coordinated, cross-partnership engagement under GPEI is ongoing and advocacy visits to facilities and NACs are regularly occurring. In 2019 to date, 27 facilities (there are currently 74 facilities planning to retain PV2) have been visited or participated in meetings clarifying PEF requirements under GAPIII. This has resulted in multiple facilities deciding not to become PEFs. A reduction in facility numbers in Canada, USA, and the Netherlands has occurred. A meeting between the Chairs of national authorities for containment (NACs) and GCC Containment Working Group (CWG) members to discuss progress, gaps and needs with containment certification activities is planned at WHO in October 2019.
Polio	SAGE expressed concern that many children have not received IPV, not only because of the shortage but also because of poor performance of routine vaccination, especially in Africa. SAGE suggested that polio programmes and expanded programmes on immunization address the issue jointly and report possible solutions to SAGE.	Apr 2019	Ongoing	The Polio Department of WHO together with the EPI team of IVB have started to plan for strategies that would improve IPV immunization coverage. For example, after each successful polio outbreak response, the POL team will work together with the EPI team in the affected country to work on solutions for improved EPI coverage.
Preferred Product Characteristics	SAGE noted the utility of Preferred Product Characteristics (PPCs) to developers and funders, and proposed that the opportunity for input into future PPCs at an early stage for any vaccine of public health importance could be included as part of SAGE's global public health mandate.	Apr 2013	Ongoing	Since the previous update, the PPCs for HSV have been finalized and and published on the PDVAC website. A target product profile (TPP) for measles/rubella vaccine on microarray patch (MR-MAP) has also been finalized following public consultation and will be posted by the time of the October 2019 SAGE meeting.

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Regulatory	SAGE recommended that the further development of the Emergency Use Assessment and Listing procedure being developed by WHO, which would allow use of a vaccine in the context of a Public Health Emergency of International Concern, be done in close consultation with relevant regulatory authorities, including those of the affected countries.	Apr 2015	Ongoing	The Regulation and other health Technologies (RHT) aims to strengthen regulatory preparedness for public health emergencies through: • Strengthening of regulatory procedures for risk-based evaluations during public health emergencies (PHEs) • Reinforcing RHTs capacity to support regulatory preparedness for PHEs • Assist countries in adapting their regulatory requirements for PHEs and using networks for expedited assessments during PHEs The scope and activities for WHO regulatory work includes support for WHO's R&D Blueprint, development of technical guidelines and standards, Regulatory Systems Strengthening, Emergency Use Assessment and Listing (EUAL), Safety monitoring and ensuring communication and coordination with different stakeholders. RHT has mapped regulatory provisions for emergency clinical trial and marketing authorization in 40 countries In November 2017, RHT organised a tabletop exercise on regulatory preparedness in a simulated emergency setting. Several activities under the norms and standards have been implemented/planned as follows: • Publication of the Guidelines on the quality, safety and efficacy of Ebola vaccines endorsed by ECBS in May 2018 and implementation workshop is planned in 2019. • Discussion of the Guidelines of Nucleic acid based vaccines of importance for priority pathogens for PHE during the ECBS meeting October 2018. • A meeting of collaborative centers networks of vaccines for standardization of priority pathogens. Following Ebola outbreaks in DRC, RHT convened a meeting with regulators of the AVAREF in June 2018 to review and discuss key regulatory considerations to facilitate implementation of EUAL for Ebola vaccine. additional work is still ongoing. Regarding the Emergency Use Assessment and Listing (EUAL) procedure, the WHO Prequalification Team took note of recommendations made during a public consultation in May 2017 and also by SAGE and initiated revision of the EUAL. The main principles of the revision includes: • a pre-emergency phase to concentrate most of the assessment activities and allow a rapid decision when the emergency is declared and a post deployment monitoring phase • Involvement of NRAs responsible for oversight of the products and NRAs of potentially affected countries at different stages of the procedure The document was published in the WHO website for comments and disseminated to several stakeholders.Comments are under collection and will be published Q1 2019. WHO has continued working with CEPI, which support product development and CT phases 1 and 2 for vaccines for emerging pathogens, with as priorities Lassa fever, MERS and Nipah. WHO ensures liaison with CEPI via a Biostandard and Assay Working Group co-chaired by WHO and CEPI and via specific Task Forces for the 3 prioritized diseases. This work addresses in particular the need to coordinate between different donors and partners. CEPI funding should accelerate the development of reference standards and reference materials for vaccines in a two-stage approach with intern standards with fast-track development paving the way to the future adoption of WHO official standards. CEPI will also support a better coordination of the collection of clinical samples for emerging diseases, which should facilitate the development of products and standards

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Reports from other advisory committees on immunization	WHO and NIBSC should develop with other stakeholders, a business plan to assure long-term security of the development of WHO reference preparations as a global public health resource and additional efforts should be undertaken to disseminate outcomes of the committees deliberations and to explain the relevance of its work to the broader immunization community.	Nov 2006	Pending	WHO and NIBSC have been working on the plan for dissemination of the outcomes of the ECBS deliberations since the ECBS 2017 meeting. Workshops/ consultations on typhoid conjugate vaccines and RSV vaccines have been organized to explain the relevance of recently adopted WHO standards to the broader immunization community in 2018 and 2019. Publication of the articles on these topics as well as on a broader range of vaccine standards in relevant journals for immunization community is planned in 2019 and 2020.
RSV	SAGE asked for preparations to be made to support global policy-making for respiratory syncytial virus (RSV) maternal immunization as well as passive immunization with long-acting mAb. SAGE emphasized the need to link maternal immunization platform strengthening with influenza, tetanus and pertussis vaccines along with preparations for potential country introductions of RSV vaccine.	Apr 2016	Ongoing	In spring 2019, the efficacy results were made public of the phase 3 clinical trial of the Novavax RSV F protein vaccine given to women in the 3rd trimester of pregnancy. In the per protocol analysis, the primary outcome, medically significant RSV Lower Respiratory Tract Infection (LRTI) in the first 90 days of life, was not met (efficacy 39% with 97.5% confidence intervals -1 to 64%.) Efficacy was higher (though not significant) against RSV LRTI with severe hypoxemia. Of note, the vaccine efficacy was significantly higher in South Africa than the U.S., and significantly prevented all-cause LRTI out to 6 months of age. Another F-protein vaccine for maternal immunization made by Pfizer has started a phase IIb trial. Regarding long-acting RSV monoclonal antibodies for prevention, a phase IIb trial of MEDI8897 (AstraZeneca/Sanofi) was completed in summer 2019 among late premature infants, showing significant 80% efficacy against RSV LRTI hospitalization; a phase 3 trial in full term infants began in July 2019. After a second round of public comment, in October 2019 the Expert Committee on Biological Standardization (ECBS) will consider approval of “Guidelines on the quality, safety and efficacy of human RSV vaccines”. A WHO-sponsored expert consultation on whether RSV infection leads to recurrent wheeze and asthma was held in February 2019. The group concluded the current evidence is inconclusive in establishing a casual association, and more evidence is needed to demonstrate if RSV vaccines/monoclonals might prevent asthma. RSV surveillance undertaken by WHO’s Global Influenza Surveillance and Response System began phase II in 2019, adding more GAVI-eligible countries and expanding to a total of 22 countries.
Second year of life (2YL)	A recommendation was made for consideration of a platform for immunization coverage in the 2nd year of life, in view of potential necessary booster doses and opportunities to catch up with incomplete vaccination, and removing the artificial barrier often experienced after the 1st birthday.	Apr 2014	Completed	Two country case studies (Zambia, presented to SAGE in April 2016, and Senegal) (WHO, JSI) and a global landscape analysis and literature review (UNICEF) have been conducted; learnings from these as well as country demonstration projects in Ghana and Malawi (CDC) have been used to inform the draft global guidance on Establishing and strengthening immunization in the second year of life: practices for immunization beyond infancy. An advanced draft of the guidance document was shared with the Immunization Practices Advisory Committee (IPAC) in Feb 2017 and the document was circulated for a final round of review in September 2017. Advocacy and demand creation packages targeting decision makers, planners, health workers and caretakers have also been developed, in collaboration with UNICEF. The guidance document “Establishing and strengthening immunization in the second year of life: Practices for vaccination beyond infancy” has been published and is available online in English, French and Portuguese (http://www.who.int/immunization/documents/WHO_IVB_ISBN9789241513678/en/) and a companion implementation handbook was published in January 2019 and is available online in English and French (Portuguese pending) (https://www.who.int/immunization/documents/ISBN_9789241514194/en/). WHO and UNICEF are moving ahead to finalize training materials for country-level staff and for building a pool of consultants trained to identify gaps and facilitate actions needed to maximize coverage of vaccines scheduled in the second year of life.

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Smallpox vaccines	SAGE recommended that WHO initiate discussions with countries in possession of smallpox vaccine to establish mechanisms for replenishment of the WHO stockpile in case of need.	Nov 2013	Ongoing	In December 2017, WHO published the 'Operational framework for the deployment of the WHO Smallpox Vaccine Emergency Stockpile (SVES) in response to a smallpox event.' This document lays out the considerations and processes needed for countries to request vaccine in the event of a smallpox outbreak. It also describes the processes by which donors can deploy vaccine to the WHO SVES, and WHO can deploy vaccine to requesting countries. WHO continues discussion with countries for their donation and replenishment of the stockpile. The Regulation and other health Technologies RHT is developing mechanisms to ensure timely deployment in countries of smallpox vaccines through development of a procedure that provides acceptable assurance of the quality, safety and efficacy of smallpox vaccines, providing technical assistance to WHO member states in building capacities for the import, registration and emergency use of smallpox vaccine and developing the capacity in member states to monitor, oversee, the safety of the vaccines for emergency use. A procedure for assessment of smallpox vaccine was developed as well as a safety monitoring guidelines. The Pre-Emergency phase of the revised EUL, will be considered for the assessment of smallpox vaccine. WHO is also mapping regulatory provisions for emergency use of medical countermeasures. WHO is currently in conversations with two Member States for the potential donation of second-generation (ACAM-2000) and third-generation (LC16m8) smallpox vaccines to the WHO SVES
Standardization of BCG strains	SAGE requested ECBS to review and report whether manufacturers have implemented their guidelines for characterization of BCG vaccines on strain, product and batch related characteristics.	Oct 2017	ongoing	Review of the evidence for characterization of BCG strains for vaccine production is being conducted and will be reported in 2019.
Strengthening of NITAGs	SAGE requested a regular update on the number of established National Immunization Technical Advisory Groups (NITAGs).	Apr 2016	Ongoing	This information is collected via the WHO/UNICEF joint reporting form and analyzed every year. The figures are included in the GVAP secretariat report, which is made available to the SAGE DoV working group and then to SAGE. A total of 134 countries now report the existence of a NITAG and 98 report a NITAG meeting six functionality process criteria – a 20% increase over 2016. These figures are included in the global report on a yearly basis. NITAG side meetings are organized back to back to SAGE meetings. A global discussion on the NITAG indicators and monitoring the impact of NITAGs at country level is on-going.

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Supply shortages	SAGE recommended that WHO could play a key role in setting up an “Exchange Forum”, helping to collect demand information from all Member States and to enhance dialogue between countries’ demand (including anticipation of schedule evolution and new introductions) and manufacturers’ supply availability and risks.	Apr 2016	Ongoing	Concerns about ongoing shortages of vaccines persist. This has been stressed through the SAGE session on vaccine shortages held in April 2016, resolution 69.25 on "Addressing the global shortage of medicines and vaccines", the fifth objective of the Global Vaccine Action Plan (GVAP), the Middle Income Country (MIC) Strategy endorsed by SAGE in April 2015 and the 68th World Health Assembly (WHA) resolution on the GVAP in May 2015. A report on ‘Addressing the global shortage of, and access to, medicines and vaccines’ was presented to the 71st World Health Assembly in May 2018.2 As a result, WHO was requested to develop a roadmap to outline the programming of WHO’s work on access to medicines and vaccines, including activities, actions and deliverables for the period 2019-2023. Efforts on addressing supply shortages will be part of the post GVAP strategy. WHO IVB Department, in collaboration with Essential medicines and health products (EMP) and with support from Linksbridge consulting funded by the Bill & Melinda Gates Foundation and MMGH consulting, has leading a Vaccine Shortage Project over the years 2016-2017. The aim of the project was to act upon the recommendations and requests of SAGE and WHA by providing concrete proposals on WHO’s role and actions to enhance information sharing for pre-empting and managing vaccine supply shortages. While all countries can benefit from this work, particular attention is paid to countries not supported by UNICEF Supply Division, PAHO, or Gavi. To ensure that any potential solution in this space builds on existing data, knowledge and processes, a first phase of the project, the Analysis of Assets, aimed to understand the extent of information available to WHO to be able to predict, pre-empt and act upon vaccine shortages. This includes both internal and external information. This phase also aimed to understand the extent of current project/mitigation work within WHO, vaccine by vaccine. This phase has been completed and a project report is available upon request. Based on the findings from Phase 1, Phase 2 of the project was focusing on development of concrete solutions to enhance WHO’s ability to address vaccine shortages with a focus on filling current gaps in information sharing and supporting self-procuring countries. Using Bacillus Calmette–Guérin (BCG) and D&T containing vaccines to prototype solutions, an informed proposal on WHO’s functions and operating model with regards to vaccine supply/demand/price data input, market analytics, output material and distribution was developed. The proposal was successfully submitted to the Bill and Melinda Gates foundation for funding and the new project, Market Information for Access to Vaccines (MI4A) was kicked off in January 2018. Under this project, WHO commits to conduct to enhance available GLOBAL vaccine market information to enhance timely access to affordable vaccines. The work will entail: i) two global vaccine market studies per year in collaboration with Linksbridge SPC and MMGH Consulting to assess global supply, demand and pricing challenges of vaccines at risk (availability & affordability). ii) development of tools and materials for countries to improve market knowledge and enhance procurement outcomes. iii) creation of an information sharing ecosystem for enhanced information exchange among key stakeholders. iv) development of guidance and strategies for suppliers and countries aimed at enhancing access. Since 2018, MI4A conducted market studies on HPV vaccines, Meningococcal meningitis vaccines (the study focuses on short term analysis of demand and supply and an update on long term forecast will be developed later in 2019, in line with the development of the Defeating Meningitis disease control strategy). In 2019 MI4A is updating the HPV study to inform SAGE discussions and additional studies are in development on measles containing vaccines and on pneumococcal vaccines.

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Surveillance	SAGE endorsed the recommendations of the ad hoc TAG for improving the quality of the IB-VPD surveillance network and urged that the objectives of this network be more clearly defined, that collaboration with other surveillance systems and laboratory networks (i.e. the polio/measles laboratory networks) be continued, and that, where feasible, activities be linked with other programmes enhancing country capacity, including implementation of the International Health Regulations. SAGE urged greater attention to integration of data systems, which would facilitate real-time analysis and performance monitoring. SAGE also noted the opportunities for integration by building upon the enhanced capacity developed by these networks to conduct surveillance for other diseases using a similar case-definition and personnel trained in applying and adhering to rigorous surveillance protocols. Both networks should continue to share experiences with the polio surveillance network. Integration efforts must be strategically designed in ways that are logical and synergistic.	Nov 2013	Ongoing	Since 2013, significant progress has been made to strengthen the Global IB-VPD and Rotavirus Surveillance Networks through recommendations from the 2013 global strategic review and annual meetings and consultations. Over the past 7 years, we have made significant progress toward strengthening the Networks and meeting those goals; however, there has been some decline in quantity and quality of surveillance data as external support has decreased. Data management processes continue to be improved toward a more systematic approach in reporting, cleaning, analysing and interpreting data. The reference laboratories are appropriately supporting sites and network laboratory performance has been successfully monitored by the global external quality assessment program as well as quality control programmes. Sentinel site and laboratory assessments are ongoing at priority sites. The most recent complete year of data available is from 2018, and it reflects the strength of the data and the network. Network data has contributed to vaccine introduction decisions, such as choice of pneumococcal conjugate vaccine (PCV) formulation, and the surveillance networks have been used as platforms for vaccine impact evaluations, particularly for rotavirus vaccines (RV). The surveillance platform has also been leveraged to monitor other VPDs, such as typhoid using the IB-VPD surveillance sites and other enteric pathogens such as norovirus, Shigella, and ETEC using the rotavirus network (Global Pediatric Diarrhea Surveillance). Moving forward, the rapid introduction of PCV and RV by Member States now requires the surveillance networks to focus on improving baseline data for sites in non-vaccine using Member States and to ensure consistent surveillance practices to monitor impact for sites that meet inclusion criteria in vaccine-using Member States, especially for pediatric diarrhea and rotavirus. A web-based data management tool is used in one Region (AMRO/PAHO) and has great potential to improve data quality and sharing across the Network. We are discussing how to better integrate IB-VPD meningitis surveillance with existing meningococcal meningitis surveillance systems. We also continue to support sites where PCV and/or RV vaccine impact evaluations may be feasible due to sufficient pre- and post-vaccine introduction data, including using secondary data sources such as hospital administrative data. Finally, one of our main activities is to work with countries on making surveillance sustainable in the long term.

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Sustainable Development Goals	Approval of a vaccination coverage indicator under the child mortality target of the Sustainable Development Goals (SDGs) has not yet been obtained. SAGE urged WHO and countries to request an aspirational immunization indicator under the SDGs.	Apr 2016	Ongoing	Several immunization partners (Gavi, Unicef, BMGF, US-CDC, WHO, Center for Vaccine Ethics and Policy NYU) have worked together to explore possible indicators to be added to the SDGs monitoring framework in addition to the currently included ones (Target 3.8.1 Universal Health Coverage composite indicator, and the Hepatitis B control strategy, three doses of Hep B vaccine). It was agreed to propose Global Vaccine Action Plan (GVAP) G2 Indicator Coverage for all vaccines in national schedule to be included for SDGs sustainability and access to health and essential medicines & vaccines goal (3.b).1. The choice of this indicator has been validated by the SAGE Decade of Vaccine Working Group. In November 2016, at the 4th meeting of the Inter-agency and Expert Group on Sustainable Development Goal Indicators (IAEG-SDG), the new accepted immunization indicator was defined as 3.b.1 Proportion of the target population covered by all vaccines included in their national programme. WHO and UNICEF were identified as co-custodians for this indicator. The indicator definition was presented to SAGE in October and was reclassified to Tier II at IAEG-SDG meeting on 28 November. The indicator definition is: - Coverage of DTP containing vaccine (third dose): Percentage of surviving infants who received the 3 doses of diphtheria and tetanus toxoid with pertussis containing vaccine in a given year. - Coverage of Measles containing vaccine (2nd dose): Percentage of children who received two dose of measles containing vaccine according to nationally recommended schedule through routine immunization services. - Coverage of Pneumococcal conjugate vaccine (last dose in the schedule): Percentage of surviving infants who received the recommended doses of pneumococcal conjugate vaccine. - Coverage of HPV vaccine (last dose in the schedule) : Percentage of 15 years old girls received the recommended doses of HPV vaccine. This indicator aims to measure access to vaccines, including the newly available or underutilized vaccines, at the national level over the life course. Indicator was reported for DTP3, MCV2 and PCV3 in February 2018 and is part of the indicator database. https://unstats.un.org/sdgs/indicators/database

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Tuberculosis vaccines	SAGE endorsed the establishment of a WHO TB vaccine technical expert group with representation from SAGE. An annual written report on TB vaccine developments should be provided to SAGE. SAGE would be provided with two-page summaries of progress every year. TB would only be included on the agenda of SAGE when there is a meaningful development of decision from SAGE required.	Nov 2011	Ongoing	WHO IVR, with the support from an TB vaccine expert working group, with further advise from PDVAC, continues to progress its activities on new TB vaccines development. Major new developments have been recently noted in the field. M72/AS01E a GSK adjuvanted protein vaccine candidate in phase IIb evaluation in Southern Africa, being tested for prevention of pulmonary TB. Two doses of M72/AS01E administered one month apart to HIV-negative adults showing evidence of latent Mycobacterium tuberculosis infection, provided 54% protection (90% CI, 13.9 to 75.4; 95% CI, 2.9 to 78.2; P = 0.04) against pulmonary TB, over approximately two years of follow-up. The study showed favorable safety. This result constitutes a major progress and provides an unprecedented opportunity to advance the field of TB vaccine towards potential public health impact. WHO is engaging leading stakeholders aiming to define the best pathway forward for accelerated availability of an effective, affordable, new TB vaccine for public health impact. GSK will soon announce its decision on identification of a development parnter that will lead to a technology transfer to a low-cost manufacturor. WHO is sponsoring a health-economic evaluation of the full public value of new TB vaccines which will include country input. H4/IC31 is an adjuvanted recombinant protein under development by Sanofi Pasteur, SSI and Aeras. A Phase II prevention of infection study in adolescents (Phase II) showed no significant protection against infection induced by H4/IC31. In the same trial, a secondary analysis showed indication that BCG revaccination induced moderate protection against sustained infection. The Gates foundation is planning on a re-investigation of this signal in another Phase 2b study in South Africa. VPM 1002 is a recombinant BCG, originally developed by the Max Planck Institute; now licensed to the Serum Institute of India (SII) and being developed with Vakzine Projekt Management (VPM), Hannover, Germany. It is currently in Phase IIb/III trials, being compared to BCG in neonates in South Africa, as well as being tested for prevention of TB recurrence in adults in India. Discussions are ongoing about neonatal BCG comparison phase 3 study design to ensure appropriate data is generated, supporting robust policy decision on possible BCG replacement. Upon PDVAC recommendation, WHO has developed guidance on preferred product characteristics for TB vaccines. The document is now publically available through the WHO IVR website: http://www.who.int/immunization/research/development/tuberculosis/en/.
Typhoid vaccines	SAGE highlighted difficulties with the lack of typhoid disease burden data in many countries to inform vaccination strategies. SAGE requested a review of the typhoid burden methodology and estimates with disease burden expansion factors.	Apr 2019	Ongoing	WHO and US CDC (with an expert Working Group) are developing a typhoid burden and risk assessment framework as guidance for countries systematically assess the burden and risk of typhoid, to support decision-making on TCV use and other control strategies. The timeline for completion of a tool is Q3 2020. WHO plans to convene a meeting in Q1 2020, with research groups generating typhoid burden estimates and additional experts, to review the methodology and estimates on typhoid disease burden to ensure appropriate interpretation and use of the data by policymakers at all levels.
Typhoid vaccines	The Nepal and Malawi typhoid vaccine trials will finish by end of 2019. SAGE decided that a potential session on typhoid should be tabled at a meeting after these trials have concluded. Data will be highly valuable to review the current policies and provide evidences for countries having not yet decided on typhoid vaccine introduction.	Apr 2019	Ongoing	The TyVAC (Typhoid Vaccine Acceleration Consortium) studies on TCV effectiveness and immunogenicity (Nepal, Malawi, Bangladesh) are on track; preliminary data from Nepal and Malawi are expected by end of 2019. In addition other TCV evaluation studies in early use settings are ongoing (incl. routine introduction in Navi Mumbai, outbreak response campaign in Zimbabwe) and preliminary results are expected to be available by end of 2019.
Un/under-immunized children	SAGE requested that WHO quickly roll out tools so that other countries can address low coverage of vaccination.	Nov 2010	Ongoing	A range of new and updated tools are being developed on the topic of strategic communications, service quality and health worker capacity, and new documentation on 'Tailoring Immunization Programmes'TIP. All updated and new guidance and tools are available on the following page: https://www.who.int/immunization/programmes_systems/vaccine_hesitancy/en/

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Vaccine coverage	SAGE recommended that WHO support new research for biological specimen collection including rapid on-site diagnostics that could improve coverage and susceptibility estimates. Improved serological surveillance techniques could be integrated with existing population-based surveys such as DHS or MICS. These research topics should be included on the QUIVER (now IVIR-AC) agenda.	Nov 2011	Ongoing	With the support from the Bill and Melinda Gates Foundation (BMGF), a rapid diagnostic test (RDT) device and prototype sample collection device Oralight have been developed. The RDT test system is based on specimen lateral flow. The tests results can be read manually or by using a reader combined with mobile phone. The RDTs intended use is for the detection of measles specific antibodies in serum and oral fluid. The prototype showed high sensitivity and specificity (91 and 94% respectively for serum and 90 and 96% for OF). On top of that, measles virus genome could be reliably detected in the POCT strips and used for genotyping, even after prolonged storage for more than a month at 20-25°C. The added advantage was that the POCT was highly thermostable and the results showed high concordance with gold standard assay used in the Global Measles Rubella Laboratory Network (GMLRN). The assay is particularly useful in endemic settings as well as in settings near elimination of even post elimination and re-introduction. During a recent meeting of the Measles Rubella Initiative on Research and Innovation this RDT came out as one of the top research priorities. It will allow monitoring disease using effective surveillance and evaluate programmatic efforts to ensure progress. It will also aid in developing and maintaining outbreak preparedness, and respond rapidly to outbreaks and manage cases. Field studies are now in phase 2 in different epidemiological and health care settings, including countries in different phases of measles control and with different health care infrastructures (India, Uganda, Malaysia, Ghana and Cameroon) to determine the operational feasibility of using RDT in combination with serum or OF in a field setting. Currently, besides the measles IgM assay for oral fluid, capillary blood and serum, a RDT for rubella IgM is being developed. Early 2020 results of all evaluation studies should become available. Efforts are also underway for technology transfer for production of the RDTs. Currently, Public Health England still is custodian of the technology. With support of BMGF development of the rubella RDTs and start-up of commercial production with one or several manufacturers is under evaluation.
Vaccine coverage	WHO to identify appropriate methods and develop guidelines for collecting, analysing, and interpreting biomarkers for validating coverage.	Nov 2011	Ongoing	Global guidelines on conducting seroprevalence survey studies on measles and rubella to identify immunity gaps in the population have been developed (url to be provided). Understanding the population immunity against measles and rubella will support the process of verifying elimination. A working group with experts in various relevant fields, including statisticians, epidemiologists, laboratory specialists, and program experts, and several consultants contributed to the development of these guidelines. It was tested subsequently in pilot studies in two different settings (post campaign/post outbreak in Mongolia 2016 , and at elimination in Bhutan 2017 integrated with hepatitis B/C, manuscripts submitted for publication). Based on the field work, the second draft guidelines were adjusted, amended and corrected where needed. Given the various advances mainly in field of diagnostics as well as the recent publication of the WHO Manual for the Laboratory-based Surveillance of Measles, Rubella and Congenital Rubella Syndrome, a third draft was developed to align with the Manual. The guidelines will provide a tool to evaluate the immune status of a target population with guidance on statistical, project and laboratory aspects of conducting such survey.

Topic	Recommendations/Action item	Meeting Date	Status	Comments and Follow up
Vaccine coverage	SAGE recommended that WHO explore alternative survey methods to improve the precision, reduce the cost and improve the usefulness of survey results to national and local immunization programmes.	Nov 2011	Ongoing	Following a thorough review of sampling methodologies; new technologies for constructing sampling frames, supervision of field work, data collection, and analysis; and alternative content, collection, analysis, presentation and linkages with other health household surveys, WHO published, first as a working draft in 2015 and as a final document in 2018, its "Vaccination Coverage Cluster Survey Reference Manual", see http://www.who.int/immunization/documents/who_ivb_18.09/en. In addition to this Manual several accompanying tools have been produced, including a tool to facilitate standardized data analysis, "Vaccination Coverage Quality Indicators (VCQI)", a sample size calculator, and practical guidance including one that focuses on post-campaign coverage surveys and another that includes model questionnaires, model protocols, reports, etc. In 2019, a White Paper to standardize and support the generation of immunization-related survey indicators, along with model questionnaires, from any household survey was published on the EPI/WHO website. Also, collaboration with DHS and MICS, on the immunization component of those large surveys is ongoing. A research agenda related to surveys was developed and published, see: https://www.ncbi.nlm.nih.gov/pubmed/30041880 and efforts are undergoing to support research, with a lit review on recall having been published https://gatesopenresearch.org/articles/3-923 and work on the KAP module ongoing as part of the [immunization] demand hub. Finally, several capacity building activities around vaccination coverage surveys have been conducted since 2015. These have included briefings with regions and selected countries, trainings for regional focal points, consultants, statisticians and immunization program officers. The largest initiative to develop capacities on the new WHO survey recommendations was the design and successful implementation of the Survey Scholar distance-learning initiative, using an approach that is based on evidence-based adult-learning methodologies for distance learning. The first such training was done in English in 2017, and the module on survey data analysis and interpretation was repeated in mid-2018. The French version was launched in Q4 2019 and is ongoing. A community of Survey Scholar Alumni has been created and, in partnership with Gavi, activities to further develop survey consultants are underway. All WHO survey related-materials are available here: http://www.who.int/immunization/monitoring_surveillance/routine/coverage/en/index2.html
Vaccine delivery research	SAGE requested that IVIR-AC explore research studies and methods including behavioural science studies for ranking reasons behind lack of vaccine delivery and other 'barriers to access'.	Oct 2015	Ongoing	IVIR-AC reviewed methods, and encourages studies on vaccine delivery costing and financing (human papillomavirus (HPV), influenza and oral cholera vaccine (OCV)) and vaccine uptake/hesitancy. Non-specific effects (NSE) of vaccination and missed opportunities for vaccination sessions were on the IVIR-AC agenda in 2016 and 2017. Economic tools for influenza vaccines were presented at the June 2016 meeting. A malaria costing tool to help countries cost and plan RTS,S vaccine in their country will be reviewed at the Sep 2017 meeting. At the March 2018 IVIR-AC meeting a proposal was presented for a WHO Guidance document on the standardization of delivery costing of vaccines to facilitate comparison of delivery costs across vaccines and to improve the quality of these costing tools/studies. Currently a Typhoid Costing Tool is under development to help countries to plan and costs the roll out of TC vaccines. At the March 2019 IVIR-AC meeting, IVIR-AC will continue to discuss research to minimize barriers and improve coverage of vaccines currently in use.
Vaccine Hesitancy	SAGE acknowledged the necessity to develop core capacities at headquarters and regional level for gaining behavioural insights that can be applied in an integrated fashion for prevention of many communicable and non-communicable diseases, as well as vaccine hesitancy. This will require the involvement of sociologists, psychologists, anthropologists, experts in social marketing, communication experts, and specific disease and vaccine experts.	Oct 2014	Ongoing	A range of activities are now ongoing in this area. There is now 1FTE at WHO HQ focused on this area, and a number of initiatives are now scaling up, both in terms of guidance being published on the WHO Vaccine Hesitancy web page, as well as jointly coordinated initiatives with UNICEF, CDC, BMGF, and Gavi through the partner 'Demand Hub'. For WHO there is focus on three main areas of work: quality services, special risk groups, and strategic and risk communications. Cross-cutting these areas is a dedicated work stream on behavioural and social data, with the development of globally standardised qualitative and quantitative tools to support countries to better assess under-vaccination. More information about this work is available here: https://www.who.int/immunization/programmes_systems/vaccine_hesitancy/en/

Topic	Recommendations/Action item	Meeting Date	Status	Comments and Follow up
Yellow Fever	SAGE prioritized head to head non-inferiority studies of all 4 WHO prequalified Yellow Fever vaccines, as well non-inferiority studies in special populations. Of particular importance, given the consequences for international travel involving IHR requirements is the duration of protection with fractional dosing, including the potential need for revaccination. Safety and effectiveness assessments should be put in place when minimal effective doses are used.	Oct 2016	Ongoing	IVR actively promotes the research agenda, and several relevant studies are in planning or execution phase. A technical consultation was held in Nov 2017, and the report is available on WHO's website. Fractional dose non-inferiority studies for all 4 prequalified vaccines have been conducted (results pending), and fractional dose studies in infants have been launched (both Africa). Immunogenicity study in DRC 1 year data have been published showing excellent results. In June 2018, Martins et al. published 8 year follow-up immunogencity data from a YF vaccine dose finding study in military personal, with very encouraging results. Fractional dose was extensively used during 2018 campaigns in Brazil, which will allow to gather more data on programmatic aspects and safety. Nov 2019 ASTMH side meeting planned to discuss progress of fractional dose studies (pediatric, comparison between 4 PQ'ed vaccines, ID administration)

XXV TAG Meeting

Twenty-Fifth Meeting of the Technical Advisory Group (TAG) on Vaccine-preventable Diseases

9-11 July 2019

Cartagena, Colombia

TAG 2019
Technical Advisory Group on Vaccine-Preventable Diseases

PAHO Pan American Health Organization World Health Organization Americas

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Acronyms	
AEFI	Adverse Event Following Immunization
AFP	Acute flaccid paralysis
bOPV	Bivalent oral polio vaccine, type 1 and 3
CCS	Containment Certification Scheme
CDC	Centers for Disease Control and Prevention, United States
CRS	Congenital rubella syndrome
cVDPV	Circulating vaccine-derived poliovirus
cVDPV2	Type 2 circulating vaccine-derived poliovirus
cVDPV3	Type 3 circulating vaccine-derived poliovirus
DAT	Diphtheria anti-toxin
DCVMN	Developing Country Vaccine Manufacturers Network
dPEF	Designated poliovirus-essential facilities
DTP3	Diphtheria-tetanus-pertussis-containing vaccine, third dose
DTP4	Diphtheria-tetanus-pertussis-containing vaccine, fourth dose
DTaP	Diphtheria-tetanus-acellular pertussis vaccine
EIR	Electronic immunization registry
EMTCT	Elimination of mother-to-child transmission
EPI	Expanded Program on Immunization
ES	Environmental surveillance
EVM	Effective Vaccine Management
EW	Epidemiological week
EYE	Eliminating Yellow fever Epidemics
GACVS	Global Advisory Committee on Vaccine Safety
GAPIII	WHO Global Action Plan to minimize poliovirus facility-associated risk after type-specific eradication of wild polioviruses and sequential cessation of oral polio vaccine use
GCC	Global Certification Commission
GNN	Global NITAG Network
GPEI	Global Polio Eradication Initiative
GVAP	Global Vaccine Action Plan
HBsAg	Hepatitis B surface antigen
HBIG	Hepatitis B immunoglobulin
HBV	Hepatitis B virus
HPV	Human papillomavirus
IEC	International Expert Committee for Documenting and Verifying Measles, Rubella and Congenital Rubella Syndrome Elimination in the Americas
IgG	Immunoglobulin G
IPD	Invasive pneumococcal disease
IPV	Inactivated poliovirus vaccine

iVDPV	Immunodeficiency-related vaccine-derived poliovirus
JRF	PAHO-WHO/UNICEF joint reporting form
LAC	Latin American and the Caribbean
MeaNS	Measles Nucleotides Surveillance database
MI4A	Market for Information for Access to Vaccines initiative
mL	Milliliter
MMR	Measles-mumps-rubella vaccine
MMR2	Measles-mumps-rubella vaccine, second dose
MNI	Maternal and neonatal immunization
mOPV2	Monovalent oral polio vaccine, type 2
MR	Measles and rubella vaccine
MR2	Measles and rubella vaccine, second dose
NAC	National Authority for Containment
NCC	National Certification Committee
NITAG	National Immunization Technical Advisory Group
OPV	Oral polio vaccine
PAHO	Pan American Health Organization
PCR	Polymerase chain reaction
PCV	Pneumococcal conjugate vaccine
PCV7	7-valent pneumococcal conjugate vaccine
PCV10	10-valent pneumococcal conjugate vaccine
PCV13	13-valent pneumococcal conjugate vaccine
PEF	Poliovirus-essential facilities
PHC	Primary health care
POSE	Polio outbreak simulation exercises
PV2	Type 2 polioviruses
RCC	Regional Certification Commission
RF	PAHO Revolving Fund for Vaccine Procurement
RIAP	Regional Immunization Action Plan
RNA	Ribonucleic acid
RTM	Remote temperature monitoring
RVC	Regional Monitoring and Re-verification Commission
SAGE	WHO Strategic Advisory Group of Experts on immunization
SDG	Sustainable Development Goals
SIA	Supplementary Immunization Activities
TAG	PAHO's Technical Advisory Group on Vaccine-preventable Diseases
Tdap	Tetanus toxoid, diphtheria toxoid and acellular pertussis vaccine
tOPV	Trivalent oral polio vaccine, type 1, 2 and 3
UHC	Universal health coverage
UNICEF	United Nations Children's Fund
VAPP	Vaccine-associate paralytic poliomyelitis

VDPV2	Vaccine-derived poliovirus, type 2
VE	Vaccine effectiveness
VPD	Vaccine-preventable diseases
VSSM	Vaccination Supplies Stock Management software
WHA	World Health Assembly
WHO	World Health Organization
WPV	Wild poliovirus
WPV1	Wild poliovirus, type 1
WPV2	Wild poliovirus, type 2
WPV3	Wild poliovirus, type 3
wVSSM	Web-based Vaccine Supplies Stock Management software
YF	Yellow fever

Introduction

The XXV Meeting of the Pan American Health Organization's Technical Advisory Group (TAG) on Vaccine-preventable Diseases kicked off on 9 July 2019 in Cartagena de Indias, Colombia. TAG Chair Peter Figueroa, PAHO/WHO Representative in Colombia Gina Tambini, PAHO Assistant Director Jarbas Barbosa, and Colombia's Minister of Health, Juan Pablo Uribe, started the meeting with remarks on the importance of the meeting to continue the Region's efforts to improve the immunization program's reach and impact at the national and regional levels, as well as to face the current challenges. Dr. Tambini mentioned that Cartagena is an appropriate setting for the meeting, both because it is Colombia's capital of Human Rights and because the country has demonstrated its commitment to immunization through one of the most updated and comprehensive vaccination schedules in the Americas. Other topics touched upon during these opening remarks included continuing to address the measles outbreaks in Brazil and Venezuela and closing immunization gaps to reach as many unvaccinated individuals as possible. Dr. Uribe expressed agreement with Dr. Tambini's comments and spoke of the history and achievements of the country's immunization program.

Update on the Regional Immunization Program

The Expanded Program on Immunization (EPI) of the Region of the Americas was created by PAHO in 1977 and has been a flagship program for the Region due to achieving the eradication, elimination and control of various vaccine-preventable diseases (VPDs) through extensive work done by PAHO's Member States. This has allowed the regional immunization program to be recognized as one of WHO's most important and successful programs in the world.

Globally, vaccination coverage has grown rapidly over the past ten years, and the number of available vaccines has significantly increased over the past 20 years. Challenges remain however, including the fact that three countries maintain endemic polio transmission; the absence of WHO measles-free regions; and 19 million children that have not completed their vaccination schedules.

Progress in the Region has been significant since the creation of the EPI 42 years ago. Comparing vaccination coverages for each of the WHO regions from 1980 to 2017, we see that progress in the Americas has been very significant, despite the presence of unvaccinated or incompletely vaccinated children. Additionally, the Region of the Americas has been the Region with the earliest and most comprehensive introduction of new vaccines (pneumococcal, rotavirus and human papillomavirus [HPV]), and the first Region to eliminate smallpox, polio, rubella, congenital rubella syndrome (CRS), measles, and neonatal tetanus. Important challenges remain, generated by population displacement, large urban growth, social crises caused by economic or political unrest, natural disasters and the high levels of inequity that characterize the Region.

Immunization activities in the Americas are coordinated and guided in accordance with the Regional Immunization Action Plan (RIAP) 2016-2020 approved by Resolution CD54.R8 in 2015 and developed under the framework of the Global Vaccine Action Plan (GVAP). A progress report of the RIAP was submitted to PAHO's Governing Bodies in 2017 and an update will be presented subsequently in 2019.

The RIAP has four Strategic Lines of Action: 1) Sustain the achievements; 2) Complete the unfinished agenda in order to prevent and control VPDs; 3) Tackle new challenges in the introduction of vaccines and assess their impact; and 4) Strengthen health services for effective vaccine administration.

This Plan consists of 13 objectives (6 strategic and 7 general) and is monitored through 29 indicators. According to information from 2018, 15 of these indicators have adequate progress, six are considered in progress and eight have less than the expected progress.

In Strategic Line of Action **1) Sustain the achievements,** some examples of progress are: The Region remains polio-free, as well as free of the endemic transmission of rubella and CRS, and Member States have maintained vaccination as one of their priorities. Unfortunately, the elimination of endemic measles in the Region was not maintained as Venezuela and Brazil reestablished endemic measles. The other 33 Member States will keep their status as "free of

endemic measles." Additionally, it is necessary to work on making individuals and communities understand the value of vaccines and their right and responsibility to demand immunizations.

Strategic Line of Action **2) Complete the unfinished agenda** has the following achievements: Haiti eliminated neonatal tetanus; we have begun to address inequity in immunization in the Region, and numerous immunization activities were conducted during Vaccination Week in the Americas (VWA) aiming at improving vaccination coverage at all levels and increasing the visibility of immunization at the regional level. However, maintaining high and homogenous vaccination coverage at all levels remains a challenge:

1) Considering coverage with the diphtheria-pertussis-tetanus containing vaccine, third dose (DTP3) as a tracer, the latter was 88% at the regional level **(figure 1)**, implying that around 1.5 million children had not been vaccinated at the age at which they should have been vaccinated (with no information available on the number of children that were subsequently vaccinated). This means that, for every 25 children in the Americas, two are left behind and one does not complete the schedule in a timely manner.

Figure 1. Vaccination Coverage by Biological in the Americas Region, 2018

2) The number of children under one year of age who have not received the DTP3 vaccine in a timely manner has increased in recent years **(figure 2**), mainly due to declining coverage in countries with large cohorts of children under one year of age, such as Argentina, Brazil, Mexico, Peru, and Venezuela. Haiti continues to have a significant number of unvaccinated children or children who complete their schedule at a later age than recommended, although their situation improved in 2018.

3) Coverage with the DTP3 vaccine analyzed by country income level (according to the World Bank) shows small differences between intermediate and high-income levels, and even though the gap has reduced in recent years, there are still major challenges for low-income countries.

4) A major challenge is not only to achieve high coverage at the national level, but to have homogeneous coverage at the subnational and local levels as well. According to 2018

data, 34% of children under one year of age in Latin America and Caribbean (LAC) live in municipalities with DTP3 coverage under 80%, that can also reach a low of 50%.

Figure 2. Populations under One Year of Age Who Have Not Been Vaccinated with the DTP3 Vaccine (in Thousands) in the Americas, 2010-2018

Significant progress has been made in Strategic Line of Action **3) Tackle new challenges in the introduction of vaccines and assess their impact,** such as the fact that 41 out of 52 (79%) countries and territories in the Region have introduced at least one new childhood vaccine (i.e. rotavirus, pneumococcal or HPV vaccines).

There is a need for more operational research to be conducted to guide immunization actions. Another gap is the absence of comprehensive strategies addressing vaccine acceptance and demand, and confidence in the safety of vaccines through advocacy, education, training, and other interventions targeting all audiences. Therefore, it is necessary to take a more holistic approach to the problem of under-vaccination, understanding the social and behavioral determinants of vaccination and involving experts in social sciences, and communication, expanding the traditional skillset of immunization program managers and staff.

With regards to Strategic Line of Action **4) Strengthen health services for effective vaccine administration**, immunization has contributed significantly to achieving the Sustainable Development Goals (SDGs) and through PAHO's Revolving Fund, the availability of vaccines has been guaranteed for most countries and territories in the Americas. Another example of progress in this area is 33 out of 52 (65%) countries and territories administer the influenza vaccine to pregnant women as a result of integration between immunization and health systems; and 14 countries (27%) have made progress in developing and/or implementing electronic immunization registries (EIRs). However, more efforts are needed to provide disadvantaged populations with timely access to vaccines, examples of these are indigenous people, migrants and populations affected by natural disasters or social crises.

Considering the four areas of the RIAP, we can see that while the immunization program has been successful thanks to the broad commitment of Member States, there are still major challenges to tackle. Some are beyond the control of immunization program, such as the political de-prioritization of immunization, program management difficulties that sometimes result from health reforms, and insufficient and delayed funding. There are also challenges directly related to the program, such as the need for appropriate strategies to ensure timely access to and availability of vaccines, information systems that allow analyses at all levels for timely decision-making, ongoing training for human resources and employing clear communication strategies at all levels.

Recommendations

- Countries should have a strong policy and legal framework to support vaccination as a human right and a social responsibility, with exemptions only for medical reasons, and with a dedicated budget for procurement and program operations, as an integral component of universal health coverage.
- Countries should promote vaccine confidence in immunization services and ensure that there is ready access to vaccination through primary health care services, as well as through a range of other opportunities, such as outreach, evening and weekend services.
- Countries should strengthen VPD surveillance and improve the monitoring of vaccination coverage and the quality and use of data to guide public health action.
- Countries need to achieve timely and complete immunization coverage in infancy and improve coverage for vaccines provided in the second year of life (e.g. DTP4, MR2 or MMR2).

Monitoring and Re-verifying Measles, Rubella and Congenital Rubella Syndrome (CRS) Elimination in the Americas

Measles Outbreaks in the Americas

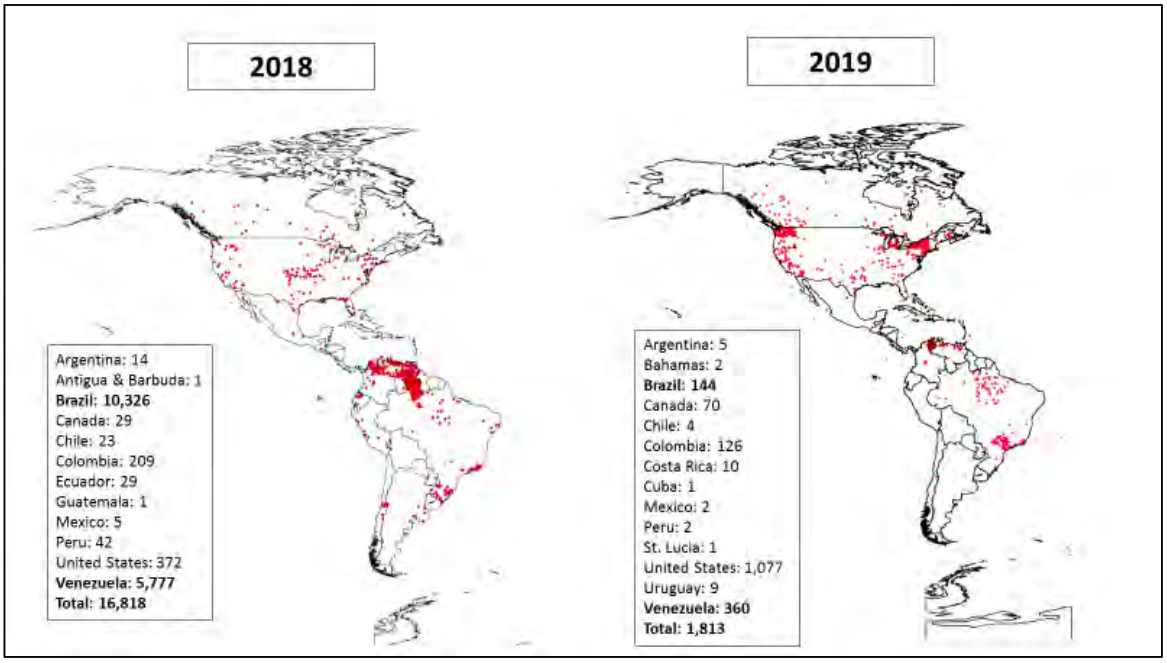
In 2018, there were 16,818 confirmed measles cases reported by 12 countries in the Region of the Americas, with a regional incidence rate of 16.8 per million population. This rate is the highest recorded during the post-elimination period. This unusual increase in cases related to low vaccination coverage in recent years in several countries. In Venezuela and Brazil, low vaccination coverage led to the reestablishment of endemic measles transmission in June 2018 and February 2019, respectively, following 12 months of continuous circulation of the measles virus (genotype D8, lineage MVi/HuluLangat.MYS/26.11) in their territories.

The rapid measles virus spread within and outside Venezuela resulted in importations and import-related cases in eight countries: Argentina (n=9 cases), Brazil (10,304 cases), Canada (n=1 case), Chile (26 cases), Colombia (335 cases), Ecuador (n=19 cases), Peru (24 cases), and the United States of the Americas (USA) (n=4 cases). Except for Colombia and Ecuador, the other six countries also reported imported cases from other regions of the world.

In 2019, there have been 1,813 measles cases in 14 countries, with an incidence rate of 1.8 per million population[1]; Brazil, Colombia, USA and Venezuela have had ongoing measles transmission since 2018, while the remaining ten countries have either interrupted transmission following isolated imported cases or are closely following up on secondary cases to ensure the rapid interruption of virus transmission **(figure 3)**.

[1] Data as of epidemiological week 25, 2019

Figure 3. Distribution of confirmed measles cases by country in the Americas, 2018-2019.



Sources: Surveillance country reports sent to PAHO/WHO's Comprehensive Family Immunization Unit, and Ministry of Popular Power of Venezuela.

During 2018 and 2019, Brazil (56%), Colombia (2%), USA (8%) and Venezuela (33%) reported the highest proportions of measles cases in the Region. The table below summarizes the main characteristics of these outbreaks. The proportions of cases by age group presented refer to two main age groups affected in each country.

Table 1. Characteristics of Measles Outbreaks Reporting the Highest Proportion of Cases in the Americas, 2018-2019*

Characteristics of Measles Outbreaks Reporting the Highest Proportion of Cases in the Americas, 2018-2019*

	Venezuela**	Brazil	Colombia	United States [a]
Total of confirmed cases	6,864	10,472	335	1,453
Ages of cases (%)	<1yr (20%); 1-4y (46%)	<1yr (17%); 15-29yr (46%)	<1yr (26%); 1-4yr (33%)	1-4yr (32%); 20-39yr (16%)
Unvaccinated [b] (%)	93%	74%	70%	89%
Affected states (%)	23/24 (95%)	13/27 (48%)	16/37 (43%)	2018: 26/50 (52%) 2019: 28/50 (56%)
Affected municipalities (%)	113/335 (34%)	99/5570 (1,6%)	34/1122 (3%)	No data
Latest onset	06/04/2019	05/25/2019	06/15/2019	06/19/2019
Genotype	D8	D8, B3	D8	D8, B3 y D4
Risk factors	Difficulty for a rapid response at the state and municipal levels; cumulative low coverage; nosocomial transmission; lack of human and logistic resources; spreading in indigenous communities	Difficulty for a rapid response at the state and municipality levels; cumulative low coverage; nosocomial transmission; lack of laboratory kits; presence of migrants in indigenous population	Migration influx flow; overload wearing of outbreak investigation; nosocomial transmission; spreading in indigenous communities	Under vaccination due to philosophical or religious beliefs; unvaccinated residents traveling internationally
Virus spreading	Quick virus spreading inside and outside of the country	Quick virus spreading to 13/27 states; Amazonas and Roraima concentrated 97% cases.	Virus spread in places with pockets of susceptible individuals in some departments; high vaccine coverage and rapid public health response has limited spread in Colombia.	Virus spread within close-knit communities due to vaccine hesitancy and other community-specific issues; high vaccine coverage and rapid public health response limited the spread in the US
Deaths	79	12	0	0

Source: ISIS, MESS, country reports to FPL-IM/PAHO *Data as of epidemiological week 26, 2019. ** Data as of 2017-2019 for Venezuela

(a) Includes all cases and outbreaks, which is defined as a chain of transmission of 3 or more cases linked in time and space.
(b) Includes unvaccinated cases, with unknown vaccination history or no data.

Despite the delicate situation of the Venezuelan health system, health authorities managed to organize a national campaign vaccinating 8.6 million children aged 6 months to 15 years old, and 460,844 individuals aged 15 years and older during the second half of 2018. This campaign that reached 97% coverage at the national level was followed by a rapid decline in measles cases. Brazil also carried out a national measles vaccination campaign, vaccinating 10.9/12 million (98%) children 1-4 years of age. In the Amazonas state, vaccination of infants aged 6 months, adolescents and young adults was additionally conducted. In Roraima, vaccination of infants was also carried out. Colombia did not conduct a national vaccination campaign, but the country has managed to successfully interrupt circulation of the virus by responding rapidly to the outbreak, stepping up efforts to find and vaccinate unvaccinated children under 5 years of age and by providing free doses of the measles and rubella vaccine to 88,819 children aged 6-11 months living in municipalities with ongoing measles outbreaks (82% coverage). The country also applied

more than 1.1 million of measles-and-rubella-containing vaccine doses to Venezuelan migrants, targeting children younger than 15 years of age.

In response to the multiple and challenging measles outbreaks in the Americas, PAHO's Comprehensive Family Immunization Unit (IM) intensified its technical cooperation by a) advocating at the highest political country level for immunization solidarity and strong outbreak response; b) mobilizing $7.4 million (USD), of which 87% were for Venezuela; c) continuing deployment of regional technical assistance and experienced consultants for outbreak response; d) conducting ten national outbreak response trainings and three sub-regional training workshops; e) strengthening in-country coordination of immunization and surveillance; and f) procuring laboratory reagents and strengthening national molecular epidemiology capacities in eight countries.

Molecular Epidemiology on Measles

Measles is an RNA virus of the *Morbillivirus* genus of the family *Paramyxoviridae*. The single-stranded negative RNA genome consists of 15,894 nucleotides which code for six structural proteins (N, P, L, M, F and H) and two non-structural proteins (C and V). Measles is probably a monotypic virus, as genetic and antigenic variations have been detected in wild-type viruses. Twenty-four measles genotypes have been identified (A, B1, B2, B3, C1, C2, D1, D2, D3, D4, D5, D6, D7, D8, D9, D10, D11, E, F, G1, G2, G3, H1 and H2). Genetic analysis of the 450 nucleotides region of the N gene has been used as a tool for molecular epidemiology to track transmission pathways, characterize outbreaks, contribute to interrupting endemic transmission and document importations.

Measles sequence data has been made available in the Measles Nucleotides Surveillance database (MeaNS, available on http://www.who-measles.org) supported by WHO. Measles virologic surveillance has been expanded through the laboratories of the global and regional laboratory network. However, in recent years, a reduction in the diversity of circulating genotypes has been observed, creating a challenge to discriminate between closely related viruses within a single genotype. The phylogenetically similar strains observed within a genotype have been designated as "named strains" that represent an epidemiologically significant viral lineage. Named lineages represent at least 50 identical sequences reported within the last two years, and from at least three different countries. Further genetic analyses allowing for a better resolution of the genetic divergences would be useful, especially to document multiple importations of the same genotype and estimates of measles virus mutation rates during long chains of virus transmission.

The Region of the Americas is experiencing a similar situation. During 2017, a total of 159 measles sequences were reported to MeaNS in four countries (Argentina, Canada, USA and Venezuela) and three measles genotypes were identified within multiple importations: B3 (52.8%), D8 (45.9%), and H1 (1.3%). Different B3 and D8 lineages were identified (five and three lineages, respectively).

In 2018, eleven countries reported a total of 460 measles sequences to MeaNS (1 in Antigua and Barbuda, 8 in Argentina, 105 in Brazil, 27 in Canada, 17 in Chile, 79 in Colombia, 16 in Ecuador, 1 in Guatemala, 2 in Mexico, 198 in the USA, and 6 in Venezuela); in 91,5% of the sequences reported, genotype D8 was identified and in 8%, genotype B3; only two sequences (0.5%) were associated with the D4 genotype. One interesting issue was related to the multiple importations of D8 genotypes and the documentation of different lineages within countries of the Region; in Argentina, two lineages; Canada, four different lineages and in the USA, six different lineages.

For the first time in the history of measles elimination in the Americas, a country in the Region had multiple importations of the same genotype and lineage. Colombia reported a total of 79 measles sequences to MeaNS in 2018; 61 of these have identical sequences (same genotype and lineage); 34/61 were identified in imported cases and 27/61 were identified in cases without history of travel. 18/79 sequences were identified with 1 nucleotide of change; 8/18 had history of recent travel and 10/18 had an unknown source.

This situation raises the concern that sequencing the N-450 gene is probably not enough to differentiate between new importations or chains of transmission. Amplifying the measles genomes of other regions can facilitate the identification of different chains of transmission. More deep sequence analysis is needed to achieve a better understanding of the mutation rate of the virus during the chains of transmission and to facilitate the identification of multiple importations of the same genotype and lineage coming from different sources.

Proposal for a Regional Framework to Monitor and Re-verify Measles and Rubella Elimination
The Regional Monitoring and Re-verification Commission (RVC) for Measles and Rubella Elimination met in June to develop consensus on the elements from the original 2011 Plan of Action for verifying elimination that should be maintained and those that need updating. The Commission agreed to the framework developed during the meeting, with substantial modifications to the original objectives, basic principles and essential criteria. The Commission also concluded that endemic countries applying for re-verification would need to document absence of transmission for more than one year, using rigorous criteria developed by the Commission. Those who did not meet the criteria would not be re-verified as free of measles.

During the TAG meeting in Colombia, TAG members emphasized the importance of using the standard and sensitive suspected measles case definition (fever and rash), as re-verification of elimination will require the review of one year of use of this case definition. TAG also reminded countries that during outbreaks, countries may consider the criteria of clinical and epidemiological links to a confirmed case for case confirmation. However, it is important that countries temporarily altering measles case definitions, such as during arbovirus outbreaks or outbreaks of other fever-and-rash-causing diseases, document their use.

Finally, countries may consider reactivating their national measles committees to monitor the sustainability of elimination, to promote the development and implementation of annual national plans for the sustainability of measles elimination, and to ensure that these reports are submitted to PAHO at the beginning of each year.

Recommendations

- TAG expresses serious concern about ongoing measles outbreaks in the Region and urges the affected countries to take urgent action to interrupt measles transmission and stop further spread of the virus.
- TAG strongly encourages the global community to set a target and develop a program for the global eradication of measles and rubella and calls on countries of the Americas and PAHO, in partnership with other Regions, to advocate for establishing this at the next meeting of the World Health Assembly in 2020.
- TAG endorses the proposed regional framework for the monitoring and re-verification of measles and rubella elimination. The standard, sensitive measles case definition should be used in all countries of the Region. Endemic countries will have to document absence of measles virus transmission for more than one year, to meet re-verification criteria.
- TAG strongly urges Member States to achieve 95% vaccination coverage levels at all administrative levels for the two recommended doses of measles and rubella vaccines and ensure high quality surveillance and rapid response. Follow-up campaigns should be conducted based on risk assessments.

Strengthening Pertussis Surveillance in the Americas

Despite the increase in vaccination coverage for DTP3 worldwide, pertussis (or whooping cough) continues to be an important cause of morbidity and mortality in children under 1 year of age and is a cause for concern in public health. The Region of the Americas is not exempt from this situation. In the last 15 years, several countries have reported the resurgence of pertussis among all population groups; on average, ten countries report outbreaks every year. Higher incidence rates have been reported in children aged less than 1 year old. The number of deaths from pertussis reported in the Region of the Americas in the last five years exceeds the number of deaths recorded by other VPDs (e.g., measles, diphtheria).

Regarding vaccination status during the last five years, regional coverage for DTP3 has not reached the regional goal of ≥95%. The heterogeneity of coverage at the subnational level presupposes the existence of pockets of unvaccinated population that could be susceptible to whooping cough. In 2018, the Region achieved 88% and 75% coverage with DTP3 and DTP4, respectively. Sixteen of the 52 countries and territories in the Americas reported coverage ≥95% for DTP3, while four of the 52 countries and territories reported coverage ≥95% for DTP4. In that same year, 4115 (27%) of the 15,170 municipalities in the Region reported coverages <80% for DTP3. It is estimated that 52% of the cohort of live births of the countries of the Region live in these municipalities.

The lack of standardization for case definitions used among countries and differences in diagnostic capacities (clinical and laboratory) makes it difficult to analyze the regional situation. For this reason, in 2014, the TAG recommended standardizing pertussis surveillance in the Region of the Americas, for which PAHO/WHO convened a working group. The group's first proposal was submitted to the TAG in 2017. However, because WHO was in the process of finalizing global guidelines for pertussis surveillance, the TAG concluded that it would consider the proposal for the regional standardization and strengthening of pertussis surveillance at its next meeting.

In September 2018, WHO published standardized global guidelines for pertussis surveillance. In February 2019, the PAHO/WHO working group held a meeting to review the regional proposal based on epidemiological surveillance standards defined by WHO. The main results of this review are as follows:

1) **Case definitions to standardize pertussis surveillance at the regional level:**

Suspected case (< 1 year of age)	Any case presenting with a cough of any duration, without other apparent cause, accompanied by at least one or more of the following symptoms: • paroxysms (fits) of coughing • inspiratory stridor • vomiting after coughing or vomiting without any other apparent cause • apnea or • Clinical suspicion of pertussis

Suspected case (≥ 1 year of age)	Any case presenting with a cough ≥2 weeks duration, or any duration in an outbreak setting, with no other likely diagnosis, accompanied by at least one or more of the following symptoms: • paroxysms (fits) of coughing • inspiratory stridor • vomiting after coughing or vomiting without any other apparent cause or • Clinician suspicion of pertussis
Laboratory-confirmed case	Any suspected case with laboratory confirmation through: • Isolation of *B. pertussis* (culture) or • Detection of the genomic sequence of *B. pertussis* by means of PCR or • Elevation of IgG for pertussis toxin in an individual ≥ 11 years of age, one year or more after administration of the last dose of vaccine.
By epidemiological link	Suspected case that has had close contact with a laboratory-confirmed case (or with a case confirmed by epidemiological link in outbreak situations) in the three weeks prior to the onset of cough
Probable case	A suspected case that does not meet the confirmation criteria nor the discarded criterion.
Discarded case	Suspected case in which another diagnosis was documented
In outbreak situations	The definition of a suspected case be modified to include cough of any duration. In case of an outbreak, samples should be collected only from the first 3-10 cases to confirm the outbreak.

2) Indicators to assess the quality of pertussis surveillance:

Indicator	Goal	Numerator/denominator
% cases with adequate investigation* (only applies if the country investigates cases) *Adequate investigation includes: completed investigation form, sample collection, line listing of close contacts. This applies in small outbreaks. If any of the above is not carried out, the investigation is considered inadequate.	At least 80%	# of suspected cases with adequate investigation / # of suspected cases x 100 (for a given period)
% cases investigated within 48 hours	At least 80%	# of suspected cases with investigation initiated within 48 hours of notification/# of suspected cases x 100 (for a given period)
% cases with at least one laboratory sample collected	At least 80%	# of suspected cases with sample collected /# of suspected cases x 100 (for a given period)

Indicator	Goal	Numerator/denominator
Respiratory sample at any age, or blood sample for children ≥11 years		
% samples received in the laboratory within two days of collection	At least 80%	# of specimens received in the laboratory within two days of collection/# of specimens collected x 100 (for a given period)
% of laboratory results reported in a timely manner Timely manner means: PCR: 2 days; Culture: 7 days; Serology (Pending) of receipt	At least 80%	# of laboratory results reported in a timely manner/# of specimens collected x 100 (for a given period)

Recommendations

- TAG urges Member States to achieve pertussis vaccination coverage levels ≥95% in all children <1 year. Full coverage with DTP4 vaccine is essential and should be monitored.
- TAG reiterates its previous recommendation on using whole cell pertussis vaccines for the primary infant vaccination series and on initiating vaccination schedules at 6 weeks of age in outbreak situations.
- TAG endorses PAHO´s revised guidelines for pertussis surveillance and urges countries to implement surveillance and improve the diagnostic capacity of the laboratory. This will strengthen the reporting and characterization of pertussis outbreaks in the Region. TAG urges countries to implement special surveillance among hospitalized children under one year of age.

Maternal Pertussis Immunization

Current Landscape of Maternal Immunization in the Americas

Maternal immunization is a promising strategy to reduce infectious-disease-related morbidity and mortality during the first weeks of life. One of the goals of PAHO's Regional Immunization Action Plan (RIAP) is establishing and strengthening maternal and neonatal immunization (MNI) platforms in the context of enhancing health services for effective vaccine administration. The Region has made important achievements such as CRS elimination in 2015 and maternal and neonatal tetanus elimination in 2017.

PAHO's TAG has previously recommended the use of the tetanus-containing vaccine, influenza vaccine and acellular pertussis-containing vaccine (the latter only in the case of outbreaks) among pregnant women. Currently, 32 of the 52 countries and territories of the Americas recommend the tetanus-containing vaccine for women at childbearing age, 34 countries recommend vaccination of pregnant women against influenza and 16 countries recommend the administration of the acellular pertussis-containing vaccine (tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine [Tdap]) in every pregnancy.

Aiming to generate evidence and document lessons about maternal immunization in Latin America, PAHO constituted the Maternal and Neonatal Immunization Group in 2016. A mixed-methods study with the objectives of understanding the state of MNI policies, strategies and practices in the capital cities of five countries (Argentina, Brazil, Honduras, Mexico and Peru) in Latin America, and describing the knowledge and perceptions of pregnant women and health workers regarding MNI has been recently completed. The knowledge gained should enable the Region to advance the use of recommended maternal and neonatal vaccines, and the introduction of future maternal vaccines such as respiratory syncytial virus and group B streptococcus vaccines that will significantly decrease neonatal morbidity and mortality.

Maternal Pertussis Immunization

Pertussis is an endemic and cyclical disease, with peaks occurring at two- to five-year intervals. The main objective of pertussis vaccination strategies is to reduce disease incidence and severe outcomes (defined as hospitalization and deaths) from pertussis infection among infants less than 12 months of age. The reemergence of pertussis has been reported in the Region with a higher incidence rate in this age group, representing one of each three reported cases.

In July 2014, the TAG reviewed the topic and recommended that the response to outbreaks of whooping cough should include: ''lowering the age for initiating vaccination to 6 weeks and vaccinating pregnant women only in areas affected by the outbreaks." By then, it was considered that there was not enough evidence for TAG to recommend routine vaccination of pregnant women.

In 2015, a revised position paper on the pertussis vaccine by WHO's SAGE incorporated evidence on the use of additional pertussis vaccination strategies for prevention of early infant mortality. In relation to vaccination during pregnancy, it was recommended that, ''Vaccination of pregnant

women is likely to be the most cost-effective additional strategy for preventing disease in infants too young to be vaccinated and appears to be more effective and favorable than cocooning. National programs may consider the vaccination of pregnant women with 1 dose of Tdap (in the 2nd or 3rd trimester and preferably at least 15 days before the end of pregnancy) as a strategy additional to routine primary infant pertussis vaccination in countries or settings with high or increasing infant morbidity/mortality from pertussis (…)''

Ever since, new evidence on Tdap administration during pregnancy regarding safety, immunogenicity, effectiveness, effect on infant immunity, cost-effectiveness and programmatic considerations has become available. Recent reviews from Gkentzi et al, 2017; Brophy et al, 2018; and Campbell et al, 2019 consistently indicate that maternal immunization with the acellular pertussis-containing vaccine, such as Tdap in pregnancy is safe. No significant safety issues have been detected and no increased risk of serious adverse pregnancy, maternal or infant events have been reported in countries currently offering Tdap vaccine for immunization in pregnancy. Regarding immunogenicity, post-immunization increases in antibody levels resulted in more than 90% of women achieving anti-pertussis toxin levels greater than or equal to 10IU/ml one month following immunization and maternal pertussis-containing immunization during pregnancy was found to result in increased infant pertussis antibody concentrations (through efficient transplacental transfer of maternal antibodies).

The effectiveness of maternal pertussis immunization in preventing infant pertussis was first demonstrated in England, by Amirthalingam et al. In 2015, three years after introducing this strategy, vaccine effectiveness (VE) against laboratory-confirmed pertussis for infants aged <3 months was demonstrated to be over 90%. The incidence in this age group remained low despite high activity persisting in those aged one year and older and VE against deaths was estimated at 95% (95% CI, 79%-100%). In the United States, the VE estimate by Skoff et al for Tdap administered during the third trimester was 77.7% (95% CI, 48.3%-90.4%) and 90.5% (95% CI, 65.2% - 97.4%) against hospitalized cases. Other studies conducted in middle-income countries in Latin America (where infant schedules use whole cell pertussis-containing vaccines) also showed that Tdap vaccination during pregnancy is effective. In Argentina, Romanin et al observed a VE estimate of 80.7% [95% CI 52.1%-92.2%] among infants <2 months of age, and Fernandes et al in Brazil estimated a VE of 82.6% [95% CI 60.8-92.3%]) in preventing pertussis among infants <2 months of age. Maternal immunization with Tdap in pregnancy also resulted in a reduction of infant disease severity and hospitalization.

The review from Brophy et al concluded that effects of the maternal acellular pertussis-containing vaccine in pregnancy on decreasing the infant's immunological response after the first doses of the primary vaccine schedule (blunting) have been observed. The clinical significance of these findings is uncertain, and to date there is no evidence of an increased risk of pertussis in infants aged 3-11 months in the United Kingdom and United States. In addition, in the majority of studies, following the receipt of the four DTaP doses with the fourth dose after 15 months of age, statistically significant differences in antibody levels and avidity were not observed between infants whose mothers received the Tdap vaccine in pregnancy and those whose mothers did not receive the Tdap vaccine in pregnancy.

A 2014 systematic review conducted by Rivero-Santana et al in several high income countries examined the cost-effectiveness of different pertussis vaccination strategies and showed that vaccination of pregnant women was the most cost-effective strategy and more effective than cocooning. Most recently, cost-effectiveness studies conducted in low- and middle-income countries have demonstrated similar results.

There is now an increasing body of evidence to support the safety, immunogenicity and effectiveness of maternal pertussis immunization and to support a recommendation for Tdap vaccination in each pregnancy, irrespective of previous Tdap immunization history or the interval between pregnancies (given the rapid waning of maternal antibody observed in studies). The existence of evidence from the Region about the impact and cost-effectiveness of Tdap vaccination during pregnancy also support this recommendation. It is noteworthy that countries considering Tdap vaccination in pregnancy should assess operational and vaccine supply issues as part of their decision-making process. Routine maternal Tdap immunization during pregnancy will provide more robust and complete protection against pertussis among infants compared to immunization in outbreak settings (or during outbreaks) only.

Recommendations

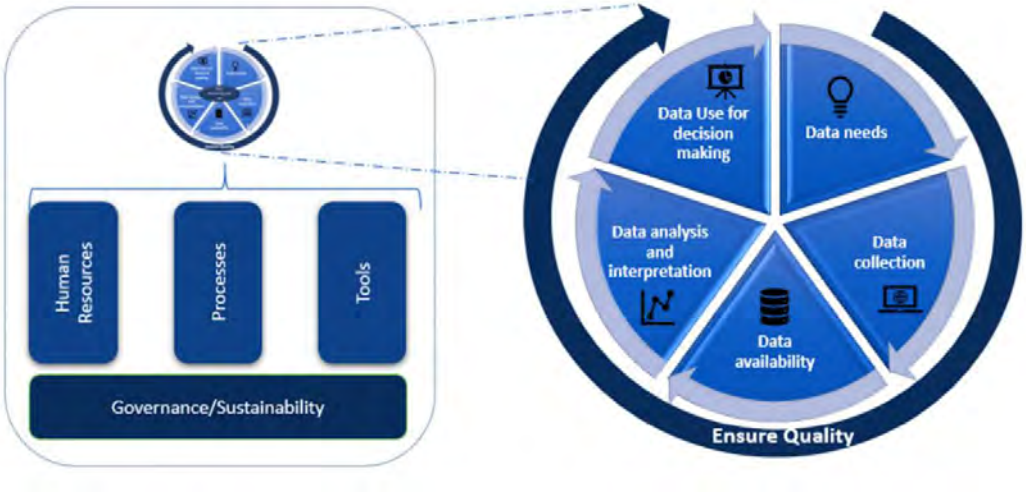
- TAG recognizes the Region's progress in maternal immunization, including pertussis and seasonal influenza vaccination. Countries must continue to monitor vaccine safety among pregnant women.
- TAG recognizes the value of vaccinating pregnant women with Tdap to protect the neonate as an effective complementary strategy to routine primary infant pertussis vaccination, particularly in countries or settings with high infant mortality from pertussis. Thus, TAG endorses the SAGE recommendation for Tdap vaccination in pregnancy, during the second or third trimesters, and at least 15 days prior to delivery. TAG also reinforces the need to sustain high vaccination coverage for DTP3 among infants and DTP4 in the second year of life.
- TAG encourages countries to monitor and report Tdap vaccine coverage among pregnant women as it is important to reach and sustain coverage of more than 50% to ensure effectiveness for this vaccination strategy.
- TAG encourages that countries whom have introduced maternal Tdap vaccination evaluate impact of the vaccine on the long-term protection of children against pertussis, particularly in countries using infant whole cell pertussis-containing vaccines.
- TAG recommends considering the vaccination of health care facility personnel with the Tdap vaccine, prioritizing maternity ward personnel and caregivers for newborns and children under 1 year of age.
- TAG encourages countries to continue documenting maternal immunization practices, associated challenges and best practices to achieve high coverage and the local impact of the strategy.

Immunization Data Quality and Analysis

Since 2002, PAHO's TAG has stressed the importance of countries strengthening data quality to guide public health action, through ongoing and systematic assessments of immunization data, and capacity-building for data analysis. To work towards that goal, TAG recommended in 2009 that countries implement and use electronic immunization registries (EIRs). During subsequent meetings, TAG expanded recommendations to include other important considerations for data quality improvement, including data collection standards, coordination with other actors, system interoperability, data monitoring and evaluation, and the use of innovative mobile health (mHealth) technologies. At the global level, SAGE recommended in 2011 that countries improve the quality and use of national and subnational coverage and surveillance data to enhance country ownership, monitoring, and accountability of immunization service delivery under the Global Vaccine Action Plan (GVAP) (2011-2020). Due to ongoing concerns pertaining to data, SAGE established a working group on the quality and use of global immunization and surveillance data in August 2017. This working group will present a topic-specific report in October 2019.

Based on work that the countries in this Region have done and using PAHO's support, existing data quality and data use frameworks, a process model was developed **(figure 4)** indicating that governance and sustainability are the foundation for data quality and use. The main pillars of data quality and use are human resources, processes and tools. These pillars support the cycle of data needs, data collection, data availability, data analysis and interpretation and finally, data use for decision-making. Each stage of the cycle is crosscut by quality and is moving towards increasing the body of knowledge and evidence of what works to increase data quality and data use, and why actions work.

Figure 4: Process Model for Data Quality and Use



The need for high quality and timely data at the local, national, regional and global levels has grown, and so has the production of information by immunization programs, such as information on new vaccines, monitoring coverage levels in new age groups and at all administrative levels, as well as information on accountability. The Region has faced these challenges by reinforcing the PAHO-WHO/UNICEF joint reporting form (JRF) as the main integrated source of information and stressing the importance of involving countries and other partners in the development of information systems at the earliest possible stages.

In countries of the Americas, data collection is conducted using a variety of paper-based tools such as home-based records, tally sheets, daily and monthly records, and EIRs. In general, the high volume of variables and high quantity of forms that staff need to complete generate an increasingly heavy workload for health workers. The development of norms and procedures and the use of EIRs are among the best practices for data collection in the Region. Ensuring integration under the umbrella of eHealth and interoperability with other systems is important for the use of digital systems.

Data must be available at all levels and to complete the data cycle, there needs to be systematic feedback to the level that is sending or originating the information. WHO and the regional offices have been working towards developing the WHO Immunization Information System (WIISE). WIISE is a collection of applications to collect, manage, analyze and disseminate worldwide immunization and VPD surveillance data reported to WHO. It will streamline processes and workflows and improve the overall governance of immunization data across the WHO system. Countries in the Americas have developed different ways to visualize data on paper (i.e. maps, monitoring charts, bulletins), as well as electronically (i.e. dashboards, web pages etc.).

The last two parts of the cycle, i.e. data analysis, interpretation, and use for decision-making, are interrelated; however, we have found a disconnect between data analysis and use, demonstrating the need to close this gap. The Region has traditionally performed aggregated

data analysis, yet the progress of countries in the Americas in implementing and using EIRs has facilitated more in-depth analyses of the individual cohort data. The use of EIRs has also prompted national teams to define new performance indicators. Moving forward, it is important to take advantage of all the functionalities that the EIR presents, including to analyze geographical information, timeliness, vaccination opportunity, etc. Ultimately, integrated analyses should guide the implementation of immunization strategies and activities that respond to the identified needs.

A recent systematic literature review conducted by PATH and PAHO entitled "Immunization Data: Evidence for Action" found evidence indicating a cyclical relationship between data quality and use. Indeed, data quality improves because of increased data use. Additionally, increased data use generates more demand for higher quality data, which in turn drives actions to improve data quality. As data quality improves, users tend to increase their trust in the data, thus reinforcing data use. We aim to create a culture of high-quality data use, whereby individuals involved in the data cycle create quality data, analyze it and generate informed decisions. Reliable data will be crucial to take the actions that keep our Region free of VPDs.

Recommendations

- TAG encourages countries to continue monitoring immunization and surveillance data quality, and to build a culture of data use for public health action at all administrative levels.
- TAG recommends that PAHO facilitate the documentation of experiences and best practices from countries that have progressed with regards to data quality and use.
- TAG encourages countries to conduct periodic evaluations of data contained in immunization registries, with guidance from PAHO as needed.

Update on the Progress towards Polio Eradication

Global Update

There has been an increase in wild poliovirus type 1 (WPV1) cases this year. As of epidemiological week (EW) 24 2019, there have been 29 cases of WPV1, compared to 12 cases during the same time in 2018. All cases are from Pakistan (75%) and Afghanistan (25%). Insecurity and access remain critical issues in these countries.

Also, there are multiple type 2 circulating vaccine-derived (cVDPV2) outbreaks occurring on the continent of Africa. The emergence of new strains of cVDPV2 in areas where mOPV2 has been used and tOPV and mOPV2 vials have been found, the recent spread of cVDPV2 into southern Nigeria, including the densely populated Lagos State, and evidence of missed transmission in Nigeria and Somalia, suggest that the situation continues to deteriorate. Insufficient coverage with IPV exacerbates the growing vulnerability on the continent to cVDPV2 transmission. Additionally, cVDPV1 outbreaks in Papua New Guinea and Indonesia and cVDPV3 in Somalia highlight gaps in population immunity due to pockets of persistently low routine immunization coverage in many parts of the world.

Major risks to global polio eradication include: growing risk of cVDPV spread, falling poliovirus type 2 immunity, weak routine immunization, low quality supplementary immunization activities (SIAs), surveillance gaps, lack of access, and population movement. To confront these challenges, the Global Polio Eradication Initiative (GPEI) has recently launched a new plan: The Polio Endgame Strategy 2019-2023. Additionally, they have published updated guidelines on polio surveillance, including polio surveillance among persons with primary immunodeficiency disorder.

Regional Update

This year marks the 25th anniversary since the International Commission for the Certification of Poliomyelitis Eradication in the Americas (ICCPE) declared the Americas free of polio. However, while recognizing and celebrating this milestone, countries of the Americas must remain vigilant. The TAG is concerned that regional coverage for the polio-3 vaccine is declining. The lowest regional polio-3 vaccine coverage since certification in 1994 was reported for the last two years (2017 and 2018). Additionally, pockets of disparity remain a concern. More than a quarter (28%) of all districts in the Region have coverage below 80%. 2018 data shows that 7 out of 10 children live in a district where coverage is below the regional standard (95%).

Currently, 33/52 of countries and territories of the Region use two or more doses of IPV, including Ecuador and Cuba, whom introduced two fractional doses of IPV following TAG's recommendation. However, 19 countries are still using only one dose of IPV. This is of concern because population immunity against type 2 polioviruses continues to decrease, as the cohort of children born after OPV2 withdrawal grows, and the potential risk of importation of cVDPV 2 rises.

Regarding surveillance, only six countries in 2018 met all three key acute flaccid paralysis (AFP) surveillance indicators (Bolivia, Cuba, Mexico, Nicaragua, Panama, Paraguay). However, the quality of AFP surveillance has not been sustained; in just the last 52 weeks, Mexico and Nicaragua have met the three key indicators. Additionally, there is lack of compliance with the standards for final classification of AFP cases.

Countries are not conducting the 60-day follow-up of AFP cases, which is a major concern, particularly in cases where an adequate stool sample was not obtained. In 2018, only 15% of cases received a 60-day (+/- 7 days) follow-up. In addition, there is late final classification of AFP cases. In fact, eight countries have AFP cases reported in 2018 that are pending final classification.

PAHO has updated the analysis of the risk of vaccine-associate paralytic poliomyelitis (VAPP) in LAC, as follow-up of the work done by Andrus et al. (1989-1991) and Landaverde et al. (1992-2011). The results show that from January 2012 to April 2016 (before the switch from tOPV to bOPV), the overall risk was estimated to be 1 case per 10.1 million doses of OPV administered. After the switch, this risk dropped to 1 case per 15.5 million doses of OPV administered. These results showed an important decrease compared to the previous risk estimations made by Andrus and Landaverde.

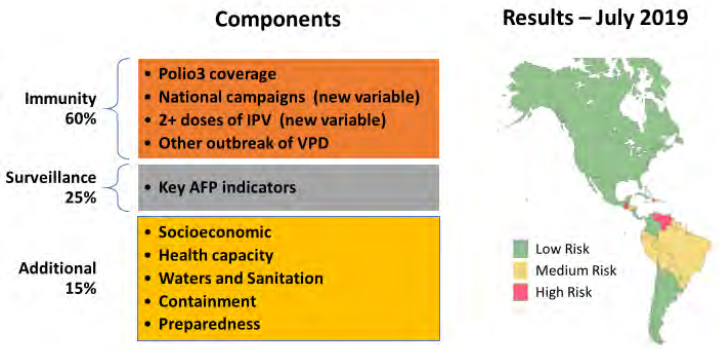
In two countries at high-risk for polio, PAHO with support from the CDC, has implemented environmental surveillance (ES) in Haiti (March 2016-current) and Guatemala (November 2018-current) to supplement AFP surveillance. Two VDPV were isolated in Guatemala (one VDPV1, one VDPV 3) through ES. These are two isolated events, and no evidence of circulating VDPV have been found to date. In the last five years, there have been three iVDPV cases notified in the Region, two from Argentina and one from Colombia. The two in Argentina received antiviral treatment with positive results. Actions have been taken according to the WHO guidelines: collection of stool samples, vaccination of family, vaccination of contacts, active case search, vaccination of the area and control and monitoring of viral excretion.

As part of the global certification process and since 2018, every country has been required to submit an Annual Report on the Documentation of Polio Eradication Status to the Regional Certification Commission (RCC). The evidence in these reports, validated by the NCCs, was used to respond to the request of the Global Certification Commission (GCC) to confirm that the Americas remain free from WPV3. All but six Caribbean countries presented their report (Antigua and Barbuda, Bahamas, Curacao, Guyana, Monserrat and St. Kitts and Nevis).

On 16 May 2019, the RCC certified that the Americas has been free of WPV3 for almost 29 years, with the last endemic case of WPV3 occurring in October 1990 in Mexico. In July 2019, the RCC updated the regional risk assessment for polio. The results show that three countries are at high-risk of having an importation or emergence of polio (Guatemala, Haiti, and Venezuela), 17 countries and territories are at medium-risk, and the remaining 24 are low-risk **(Figure 5)**.

In coordination with WHO, PAHO has updated the regional standard operating procedures for responding to a poliovirus event and outbreak. The RCC has requested that all countries have a national outbreak response plan. All countries and territories, except for Antigua and Barbuda, Curacao and Montserrat have submitted at least one version of their national plan. After each submission, PAHO conducts detailed reviews of the plan and provides recommendations to update the plan. As of July 2019, only 29 countries have conducted polio outbreak simulation exercises (POSE).

Figure 5. RCC Polio Risk Assessment



Poliovirus Containment Status

Efforts to contain poliovirus type 2 were implemented progressively in 2016 and 2017 and intensified in 2018. WHO has published guidance to minimize risks for facilities collecting, handling or storing materials potentially infectious for poliovirus.

The SAGE Polio Working Group met in February 2018 to harmonize recommendations between SAGE and GAPIII on the post-eradication polio immunization schedule and to review other issues regarding GPEI. Regarding immunizations requirements for countries with poliovirus essential facilities (PEFs), SAGE recommended that countries implement a routine immunization schedule with a minimum of two IPV doses, maintain high population immunity with ≥ 90% IPV2 coverage among infants in the area surrounding the PEFs (100 km), have outbreak plans specifying responses to containment breaches, and conduct outbreak simulation exercises.

At the 71st World Health Assembly in May 2018, WHO Member States unanimously adopted Resolution WHA71.16, urging international commitment to full implementation of GAPIII requirements. With adoption of the resolution, countries are expected to complete inventories of type 2 polioviruses (PV2), destroy unnecessary PV2 materials and advance their inventories of WPV1 and WPV3 materials in accordance with WHO guidance. In addition, countries must reduce the number of facilities designated to retain polioviruses to a minimum, appoint a national authority for containment (NAC) by the end of 2018 and formally engage designated PEFs in containment certification by no later than the end of 2019.

Poliovirus containment includes management of biorisk in laboratories, vaccine production sites, and in other facilities that retain the viruses after eradication; the initial milestone is for

containment of PV2. By August 2018, 29 countries had designated 81 facilities to retain PV2 materials; 22 of them had established a NAC.

Implementation of the GAP III in the Americas

The Region is committed to completing all goals outlined in the Polio Eradication and Endgame Strategic Plan, including the GAP III, which has been adapted for the Region as the Regional-GAP III, endorsed by PAHO's TAG in July 2015. All countries have submitted an average of four reports (range 2-6) on Phase I of GAP III: containment of WPV2/VDPV2 and Sabin2 to the RCC. Between March 2016 and October 2018, the RCC reviewed 99 updated containment reports during RCC meetings. In 2017, the RCC validated 32 switch reports, including the retrieval and destruction of all vials of tOPV.

In an October 2018 meeting, the RCC fully validated 18/23 (22 countries + 1 Caribbean Sub-region) expected reports for infectious and potentially infectious WPV2/VDPV2 materials and 16/ 23 for infectious Sabin2 materials. By October 2018, five countries in the Region had designated 20 Poliovirus Essential Facilities (dPEFs), Brazil: 1, Canada: 5, Cuba: 1, Mexico: 1, and USA: 12. Eighteen of these will retain WPV2/VDPV2 and Sabin2. In agreement with WHO's Containment Certification Scheme (CCS), the five countries with dPEFs have nominated a NAC. Six dPEFs have submitted the documentation required for the Certificate of Participation (CP) to the NAC for the United States and to the GCC, which is the first step of the global certification process. PAHO and WHO provided a second regional auditors training on April 2019, to support the CCS implementation in the five countries with dPEFs.

Regarding WPV1 and WPV3 materials, 16/23 reports have received RCC validation for inventory of facilities and countries are advancing with the elimination of all unneeded WPV1 and WPV3 materials. Resolution **"**WHA71.16 Poliomyelitis – containment of polioviruses" was presented at the 56th Directing Council and the 70th Session of the Regional Committee of WHO for the Americas in Washington, DC, 23-27 September 2018. A report about the implication and progress in the Region was presented and is available at: http://bit.ly/2krq9vY

In January 2019, PAHO Director, Dr. Carissa Etienne, sent letters to the Ministers of Health of all the countries of the Region of Americas to urge their personal engagement and leadership to fully implement Resolution 71.16 to ensure the long-term sustainability of the eradication of poliomyelitis. For countries with dPEFs (Brazil, Canada, Cuba, Mexico and USA), the letter highlights the commitment to apply strict safeguards to keep their countries and the world safe from the risk of facility-associated re-introduction of poliovirus.

The RCC has requested that all countries submit updated containment reports by August 2019, with a complete inventory for type 2 polioviruses, advances for polioviruses types 1 and 3, and destruction of all unneeded poliovirus type 1 and 3 materials. These updated country reports will be reviewed at the 11th RCC meeting planned for October 2019. All dPEFs should have formal engagement with the CCS process no later than 31 December 2019.

Recommendations

- TAG urges countries to fully implement the end game strategy for polio eradication, including maintaining high vaccination coverage, conducting active AFP surveillance, meeting poliovirus containment requirements, conducting risk assessments, developing and implementing mitigation plans and updating outbreak response plans.
- The TAG strongly recommends that the 19[2] countries that currently use only one dose of IPV, introduce a second IPV dose into their routine immunization schedules.
- In countries where VDPV is detected through environmental surveillance, such as Guatemala, TAG underlines the importance of countries maintaining high vaccination coverage and high-quality surveillance. TAG supports the decision of Guatemala to conduct a nationwide vaccination campaign using bOPV and MMR vaccines. Other high-risk countries in the Region should take appropriate measures to prevent the re-introduction of WPVs or emergence of cVDPVs.
- TAG recommends that PAHO adapt the SAGE Primary Immunodeficiency Guidelines for the Region.

[2] Belize, Bolivia, British Virgin Islands, Curaçao, Dominica, Dominican Republic, El Salvador, Grenada, Guatemala, Guyana, Haiti, Nicaragua, Paraguay, Saint Kitts and Nevis, Saint Lucia, Suriname, Trinidad and Tobago, Islands of Turks and Caicos, and Venezuela.

Update on the Yellow Fever Situation in the Americas and Yellow Fever Vaccination

Epidemiological Situation of Yellow Fever

Emerging and reemerging diseases pose a continuing threat to global and regional health security. The increasing incidence and geographical spread of arboviral infections, such as the yellow fever (YF) virus, are among the most significant public health concerns in the Americas. In this context, the PAHO/WHO Strategic Plan 2014-2019 includes the commitment to support countries in building and upgrading their surveillance and control mechanisms for diseases with a high public health impact.

The YF virus is enzootic in 13 countries of the Americas. In the last several decades, sporadic human cases or limited clusters have been reported following sylvatic exposure, mainly in Bolivia, Brazil, Colombia and Peru. However, a significant increase of human cases has been reported in Brazil since December 2016. Overall, approximately 2,200 confirmed human cases and among them 745 deaths have been reported over two subsequent transmission seasons (May-December 2016-17 and 2017-18). During the 2018-19 monitoring period (until epidemiological week 20, 2019), the number of human cases (82) has decreased by 93.7% compared to the same period in 2018 – 14 deaths have been reported and 48 epizootics confirmed. The human cases followed an epizootic wave that moved progressively from the Amazon basin towards the Atlantic coast of Brazil and reached and bypassed the outskirts of metropolitan areas. No evidence exists that transmission by *Aedes* spp., what is commonly referred to as urban yellow fever, has occurred. Rather, the situation in Brazil during the last three years highlights the risk of exposure via sylvatic vectors that residents of urban and peri-urban areas adjacent to ecological corridors face. Brazil adopted the use of fractional dose yellow fever vaccination in three states (São Paulo, Rio de Janeiro and Bahia) to respond to outbreaks and the risk of urbanization of YF. In 2019, Bolivia has reported 1 confirmed case and Peru has reported 8 human cases (3 confirmed) and 3 deaths.

Yellow Fever Vaccination

The recent YF outbreaks in the Region have highlighted the importance of strong routine YF immunization programs and vaccination campaigns to mitigate the risk of exposure along ecological corridors and prevent large urban YF outbreaks. Countries in the Americas follow PAHO's TAG recommendations to prevent and control YF in the Region, which include:

- Universal introduction of the YF vaccine in national immunization programs for children aged 1 year (and <2 years old) in countries with endemic transmission (co-administration with measles and rubella-containing vaccines, understood as administration of two vaccines at same vaccination visit),
- Preventive vaccination campaigns for at least 95% of populations aged older than 2 years living in enzootic areas during interepidemic periods,
- Vaccination campaigns in response to outbreaks or epizootics (including use of fractional doses in response to outbreaks in case of insufficient vaccine supply), and
- Vaccination of travelers to areas with a risk of YF virus transmission.

- Moreover, endemic countries are encouraged to seize the opportunity of outreach immunization activities to increase vaccination coverage among the routinely targeted groups.

In 2017, TAG endorsed the use of fractional YF vaccine doses in response to outbreaks among individuals <2 years old, in the context of limited YF vaccine availability. In 2018, TAG reiterated its endorsement and indicated that children aged <2 years old, pregnant women and individuals known to be HIV-infected should be vaccinated using a standard 0.5 ml dose, given the lack of data on immunogenicity and reactogenicity in those population groups.

All 13 endemic countries in the Region have included the YF vaccine in their national vaccination schedules with a reported coverage for 2018 in children at one year of age of 63%. According to PAHO's Revolving Fund, only half of the countries' vaccine needs have been met over the past ten years due to global supply issues, resulting in a substantial accumulation of susceptible populations/suboptimal population immunity in the Region. Based on that and preparing for the future, a tool has been developed for countries to estimate the susceptible populations in the risk areas, which was presented during a workshop in Peru in November 2018. It is expected that this information will serve as the basis for and drafting a short- and medium-term vaccination forecast plan to inform the WHO Global Strategy to Eliminate Yellow Fever Epidemics (EYE), which is a global framework for accelerated YF control for the period 2017-2026.

Co-administration of measles and rubella-containing vaccines and yellow fever vaccines
PAHO and WHO recommend that live, attenuated vaccines should be co-administered, or administered at least four weeks apart. In most countries, measles and rubella (MR) or measles, mumps and rubella (MMR) and YF vaccines are co-administered to children at 12 months of age. However, some countries, namely Argentina, Colombia, Panama and Peru, have introduced changes in their vaccination schedules, postponing administration of the YF vaccine to the age of 15 or 18 months, based mostly on the number of doses of different vaccines administered at 12-month visit and the potential interference of these two vaccines.

In 2011, a study in Brazil found a significantly decreased immunogenicity against YF, rubella, and mumps viruses when MMR and YF vaccines (full dose) were co-administered compared with administration at different visits separated by four weeks. After these results were published, WHO and PAHO's TAG urged that additional studies be conducted to obtain further evidence on the co-administration of these two vaccines and noted this study as a potential caution regarding the co-administration of these vaccines. In order to answer this research question, the Ministry of Health of Argentina, PAHO, and the Centers for Disease Control and Prevention (CDC) conducted a phase IV, open-label randomized controlled trial to determine if seroconversion rates for measles, mumps, rubella, and YF viruses after co-administration of MMR and YF (full dose) vaccines is non-inferior to seroconversion after sequential administration of the vaccines, separated by four weeks. The study was conducted at four health facilities in the Misiones Province in Argentina from 2015 to 2018 and included children aged 12-13 months.

Seroconversion rates were high for all antigens (95-98%) when the vaccines were co-administered and when they were administered individually. In the intent-to-treat analysis, co-administration was non-inferior to individual administration for all antigens. Looking at the magnitude of antibody titers, there was no significant difference between groups in the distribution of antibody titers for measles, but the titers for rubella, mumps, and YF were significantly lower when the vaccines were co-administered than when they were individually administered. However, the observed titers were substantially greater than the level needed for seroconversion in both the co-administration and individual administration groups. It is unknown whether the small, but significant, difference in titers has any impact on long-term immunity. There was no evidence of safety concerns.

These study results, along with results from two other randomized controlled trials on potential interference between YF and measles-containing vaccines, were presented to the WHO's Strategic Advisory Group of Experts (SAGE) on immunization in October 2018. In addition to the study findings, the potential programmatic implications (missed opportunities for YF vaccination, given that only one dose of YF vaccine is recommended in comparison to two for MR/MMR, which provides a second opportunity for vaccination and a potential decrease in vaccination coverage) of delaying one of these vaccines to a later vaccination visit were discussed. To highlight the potential implications, vaccine coverage figures from four countries in the Americas region that initially co-administered YF and MMR vaccines at the 12-month visit and then moved YF vaccine to the 15 or 18-month visit were shown. In all four countries, vaccination coverage dropped substantially in the year that the vaccination schedule was changed. All countries have shown some recovery in their coverage, but there is still a difference of approximately 15 percentage points in two of the countries, with smaller differences in the other two countries. The conclusion was that delaying vaccination with one of the vaccines to a later visit instead of co-administering them would probably have a far more deleterious effect on population immunity than any potential reduction in the magnitude of the immune response due to co-administration.

Considering the scientific and programmatic implications, SAGE endorsed the following recommendations: WHO maintains its current guidance stating that MR/MMR and YF vaccines should be administered at the same visit or at least four weeks apart, according to the schedule that will maximize coverage for all antigens in the national immunization schedule [*removing all qualifications/precautions about co-administration].* Additional research is needed to determine if the lower titers or antibody concentrations observed following co-administration of MR/MMR and YF vaccine will impact long-term immunity and cause secondary vaccine failures.

Recommendations

- TAG stresses the importance of achieving yellow fever vaccination coverage levels of 95% in endemic areas through optimal routine immunization and campaigns where indicated.
- In view of the available evidence supporting coadministration of MR/MMR and YF vaccines and the experience of increased drop-outs when YF vaccination is scheduled beyond 12 months of age, TAG recommends that both vaccines be given during the same

visit at 12 months. If administered separately, they should be at least four weeks apart and full coverage with both vaccines should be ensured.

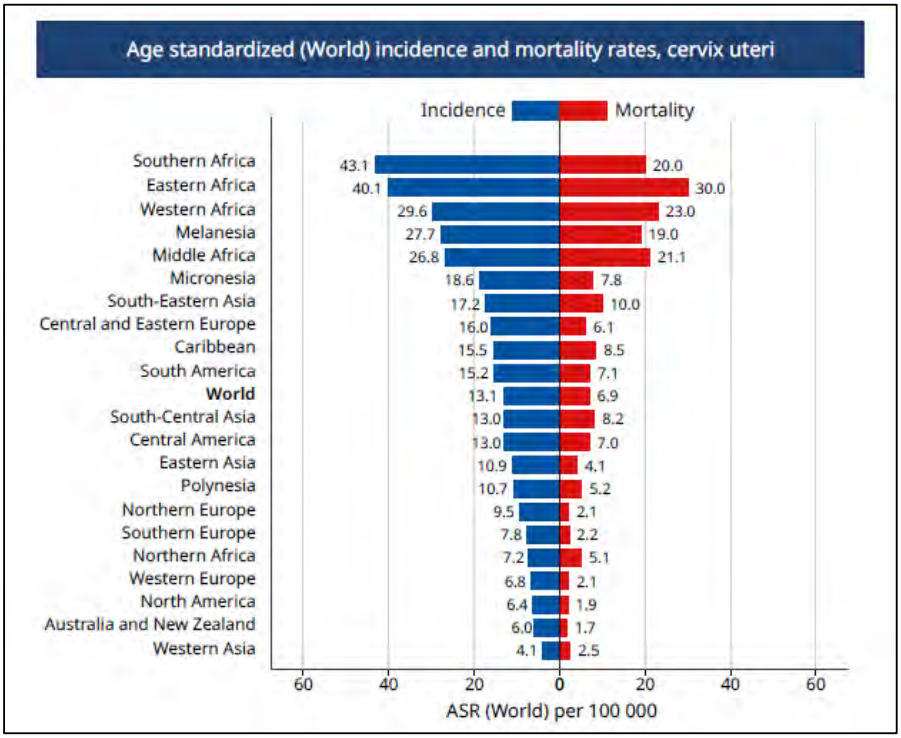
- TAG recommends that further research be conducted in the Region to examine the effect of lower antibody titers against rubella, mumps and YF viruses observed after co-administration on long-term immunity and to rule out the possibility of secondary vaccine failure.

Elimination of Cervical Cancer as a Public Health Problem

Human papillomavirus (HPV) is one of the most common infections of the reproductive tract, responsible for a variety of cancers, such as cervical cancer, and other conditions in both men and women caused by persistent infection with high-risk types of HPV. Cervical cancer can be prevented by vaccination against HPV and by screening and treatment of precancerous lesions.

In the Region of the Americas, cervical cancer is the fourth leading cause of death for women. However, it is the leading cause of cancer death among women in eleven countries in the Region (Belize, Bolivia, Dominican Republic, El Salvador, Guyana, Haiti, Honduras, Nicaragua, Paraguay, Suriname, and Venezuela), and is the second leading cause of cancer death in twelve countries in the Region (Brazil, Dominica, Ecuador, Grenada, Guatemala, Jamaica, Panama, Peru, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, and Trinidad and Tobago). An estimated 83,200 women in the Americas are diagnosed with cervical cancer each year, and 35,680 women die from the disease every year. More than half of these women (52%) are under 60 years of age. The global incidence and mortality of cervical cancer is presented in **figure 6**.

Figure 6. Global Incidence and Mortality of Cervical Cancer, the Americas



Source: The Global Cancer Observatory, May 2019

Cervical cancer screening programs have been established in almost every country in the Region since the early 1970s, and cervical cancer treatment services have been developed in almost every country, although there are significant differences in access. Access to palliative care also

remains a challenge, with only ten countries reporting palliative care services. Significant progress has been noted in disease prevention and control; however, major gaps and challenges remain in reducing incidence and mortality and in preparing the ground for the elimination of cervical cancer as a public health problem.

In 2016, with the aim of strengthening cervical cancer initiatives, the United Nations Joint Global Programme on Cervical Cancer Prevention and Control was established to provide Member States with coordinated technical cooperation through relevant United Nations programmes in order to enhance all initiatives against cervical cancer. In addition, WHO and other United Nations partners are developing a new global cervical cancer elimination strategy to be presented to the World Health Assembly in 2019. These global and regional plans, together with the Prevention and Control Plan 2018-2030 for the Region of the Americas, will contribute to the achievement of the SDGs, in particular, the following targets by 2030: *3.4:* "to reduce by one third premature mortality from non-communicable diseases;" *3.7:* "to ensure universal access to sexual and reproductive health-care services;" *3.8:* "to achieve universal health coverage;" and *5.6:* "to ensure universal access to sexual and reproductive health and reproductive rights." These strategies include HPV vaccination, screening, early treatment, and palliative care.

The Prevention and Control Plan 2018-2030 for the Americas

This plan presents guidance to Member States and the Pan American Sanitary Bureau to strengthen their capacity and establish innovative and effective evidence-based strategies to accelerate the reduction of cervical cancer incidence and related mortality. The plan sets out the following four strategic lines of action:

1. Improve the organization and governance of cervical cancer programs, information systems, and cancer registries;
2. Strengthen primary prevention through information, education, and HPV vaccination;
3. Improve cervical cancer screening and treatment of precancerous lesions through innovative strategies;
4. Improve access to cancer diagnosis, treatment, rehabilitation and palliative care services.

Regarding cervical cancer screening, almost all Member States have stated that these services are available. However, for the program to have an impact, screening coverage must reach at least 70% of the target population. In the Region of the Americas, only seven countries have reported this level of coverage. To have an impact on the burden of disease, significant improvements need to be made in order to reach the 32 million women between 30 and 49 years in the Region who must be screened.

HPV Vaccination as a Strategic Line for the Cervical Cancer Prevention and Control Plan

The first prophylactic HPV vaccine was licensed in mid-2006. Currently, there are three vaccines on the market that can be used to prevent high-risk HPV types: the bivalent vaccine, Cervarix; the quadrivalent vaccine, Gardasil; and the 9-valent vaccine, Gardasil 9. In the Region as of 2018, the PAHO Revolving Fund offers the bivalent and the quadrivalent vaccines.

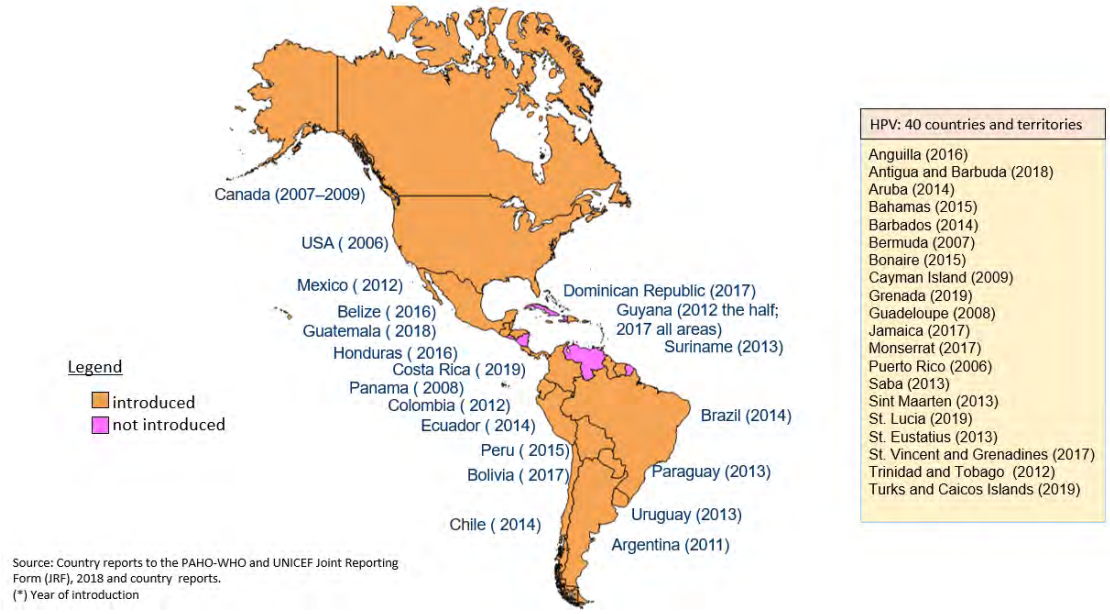
The introduction of the HPV vaccine into the EPI in the Americas began in 2006, with the United States being the first country to introduce the vaccine. By June 2019, forty countries and territories the Region of the Americas had introduced the HPV vaccine into their national immunization programs. This indicates that 89.6% of girls in the Region live in countries where the HPV vaccine has already been introduced into the national schedule. The most commonly used vaccine is the quadrivalent (31/40), followed by the bivalent (7/40); only two countries have used the 9-valent vaccine. Eight countries report vaccinating boys and girls (JRF, 2018): Antigua, Argentina, Barbados, Bermuda, Brazil, Canada, Panama and the USA. WHO data from 2018 shows that in the Region of the Americas, 69% of the countries have introduced the HPV vaccine into the EPI, followed by Europe (EURO) with 64%, Western Pacific Region (WPRO) 48%, South-East Asia Region (SEARO) 27%, Africa (AFRO) 17%, and Eastern Mediterranean Region (EMRO) 5%. An analysis of coverage from 2014 to 2016 showed that in the countries under study, 27% (14) had coverage ≥80% and 25% (13) had coverage less than 50%. In the Region of the Americas, the coverage among girls during 2018 ranged from 2% to 97%, 17% (4) had coverage ≥80% and 46% (11) had coverage less than 50%, according to 24 country reports in the JRF. Analysis of vaccination coverage has shown that in order to achieve high coverage, several vaccination strategies must be adopted and vaccination in schools must be prioritized and considered part of the "new immunization routine."

In 2017, PAHO's TAG endorsed the SAGE's recommendation, reaffirming the importance of prioritizing high coverage among cohorts of adolescent girls to ensure complete protection against HPV in girls and herd immunity in populations of boys. Countries should prioritize vaccination with two doses in girls aged 9 to 14 years with a six-month interval between doses.

Since licensure in 2006, over 270 million doses of HPV vaccines have been distributed (2016 data). The WHO Global Advisory Committee on Vaccine Safety (GACVS) released its latest review in July 2017, reasserting that the HPV vaccine is extremely safe, that vaccine-associated events are mild and moderate, with spontaneous resolution. Data analyzed by GACVS show that the risk of anaphylaxis has been characterized as approximately 1.7 cases per million doses, and syncope was established as a common anxiety or stress-related reaction to the injection.

In October 2017, PAHO held a workshop in Antigua, Guatemala, with participation from 24 countries in the Region, to share experiences on introducing the HPV vaccine as a follow-up to TAG recommendations from 2017. During this meeting, countries discussed the main lessons learned, such as the difficulty in reaching the vaccine coverage target of 80% of girls. In line with other international findings, school-based vaccination has been shown to improve coverage in the Region of the Americas. Regarding communication, it is important to have an integrated and continuous communication plan, including crisis response, and to develop messages according to each audience. As part of the commitments made at the workshop, PAHO is finalizing guidelines to standardize the calculation of HPV vaccine coverage and estimate the impact of vaccination.

Figure 7. Countries and Territories (n=40) with HPV Vaccine in the Region of the Americas, June 2019



HPV Vaccine Supply: Constrained Market Conditions for PAHO Revolving Fund

The HPV market is transitioning in 2019. WHO has prequalified three vaccines from two manufacturers: the bivalent (GSK), quadrivalent, and 9-valent (both Merck). However, GSK is planning to exit the market and the 9-valent vaccine will not be available to the Revolving Fund, leaving the quadrivalent vaccine as the sole presentation available during the period 2020-2022. This situation will persist until new suppliers from India and China (Serum Institute of India LTD "SII", Zerun Biotech and Innovax) are expected to reach WHO prequalification (or local registration). GSK recently indicated to PAHO it may return to the market in 2022.

While HPV vaccine supply is currently enough to meet yearly regional demand (3 million doses), constrained conditions will exist in 2020 beginning with the anticipated transition of national programs from the bivalent vaccine. Special attention to all elements in our regional supply chain will be necessary. Additionally, the Revolving Fund will continue to work to improve the HPV vaccine supply outlook by networking with global partners aligned with the WHO Director General's call to action on cervical cancer elimination by 2030.

Recommendations

- TAG expresses deep concern over the current challenges facing the supply of HPV vaccine and stresses the importance of meeting countries´ needs in order to reduce the burden of cervical cancer. TAG calls on the global public health community to challenge HPV vaccine manufacturers to be operationally and ethically responsive to global vaccine supply needs and align with PAHO/WHO´s call for action for elimination of cervical cancer.

- In view of the current supply challenge, all countries administering vaccines to girls and boys should prioritize vaccination of girls, achieving HPV coverage >80%. This will induce herd immunity and protect both girls and boys.
- TAG encourages countries to implement school-based HPV vaccination and communication plans to accelerate vaccine uptake and maximize vaccination impact.

Strengthening the Decision-Making Capacity of National Immunization Programs

In this section, we present an update on the progress of countries and territories of the Americas establishing National Immunization Technical Advisory Groups (NITAGs) in the Americas and on their performance, with the aim of strengthening decision-making on immunization. As an example of country progress generating valuable evidence for decision-making and sustaining investments in new/underutilized vaccines, we also present the findings of a multi-country study demonstrating the impact of pneumococcal conjugate vaccines on children mortality.

Update on the Status of NITAGs in the Americas

Ministries of health in the Americas have established NITAGs or equivalent independent groups to strengthen decision-making processes and outcomes regarding vaccines and immunization. Comprised of multidisciplinary experts, these advisory bodies provide independent, evidence-based guidance to national health authorities on immunization policy. While the roles and responsibilities of NITAGs in policy formulation vary by country, the committees are considered vital to ensuring a transparent and credible process for decision-making for a range of immunization issues, including the introduction of new vaccines, updates in existing vaccination policies, and monitoring of immunization-related progress and impact.

Both WHO and PAHO have recommended the establishment of independent NITAGs since the early 2000s. Through their endorsement of the regional adaptation of the GVAP, PAHO Member States committed to establishing functional NITAGs in at least 18 countries by 2020. By global standards, the Americas consider NITAGs to be functional if they meet the following indicators:

- Legislative or administrative basis for the advisory group,
- Formal written terms of reference,
- At least five different areas of expertise represented among core members,
- At least one meeting per year,
- Circulation of the agenda and background documents at least one week before meetings,
- Mandatory disclosure of any conflicts of interest.

In 2019, 41/44 (93%) countries/territories in the Americas that shared information with through the PAHO-WHO/UNICEF joint reporting form (JRF) reported having an active NITAG. A sub-regional TAG called the “Caribbean Immunization Technical Advisory Group” or CiTAG, was created in 2018 and advises 20 English and Dutch-speaking Caribbean countries/territories on immunization. Of the 21 active NITAGs (20 NITAGs and the CiTAG), 18 met the GVAP/RIAP indicator of good functionality, thus meeting the set RIAP target of establishing 18 functional NITAGs by 2020. Of three countries not reporting active NITAGs, one country reported that its NITAG was being created (the Dominican Republic) and another that it was being reactivated (Ecuador). Haiti was the latest country to establish a NITAG and will be holding a formal induction meeting for newly appointed members in August 2019. Two countries with active NITAGs reported not disclosing interests of NITAG members. The other indicator that affected good functionality was the inclusion of at least five main expertise areas in the core membership. While

countries have made significant efforts towards establishing clear policies and procedures for the declaration and management of interests, it remains an important challenge in the Region. Another crucial characteristic of a good NITAG that is not captured by the GVAP/RIAP indicators is the independence of its core members. Several NITAGs in the Region still include members that have direct or indirect supervisory relationships within the immunization program or are employees of ministries of health.

Experience during the last decade has shown that establishing and strengthening NITAGs is critical to improve leadership in making informed decisions about the introduction and financial sustainability of vaccines. Moreover, NITAGs increase the credibility of the government by increasing its capacity for rigorous, transparent evidence-based decision-making. NITAGs can potentially deflect pressure from narrowly focused lobbying groups, including industry, and anti-immunization groups, and allow/obligate members to abstain from decision-making on issues from which they might benefit. NITAGs also help anticipate the needs of immunization programs. For example, the NITAG in Argentina had been monitoring the epidemiological situation of meningococcal disease long before vaccine introduction was considered. In Chile, the NITAG recently examined data from national electronic immunization registries (EIRs) in response to rising concerns about vaccine hesitancy. Finally, in the event of an adverse event following immunization (AEFI) or the questioning of an existing immunization policy, NITAG support is crucial and can neutralize public backlash.

Through PAHO/WHO's technical cooperation on NITAGs in the Region, we have learned that having a solid administrative and legal basis is key to preserving NITAG activity. Moreover, defining clear communication channels between NITAG and the secretariat, as well as a work plan aligned with the needs and priorities of the immunization program, have contributed to a positive evolution of ministry of health/NITAG relations. The use of local data by leveraging existing surveillance and research platforms, and strong support from the secretariat to prepare a solid evidence base have increased ownership of the recommendations. NITAG reporting at a high political level has facilitated acceptance of recommendations by ministries of health. NITAG members' flexibility to attend ad hoc meetings has facilitated addressing pressing requests from health authorities in a timely manner.

There are many opportunities for NITAG growth in the Region, such as the expansion of expertise profiles to include additional specialties such as social sciences, health economics and civil society representation on the committee or as liaison or ex-officio members. Also, NITAGs could benefit from updating their standard operating procedures periodically to increase efficiency and transparency. NITAG secretariats that need additional support for the review and appraisal of immunization evidence may explore leveraging national capacities by collaborating with academic institutions or other government entities that could provide that expertise. Finally, written policies for the management of potential conflicts of interests are essential but should be complemented by good practices in addressing perceived interests. A good practice from the Chilean NITAG consists in declining invitations to events funded by the pharmaceutical industry to avoid perceived conflicts of interest. Members also systematically disclose the position from which they make public statements (i.e. as a NITAG member or individually).

To address the frequent problem of membership terms ending simultaneously, NITAGs could revise the membership renewal procedure so that there is enough time for a successful transition and for experience gained by NITAGs to be preserved over the years. NITAGs could also benefit from increasing visibility among peers and among the general population to strengthen confidence in immunization programs and policies. Finally, NITAGs may benefit from exchanges with other NITAGs to share technical resources, experience, and lessons learned.

In 2016, the Global NITAG Network (GNN) was launched as a global initiative to facilitate exchanges between NITAGs about their experience, processes, evidence reviews, recommendations and policy decisions. By joining the GNN, NITAGs can receive timely updates on useful global and regional resources, publications from other NITAGs, and upcoming GNN support activities. To date, nine NITAGs from the Americas including the CiTAG, have joined the network and six have attended GNN meetings. The next GNN annual meeting will be held in Atlanta, USA and NITAG participants will also be invited to the ACIP (the USA NITAG) meeting.

In response to a request from GNN members, the CDC, with PAHO/WHO and NITAG partners, developed a short, user-friendly NITAG assessment tool that examines three areas of performance: functionality, quality of work processes and outputs, and the integration of the committee into the ministry of health policy process. It is currently available in English, Spanish and French for use by NITAGs in external, peer-to-peer or self-evaluations. The tool was successfully piloted in Chile in 2018 with support from the CDC.

Using Secondary Data to Demonstrate the Impact of PCV on Children Mortality – an Innovative Approach to Generating Evidence for Decision-making

We hereafter present the findings of the study entitled "Declines in pneumonia mortality following the introduction of pneumococcal conjugate vaccines in Latin American and Caribbean countries," conducted by Lucia H. de Oliveira*, Kayoko Shioda*, Maria Tereza Valenzuela, Cara B. Janusz, Analía Rearte, Alyssa Sbarra, Joshua L. Warren, Cristiana M. Toscano, Daniel M. Weinberger, country representatives: (as group author of study team):

Pneumococcal infections, caused by *Streptococcus pneumoniae,* are one of the most important causes of disease and death among children under 5 years of age throughout the world. Currently, 143 countries globally have introduced pneumococcal conjugate vaccines (PCVs). Therefore, it is critical that their impact on disease morbidity and mortality is measured. In this study, we estimated declines in mortality due to pneumonia in ten countries in Latin America and the Caribbean (LAC) – Argentina, Brazil, Colombia, the Dominican Republic, Ecuador, Guyana, Honduras, Mexico, Nicaragua and Peru. Trends in death due to pneumonia from 2005 to 2015 were analyzed, adjusting for unrelated trends, to estimate declines in pneumonia mortality that occurred in the post-vaccine period. The analysis mostly used the synthetic control method that allows to account for the effects of confounders changing over time, and in settings where it was not possible, seasonal-trend decomposition plus principal component analysis, which first extracts smoothed trends from the control time series and uses them to adjust the outcome.

All analyses and data cleaning were performed in R (Vienna, Austria). In total, there were 73,912 deaths due to pneumonia among children aged 2-59 months during the study period. The reported incidence of death due to pneumonia per 10,000 among children aged 2-59 months in the pre-PCV period ranged from 7.8 in Argentina to 29.6 in Peru. Most countries showed some evidence of a decline in mortality due to pneumonia among children aged 2-59 months following the introduction of PCV and approximately 4500 pneumonia deaths have been averted in this age group since PCV introduction in the ten countries studied. This study has demonstrated that it is possible to evaluate PCV impact in childhood mortality in LAC countries, where routinely collected data from national mortality registries are available. The results confirm the importance of PCVs as a public health intervention, given that these vaccines are showing a great impact on child mortality.

Recommendations

- TAG commends countries and territories for their progress in establishing NITAGs and recognizes their role in strengthening evidence-based decision-making, program sustainability and promoting confidence in immunization.
- TAG stresses that NITAGs must be independent and have written policies for the declaration and management of potential conflicts of interest.
- TAG encourages Member States with established NITAGs to document their lessons learned and calls on PAHO/WHO to facilitate exchanges and peer-to-peer support between NITAGs both within the Region and globally.

Strengthening Cold and Supply Chain Operations and Vaccine Management in the Americas

Cold chain operations in the Americas were built on four pillars: training in program management, research and testing when developing refrigeration equipment for safe vaccine storage, information flow in the EPI program, and cold chain evaluations. However due to recent advancements in technology to manage the cold chain, the use of digital technologies, continuous temperature monitoring devices and software, and the use of newer refrigeration equipment have been added to the fundamental pillars of cold chain operations.

At the beginning of the 2000s, the introduction of several new and expensive vaccines, like rotavirus, and single-dose MMR, PCV, and HPV, as well as increases in the population of each country, gave ministries of health the challenge of rapidly increasing their cold chain storage capacities. This experience in the Region of the Americas provided a model for many countries in other regions to follow in planning increases in their cold chain storage capacities.

To assist ministries of health, PAHO's technical cooperation has focused on three management areas: 1) providing training courses to national immunization staff, 2) providing technical cooperation to build new cold chain facilities and/or new cold rooms, and 3) evaluating cold and supply chain operations. Together, these efforts are strengthening countries' abilities to assure that vaccines are kept potent and that no health service runs out of vaccines and related supplies.

Training

One of the elements necessary to obtain outstanding program performance is having well-trained, informed health workers and managers, who are also updated on new technologies. To this end, PAHO's Comprehensive Family Immunization Unit (IM) has completed the following work:

1) Updated the Cold Chain Module and Modules for the Use, Installation, Maintenance and Troubleshooting of Solar Refrigeration Equipment. A total of 540 persons have been trained with these training materials.

2) Conducted five international training workshops between 2012–2018 in Colombia (2), Dominican Republic, Jamaica and Nicaragua, with more than 700 health staff trained. The workshops covered topics including cold chain, supply chain, vaccine management, temperature mapping and studies to monitor temperature during vaccine distribution throughout the supply chain.

3) Fifteen courses regarding management of the supply chain and distribution of vaccines were carried out between 2010-2018 in Bermuda, Bolivia, Dominican Republic, Haiti (2) Honduras (2), Jamaica, Mexico, Nicaragua, Paraguay (2), Peru, Suriname, and Venezuela. Specifically, the stand-alone version of the Vaccination Supply Stock Management software program (VSSM) and the web-based version of the program (wVSSM) were reviewed. These events trained a total of 448 people and the courses were celebrated.

4) It is fundamental to evaluate the performance of cold and supply chain operations to strengthen the management capabilities of health staff and supervisors. IM efforts have carried out eight evaluations on VSSM and wVSSM between 2011-2018 in the Dominican Republic, Haiti, Honduras (2: VSSM and wVSSM), Jamaica, Mexico, Nicaragua and Paraguay to obtain outstanding country performance in these operations.

5) A second management tool, Effective Vaccine Management (EVM), was introduced in 2013. Training with this tool was initiated with seven courses, starting in 2013. By 2018, a total of 185 people was trained in EVM courses in five countries: Bolivia, Cuba, Guyana (2), Honduras (2), and Nicaragua.

Technical Cooperation to Build New Cold Chain Facilities and/or Cold Rooms

Member States have scaled up their cold chain operations and vaccine management with technical cooperation provided by PAHO's IM regional office. Over the last 15 years, Member States have quickly built new cold chain facilities or established new cold rooms to accommodate new vaccines for a growing population. With the introduction of PCV, rotavirus and HPV vaccines during the last two decades, Colombia, Honduras, Nicaragua, Paraguay and other countries have built new warehouses to increase vaccine storage at both national, central and sub-regional levels. These efforts have focused on expanding cold chain capacity beyond the national level, which has resulted in a decrease in the costs related to expanding cold chain storage capacities at the national level only. More importantly, having additional vaccine storage space at sub-regional levels has provided program managers with more flexibility in managing supply chain operations and responding to unplanned service level requests for additional vaccine supplies.

Evaluating Cold Chain and Supply Chain Operations

EVM is a management tool that assists managers in determining whether distribution points for supplies and vaccines are optimal to achieve their goals and avoid stock-outs at service levels. EVM evaluations identify needs and weaknesses in management operations, infrastructure gaps and supply operations. The EVM tool collects information on nine criteria to evaluate performance on these operations, aiming to document outstanding performance and conditions needed for effective performance, as well as to highlight those areas that require improvements and/or strengthening interventions to assure that these operations achieve their objectives in supporting immunization services. To date, five countries – Bolivia (2016), Guyana (2014), Haiti (2013-2018), Honduras (2015) and Nicaragua – have completed EVM evaluations. Honduras and Nicaragua achieved the highest EVM scores when compared to other countries in other regions (to date) that have carried out EVM evaluations. These EVM evaluations allowed the countries to purchase new refrigeration equipment, in addition to using new temperature monitoring devices. Moreover, the EVM results recommended the expansion and improvement of storage facilities.

New Tools and Technologies

The introduction of new, expensive vaccines mandated the need to continuously monitor vaccine temperatures to assure that each person is vaccinated with a potent vaccine. Therefore, IM advocated for and supported the introduction of remote temperature monitoring devices (RTM)

for cold rooms and continuous temperature monitoring devices for facilities using refrigerators/freezers. With the new digital technologies, the IM began training national staff from all countries in either international (5) or national (8) workshops. Among the many topics covered by these workshops, participants were trained in continuous temperature monitoring devices and RTM, using cell phone technology and e-mail alerts to receive temperature deviations from the monitored equipment. This has facilitated not only better management, but also allowed for rapid response to act in the event of energy or mechanical equipment failures.

As the immunization cold chain and supply chain became more complex, it also became imperative for countries to examine their operations and assure that managers at all levels had "end-to-end visibility" of all their operations. To this end, IM introduced the wVSSM[3]. VSSM is a vaccine and commodity inventory application, which allows managers to receive information on stock levels for vaccines and other commodities, their location, expiration dates, and other important information to ensure that no immunization services suffer from vaccine or supply stock-outs and helps protect vaccines and syringes from reaching their expiration dates. Moreover, wVSSM allows for a traceability of lot numbers of vaccines and syringes that need to be recalled.

The major challenge that management has faced in effectively using wVSSM is assuring that all health service points have access to the internet. Fourteen countries have installed VSSM, six of which are now using wVSSM (Dominican Republic, Honduras, Jamaica, Mexico, Nicaragua and Paraguay).

PAHO has always advocated for the principle of health equity and in this respect, the countries in the Region have extended their immunization services to more populations, especially those living in remote areas. IM has developed projects and/or assisted countries to introduce solar powered refrigerators. By 2008, IM had provided technical cooperation to almost all countries in the Region in the installation, maintenance and use of solar refrigeration equipment.

An Achilles heel affecting the management operations of the cold and supply chain is the flow of information throughout the system, due to the lack of digital equipment and access to the internet at lower administrative levels. These constraints will make it difficult to achieve the vaccine coverage goals set forth in the Decade of Vaccines Plan and in the upcoming immunization strategy plan. Together, EVM and wVSSM can provide the required information to make the best decisions and prepare effective budgets as part of each country's annual plan of action. It is worth noting that the TAG in Panama (2017) recommended the implementation and use of both EVM and wVSSM tools.

2018 JRF results on cold and supply chain practices indicated that only 15/42 LAC countries are using an electronic/digital tool to manage their vaccine stocks down to the lower administrative

[3] In 1997 PAHO introduced inventory software called Commodities and Logistics Management (CLM) in a few countries. The US-CDC and Management Sciences for Health developed CLM for health for managing medical supplies in public health warehouses. VSSM was introduced in 2010, beginning with Nicaragua and Paraguay.

levels. Twenty-three/42 countries indicated that they do not employ technologies at the sub-national level to continuously monitor vaccine storage temperatures. Of the 19 countries that indicated that they use technologies to continuously monitor vaccine storage temperatures, the range of establishments that have such abilities range from 100% to 50%. Regarding the confirmation of countries having a supply chain manager, 27 countries indicated yes, and 11 countries indicated that there is no manager in place. The analysis of these results indicates that countries need to invest in more management skill building and resources to ensure that they have excellent cold and supply chain operations at all levels.

As was stated in the early editions of the EPI Newsletters, today more than ever, governments need to provide the required funds to support their immunization program operations. Managers at all levels need to prepare their annual plans of action and activities (emphasizing new technologies, cold chain equipment, temperature monitoring devices, among others) and their corresponding budgets to guarantee that the required funds are allocated by the budgetary authority. Providing potent vaccines will save money and prevent VPD outbreaks and premature deaths from occurring.

Recommendations

- TAG urges each country to conduct and maintain a cold chain inventory and assessment and, also using this information to plan and make informed equipment purchases.
- TAG recommends that countries implement the use of new, well-accepted and tested technologies to manage cold and supply chain operations, such as prequalified refrigerator equipment, continuous temperature monitoring devices, and inventory control management tools. Countries should purchase prequalified equipment.
- TAG encourages each country to assure that their annual plans of action include investments in, but not limited to: training, supervisory activities, incorporation of new technologies, repair and maintenance of equipment and evaluation activities.

Improving Access and Timely Supply of Vaccines/Syringes through PAHO's Revolving Fund

Update on the Global Market, Pressing Supply Challenges and Vaccine Affordability for the Region

PAHO's Revolving Fund (RF) for Vaccine Procurement continues to be a key component of technical cooperation for immunization in the Americas and for the timely access of high-quality vaccines to 41 countries and territories in the Region at the lowest prices. In addition to its contributions to the elimination of VPDs, the RF continues to support the rapid uptake of new and under-utilized vaccines. The RF has been following through with the implementation of TAG recommendations from 2017. Successes have been a shared responsibility across the Region in confronting the challenges of global vaccine markets, implementing appropriate acquisition strategies, refining accurate country vaccine demand plans and aligning with national budgets and financing to minimize the risk of vaccine supply interruptions.

Challenges within the Global Vaccine Market and Supply

Vaccine markets present ongoing challenges for countries participating in the RF. For a significant number of vaccines, there are a limited number of manufacturers, restricting the global supply base, limiting competition and affordable prices. Production timelines are often lengthy and require considerable and careful planning. The RF continues networking with international partners and suppliers during production, including the GPEI, the EYE Strategy, and the Market for Information for Access to Vaccines (MI4A) initiative at WHO, as well as during UNICEF's annual meeting with suppliers. Similarly, the RF participated in the annual meeting of the Developing Country Vaccine Manufacturers Network (DCVMN) last held in Kunming, China in November 2018.

The Region is concerned with the constrained conditions of the HPV vaccine market. Currently, WHO has three prequalified vaccines from two manufacturers, all of which protect against HPV 16 and HPV 18, the main strains that cause cervical cancer, as shown in **Table 3.**

Table 3. Summary of Demand for HPV Vaccines through the RF, 2019

Manufacturer	Type	WHO prequalification	Availability to PAHO RF	RF Demand Forecast 2019 (doses)
GSK (Belgium)	Bivalent	2009	Through 2019	500,000
Merck (USA)	Quadrivalent	2009	Indefinite	2,500,000
	9-Valent	2018	Not available	

The HPV market is transitioning in 2019. GSK is exiting the market, leaving Merck as the sole supplier from 2020-22 until new manufacturers from India and China (Serum Institute of India LTD "SII," Zerun Biotech, and Innovax) are expected to reach WHO prequalification (or local registration). GSK indicated recently (May 2019) that it may return to the market in 2022.

While the HPV vaccine supply is enough to meet regional demand needs in 2019, constrained conditions will exist in 2020, beginning with the anticipated transition of six national programs

from the bivalent vaccine. Given these challenges, special attention to all elements in our regional supply chain for this vaccine are required. Additionally, the RF has been an active participant in the MI4A initiative at WHO and in the preparation of a market study analyzing the global demand and supply outlook for the HPV vaccine, aligned with the Director General's call to action on cervical cancer.

The supply of IPV and YF vaccines also present unique challenges for the Region. Supply constraints of prior years' market conditions for IPV improved in 2019 for the RF to adequately address the regional demand estimated at approximately 8.6 million doses. The current status of IPV demand and supply for 2019 is summarized below in **Table 4:**

Table 4. Summary of Demand for IPV Vaccines through the RF, 2019

UPDATE DEMAND IPV 2019 (as of 30 June)

TOTAL ADJUSTED REGIONAL DEMAND (doses)
8,600,000

IPV PRESENTATION		ALLOCATION Dec/18		PROCURED (30 June-19)	CONFIRMED Q3-Q4 2019	TOTAL ESTIMATED 2019	
PFS	1 ds	3,000,000	% DEMAND	1,810,000	910,000	2,720,000	
MULTIDOSE VIAL	5 ds	2,600,000		1,130,000	630,000	1,760,000	2,960,000 *
	10 ds	3,000,000		550,000	650,000	1,200,000	
TOTAL		8,600,000	100%	3,490,000	2,190,000	5,680,000	

* This demand may be revised following July 2018 TAG Regional meeting

Unfortunately, seven countries reported that there were interruptions in supply due to one of the following reasons, e.g. budgetary or financial issues, delays in shipments/deliveries, switches to fractional doses, and other countries that use combined vaccines containing IPV and use IPV only as booster and for travelers, according to the 2018 JRF. These are under review with the concerned countries attending the TAG meeting.

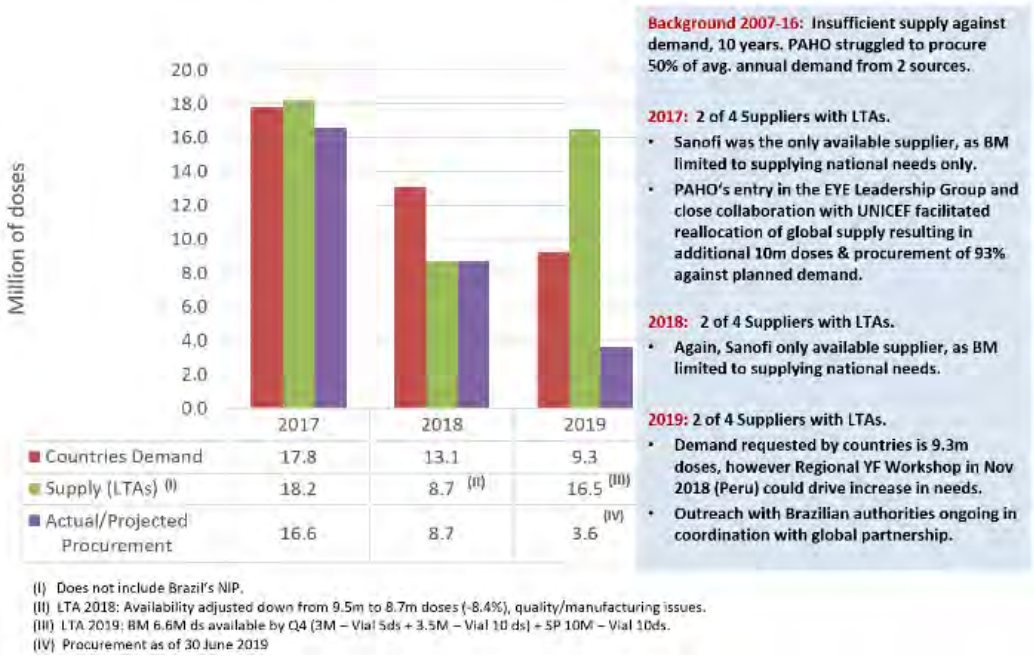
Comments from Member States attending PAHO's Directing Council in September 2018 directed the RF to maintain its "readiness" in case of any changes in the global IPV supply situation. Accurate demand forecasts together with close monitoring of national inventories (stock reach), will continue to be fundamental tools for the allocation of available vaccine supply, either to cover current needs or additional doses required for the remaining countries considering changing to the 2-dose schedule.

For 2020, the RF expects to have enough supply from the two WHO prequalified manufacturers to meet regional demand. The RF will continue to network with global partners and with manufacturers to assure the supply to Member States as part of continuous efforts to maintain polio eradication in the Region of the Americas.

The yellow fever outbreak in Brazil impacted the availability of YF vaccine supply to endemic countries in the Region, reducing the RF supply plan for 2017 by approximately 60%. Proactively, the RF continues to engage with WHO and UNICEF colleagues as the governing structure for the global EYE Strategy evolves. The RF was named to the Leadership Group together with WHO, UNICEF, and GAVI representatives and is also part of the Supply Sub-committee.

Special attention continues to be given to the eleven YF endemic countries of the Region. In view of the buildup of susceptible populations in these countries, a regional workshop was convened in November 2018 to protect at-risk populations, prevent international spread, and to respond to outbreaks.

Figure 8. Demand Supply and Procedures of Yellow Fever Vaccine, PAHO Region, 2017-19



Technical Support to Countries in Demand Planning & Monitoring

Carefully reviewing and analyzing country demand plans continues to be necessary for the RF and there are opportunities to improve their accuracy. As of 2019, only four countries have maintained demand planning accuracy above 80% on more than 80% of the vaccines planned and procured through the RF. To continue strengthening demand planning for countries, several initiatives are under consideration including a training network to improve country knowledge and practices. In close collaboration with PAHO's IM unit, the RF provided regional trainings on vaccine demand planning and in joint country level workshops.

In preparation for the review of 2020 demand plans from countries by end of June 2019, the RF held WebEx orientation sessions with participating countries to review the planning process and use of the updated PAHO 173 tool. As of July 2019, 31 of 41 countries (76%) have already submitted their annual plans for 2020.

Budget and Financial Considerations for the RF

Accurate demand plans should be backed up with a reliable budget and financing from national resources. The RF monitors financial situations through aging of invoices received by countries following the receipt of goods in-country. If more than 60 days elapse from the date of the invoice

receipt, the country is considered in arrears and not eligible for continuing to have access to the RF credit line.

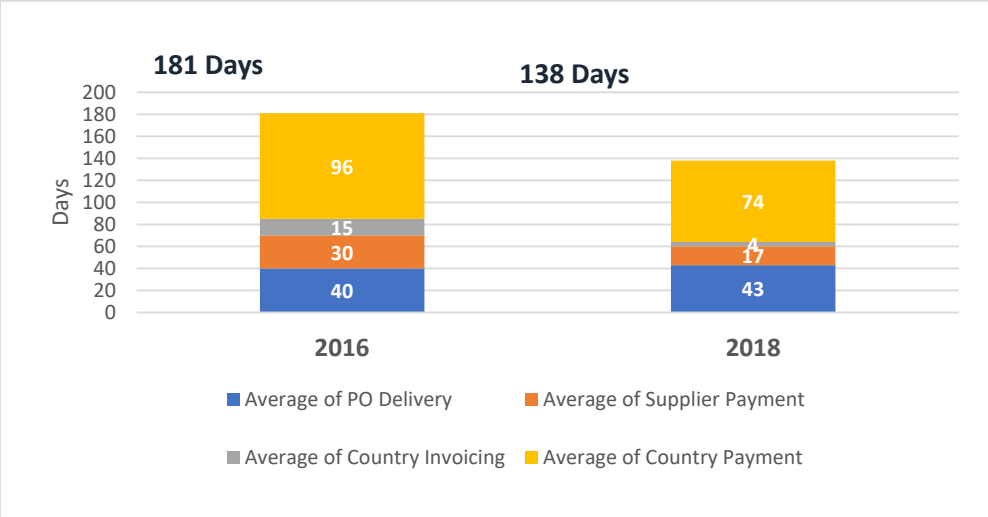
As of 30 June 2019, there were 23 countries in arrears to the RF as shown in **Table 5**. This represents a four-fold increase over the same period last year, June 2018. This is a cyclical concern for the RF. The RF remains committed to both monitoring this situation in a monthly manner with PAHO's Department of Procurement and Supply Management (PRO) and PAHO country offices and improving the visibility of payment performance by countries, along with other financial statements for countries.

Table 5. Financial Situation of Countries Participating in RF Credit Line, June 2018/June 2019, Aging (Days)

	NUMBER OF COUNTRIES				
Date	**1-30**	**31-60**	**61-90**	**91-180**	**181+**
End June 2018	1	0	0	2	3
End June 2019	3	9	12	6	5

The RF also monitors credit line turnover. One of the findings from the RF Assessment in 2017-18 was the underperformance of that turnover. **Figure 9** compares average number of days for Procurement Order (PO) deliveries, Supplier Payments, Country Invoicing and Country Payments for 2016 and 2018.

Figure 9. Revolving Fund Line Turnover, 2016-2018



Upon comparing data from 2016 and 2018, improvements are noted in a total reduction of time from 181 to 138 days resulting from improvements in average times for country invoicing and payment, respectively. Nevertheless, the performance target identified in the RF Assessment is for 1.5 turns per year of the credit line, up from .92 turns measured during the Assessment. More on key points from the RF Assessment follow below.

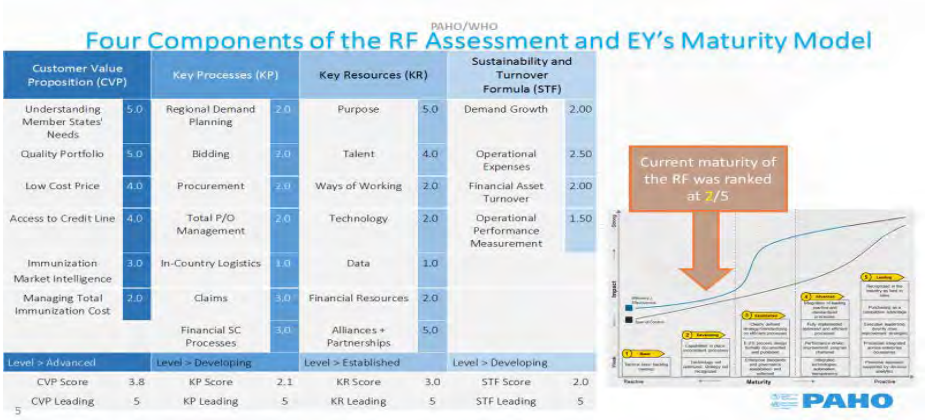
RF Assessment by Ernst and Young (2017-18)

To improve RF performance, an external assessment was conducted in 2017-18 funded by a variety of resources including Member States (procurement fee revenue), PAHO's regular budget, and a WHO grant from the Bill and Melinda Gates Foundation.

The independent Ernst & Young report assessed the RF's current operating model, mapped drivers of change in the operation, and provided short-term and long-term recommendations to preserve the relevance and sustainability of the RF. These were presented by the Ernst & Young team to PAHO's Director and Executive Management team on 18 December 2018. Over the past six months, these recommendations have been reviewed internally by the RF Working Group for a discussion with the Director on 1 July 2019. The following is a summary of key findings. A public version of the report will be made available soon.

The four basic components of the Assessment were the RF's Customer Value Proposition (CVP), Key Processes (KP), Key Resources (KR), and its Sustainability and Turnover Formula (STF). The current state of these components was assessed and benchmarked using a maturity model with a range of scores from 1 to 5, where 1 corresponds to a basic level of maturity and 5 to a leading level, calibrated by best practices in relevant comparable Group Purchasing Organizations (GPO). The results are summarized in **figure 10**.

Figure 10. The Four Components of the Revolving Fund Assessment and Maturity Model



Recommendations

- TAG encourages PAHO to keep updating countries on vaccine markets and to implement proactive responses to specific vaccine issues.
- TAG encourages PAHO to continue supporting global efforts to improve access to affordable vaccines, including regional pooled procurement initiatives beyond PAHO Member States.
- TAG welcomes the report of the RF Assessment and supports the transformational program of work to increase the efficiency and further enhance the support of the RF to countries while maintaining its core principals.
- TAG urges countries to make their payments to the RF in a timely manner.

Pneumococcal Conjugate Vaccines: New Evidence and Use Among the Elderly

Infections caused by pneumococcal bacteria can be serious, especially in the elderly, and infections caused by many of the pneumococcal serotypes are preventable by vaccines. A conjugate vaccine covering 13 of the over 90 serotypes of streptococcus pneumoniae has been licensed for adults (PCV13) and has shown to be efficacious. However, few countries recommend PCV13 for routine use among older adults because pediatric vaccination programs have reduced the overall circulation of pneumococcal strains included in the 13-valent vaccine, as well as the exposure of older adults to these strains. In LAC, 37/52 (71%) countries and territories have introduced PCV10 or PCV13 into national immunization programs for infants.

Experience from the US and Europe: Invasive Disease among Adults Aged 65+ Years

The United States was the first country to introduce PCV for children, starting with the 7-valent conjugate vaccine (PCV7) in 2000 and changing to PCV13 in 2010. In late 2014, the USA also made a recommendation for PCV13 to be given routinely to all adults age 65 years and older. Data from the U.S. Active Bacterial Core surveillance (ABCs), which tracks invasive disease episodes and collects isolates for serotyping, shows a large reduction in disease caused by vaccine serotypes among adults aged 65 and older after both PCV7 and PCV13 introduction. Disease rates did not change following the introduction of PCV13 for older adults in late 2014. In 2016, few of the remaining cases among either adults or children were caused by vaccine serotypes. While vaccine serotype 3 was the most common serotype among adults, the rates of disease caused by serotype 3 did not change following PCV13 introduction in both children and adults. No increase was seen among older adults in invasive disease caused by nonvaccine serotypes in the years following PCV13 introduction.

Data from surveillance for invasive pneumococcal disease (IPD) conducted in European countries, aggregated through a program called SpIDnet/I-MOVE+, indicates an indirect benefit of childhood PCV programs on disease caused by the serotypes that are included in PCV10 and PCV13 among older adults, like that noted in the USA. In contrast to the situation in the USA, however, a year-on-year increase in non-PCV13 serotype incidence, suggesting serotype replacement disease, was observed among European surveillance sites. This replacement effect was of similar magnitude for disease caused by serotypes included in the 23-valent pneumococcal polysaccharide vaccine, but not in PCV13 and for serotypes not included in any vaccine. SpIDnet/I-MOVE+ results indicate a large indirect effect of childhood PCV programs on IPD caused by the serotypes that are included in both PCV10 and PCV13 among older adults. However, the year-on-year increase in non-PCV13 serotype incidence, suggesting serotype replacement in disease, was observed in all sites.

We conducted a critical appraisal of the published and unpublished literature on pneumococcal disease burden in LAC to assess the data available on the remaining burden of disease in older adults (adults aged ≥65 years) that could be prevented if PCV13 were recommended for this age group. A review of four electronic databases and inquiries with experts familiar with pneumococcal burden of disease studies in LAC identified 175 potential data sources.

Among these, 13 relevant data sources, including eight publications and five unpublished documents met the inclusion criteria. Most studies (n=8) were from Brazil, and all except two (from Uruguay) were from countries using PCV10 in their infant immunization programs. Studies of invasive disease (n=3 for adults), pneumonia hospitalizations (n=3) and pneumonia mortality (n=2) showed that disease rates overall were increasing among adults age 65 years and older, a trend that began before PCVs were introduced for children. Analyses comparing changes in rates of pneumonia hospitalizations and mortality after pediatric PCV introduction showed mixed results, with some studies showing a decrease in disease among the elderly and others not detecting any change or an increase in rates. Studies of invasive disease showed that disease caused by serotypes covered by the PCV used in the country's pediatric program dropped after the programs began. Carriage studies (n=3), all of which were from Brazil, showed that limited adults are being exposed to PCV10 serotypes in recent years.

In summary, the studies identified were limited in number and quality by the lack of standard surveillance in LAC, surveillance that monitors rates of disease caused by vaccine serotypes. In addition, the underlying increasing trend of pneumonia and invasive disease rates in the elderly, likely due to population aging and improved access to healthcare, made interpretation difficult for the available studies. The expert group that reviewed the evidence concluded that in countries with robust pediatric PCV programs, the benefits from PCV13 vaccination for all older adults is likely to be limited. Certain groups at very high risk of pneumococcal disease, such as immune-compromised individuals may be more likely to benefit from receiving PCV13 than healthy older adults.

Recommendations

- TAG reiterates its previous recommendation to achieve high PCV vaccination coverage in infants and young children. Evidence indicates that high coverage in this age group indirectly reduces the burden of disease in the elderly and introduction of PCV13 for all older adults is likely to have limited benefit and is not cost-effective.
- Countries should improve the epidemiological surveillance of *Streptococcus pneumoniae* invasive disease in older populations to measure the indirect effects of the vaccination in infants.
- Countries should carry out carriage studies to quantify the remaining burden of vaccine type disease and carriage in children <5 years of age, to determine the extent of vaccine type *pneumococci* circulation in the community, putting older adults at risk of disease.

Access, Acceptance and Demand: Challenges in Vaccination

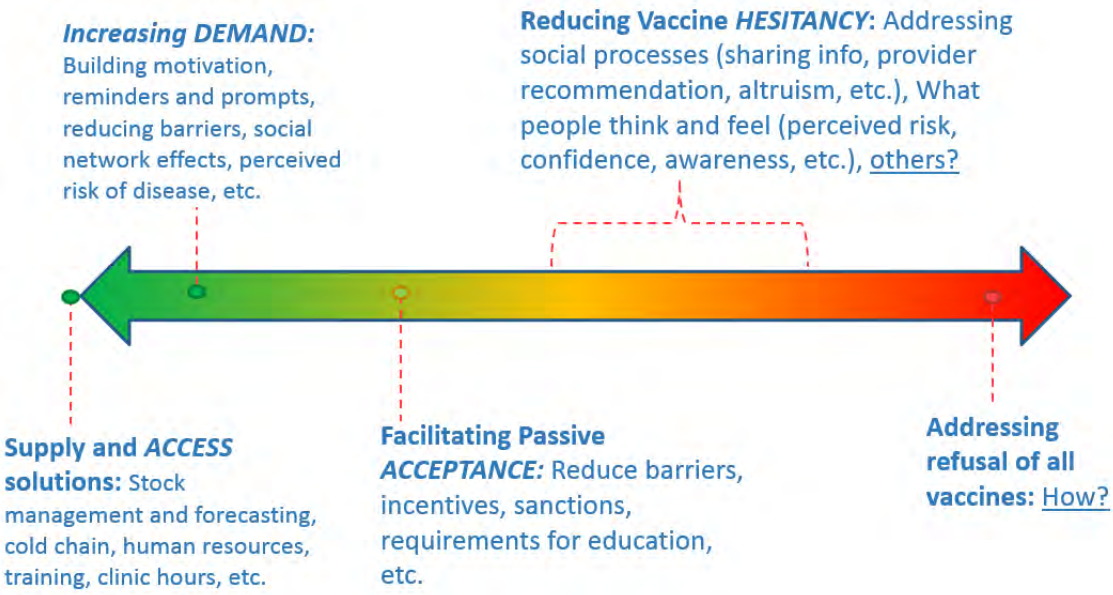
Despite the Region´s achievements in immunization, challenges persist and a decline in vaccination coverage levels has been observed in recent years at national and subnational levels. Various factors pertaining to immunization programs themselves, the health sector or the local socio-economic context may have negatively affected vaccine supply and demand, resulting in suboptimal immunization performance **(figure 10)**.

Past program evaluations and studies conducted in LAC to date have suggested that barriers to vaccination have mainly been associated with vaccine availability and access to immunization services reflecting programmatic and logistical issues. Four studies conducted in Colombia, Dominican Republic, El Salvador, and Guatemala in 2010-11 confirmed that missed opportunities for vaccination of young children under the age of five, were associated with difficult geographic access, inadequate organization of health services, limited availability of vaccines/supplies and of immunization staff. These studies also highlighted the negative impact of healthcare professionals' practices on vaccine schedule completion, such as not requesting the vaccination card during consultations. The current high turnover of immunization staff reported by countries, and the insufficient training and awareness of healthcare workers/providers about VPDs are also affecting both vaccine supply and demand. Finally, misinformation and lack of perception of the risk and seriousness of VPDs in the community may also play a role in decreasing vaccine uptake. Related to this latter issue, WHO has recently included vaccine hesitancy – a delay in acceptance or refusal of vaccines despite availability – in its list of top ten global public health threats.

While LAC have historically benefitted from a generally high confidence in vaccines, as identified in 2016 through a survey conducted in nine countries of the Americas reporting a general tendency among interviewees to agree that vaccines for children are important, safe, effective and compatible with religious beliefs, recent communication crises in the Region associated with the use of HPV vaccines and yellow fever fractional doses have underlined that vaccine confidence can be fragile and that recuperating it can be a difficult and lengthy process. Similarly, and at the global level, escalating concerns related to vaccine hesitancy and learning from programs that have seen safety or other events contribute to declines in coverage, prompted WHO's SAGE to put forward recommendations in 2017 to all countries, to conduct assessments of vaccine acceptance and demand.

Since 2015, the JRF has collected data on vaccine confidence and hesitancy by asking respondents to list the top three reasons for hesitancy to accept vaccines according to the national schedule in their country. However, this information is insufficient to guide countries' public health actions and published data on the topic are scarce in LAC. Reliable measures to better understand why people are not being vaccinated are needed to ensure that evidence informs the design and evaluation of more tailored and targeted interventions to increase vaccine uptake. Standardized, validated measures to assess reasons for under-vaccination will also facilitate future comparison across and within countries/regions and monitoring of trends.

Figure 11. Increasing Vaccination Model: Strategies to Address Stages on the Continuum



Once countries have established a diagnosis of reasons for under vaccination, immunization programs may draw on their experience to address immunization system issues through improving vaccine availability, supply, outreach services, and health workers training among other interventions. Nevertheless, some of the current obstacles may require expertise extending beyond the scope and traditional competencies of the immunization program, such as social sciences. Indeed, under-vaccination and non-vaccination linked to healthcare providers and parental knowledge and attitudes may require formative research skills and local interventions. Thus, multi-faceted, innovative approaches are needed to reach the under-vaccinated and unvaccinated, requiring multidisciplinary and intersectoral efforts to strengthen social mobilization, education, and advocacy.

Experience from other Regions, especially the WHO European Region, has shown the importance of moving away from the traditionally supply-oriented immunization programs to applying a more people-centered and comprehensive approach, built on listening to the intended beneficiaries and considering the complexity and the wide range of factors influencing vaccination uptake.

“WHO was established to advance human health—and human behavior is a core determinant of human health and well-being. Now is the time for this fact to be fully accommodated in its structure and programs (Omer and Butler, 2019).” As we enter this exciting era of WHO transformation, it is an important reminder that human behavior is a critical component to be studied and considered when developing public health policy recommendations. It is important to examine reasons for under-vaccination in the Region in a systematic manner and build an evidence base to design effective interventions. Factors such as individual motivation, attitudes and beliefs, but also social, community and cultural factors, legislative, institutional and structural factors should all be considered.

Recommendations

- TAG urges PAHO to develop a regional strategy for vaccine access, acceptance and demand, and support countries in identifying social and behavioral determinants of vaccination and addressing barriers to vaccination.
- Countries should use theory-based approaches to identify local barriers and drivers to vaccination and use these insights to develop tailored, evidence-based interventions to reach vaccination target populations, evaluate their impact and share their findings with other countries.
- Countries should strengthen their preparedness and response to vaccine communication crises which have the potential to erode trust in vaccines and in health authorities delivering them.

Diphtheria in the Americas

Thanks to countries' significant progress in immunization, the Region of the Americas has been free of diphtheria for several decades. However, in recent years, large diphtheria outbreaks have affected Haiti and Venezuela. We describe their epidemiological situation below.

Haiti

Since the beginning of the outbreak in 2014 (EW 51) and through 2019 (EW 16), 271 confirmed cases of diphtheria have been reported based on laboratory confirmation or an epidemiological link to a confirmed case. Cases have been reported from all 10 departments of the country. The cumulative incidence rate for the period from 2014 to 2019 (EW 22) is 2.5 per 100,000 inhabitants. The case-fatality rate among cases confirmed by laboratory or epidemiological link was 50% in 2014, 23% in 2015, 39% in 2016, 8% in 2017, 13% in 2018, and 17% in 2019. In 2019, the highest incidence rate to date has been reported among children 5 to 15 years of age, followed by those 1 to 5-year-old. There is a slight predominance of female cases.

Venezuela

The diphtheria outbreak that began in July 2016 (EW 26) is still ongoing. Since the beginning of the outbreak until EW13 of 2019, 1,711 cases have been confirmed by laboratory, clinically, or by epidemiological link to a case. Cases have been reported in all states. The cumulative incidence rate is 5.9 cases per 100,000 inhabitants. A total of 317 deaths were reported (. In 2019, the highest case-fatality rate occurred in the age group of 5 to 9 years-old (7%), followed by 10 to 15 years-old (4%). Since EW 43 of 2018, the outbreak has been concentrated in people over 18 years of age.

Outbreak Response Activities

In Haiti, outbreak response activities have been focused on communes with reported cases, aimed at children from 1 to 14 years old. To date, vaccination campaigns have been carried out in 44 of the 140 communes of the country. As of May 2019, 1.1 million children aged 1 to 14 have been vaccinated. The reported official coverage is 78%. From May 2-6, 2019, a campaign was carried out in 78% communes of the departments of Ouest and Artibonite. The results of this last campaign are pending publication. Health care workers have not been vaccinated.

In Venezuela, the outbreak response vaccination campaign was initially carried out in nine departments, and progressively expanded throughout the country. As of May 2019, 4.6 million children aged 7 to 15 years have been vaccinated, most of the states have reached ≥95% coverage, except for seven states where vaccination activities are ongoing: Anzoátegui, Apure, Bolívar, Cojedes, Falcón, Portuguesa and Trujillo. In addition, the states that have already reached coverage ≥95% continue to monitor actions to ensure that no pockets of unvaccinated children remain. Health care workers have been vaccinated.

In addition to the vaccination campaigns, both countries have carried out the following activities: i) updating the national surveillance guidelines, following WHO's new epidemiological surveillance standards; ii) conducting training workshops on case and contact management; iii)

training supervision on the prevention and control of infections associated with health care; and iv) acquisition of diphtheria antitoxin (DAT), which at the beginning of the outbreaks was difficult to achieve, but starting in 2018, has been available through the RF.

Vaccination Schedule and Coverage

The primary vaccination schedule for both countries includes three doses of pentavalent vaccine (DTP + Hep B + H. influenzae). The vaccination schedule in Haiti includes only one booster dose, administered 1 year after the administration of the third dose of the pentavalent vaccine. The Venezuelan vaccination schedule includes three booster doses: at 18 months, 5 years, and 10 years of age.

Vaccination of other age groups in Haiti includes women of childbearing age, as part of the prevention against maternal and neonatal tetanus, and in Venezuela, women of childbearing age, health care workers, and older adults.

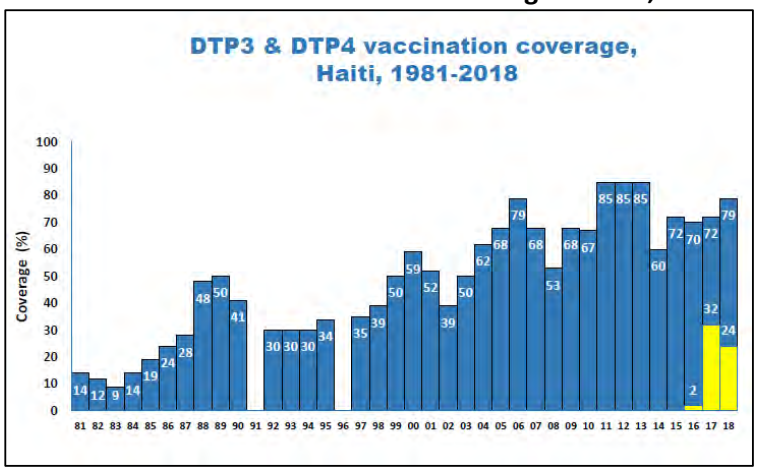
Table 5. Diphtheria Vaccination Schedule, Haiti and Venezuela, 2018

Country	1st dose	2nd dose	3rd dose	4th dose	5th dose	6th dose
Haiti	6 weeks	10 weeks	14 weeks	1 year after 3rd dose		
Venezuela	2 months	4 months	6 months	18 months	5 years	10 years

Source: PAHO-WHO/UNICEF 2019 JRF on immunization (2018 data).

In Haiti, vaccination coverage for DTP3 has historically been low. In the case of DTP4 coverage reported in 2018, a deterioration was observed with respect to the previous year (2017: 32%, 2018: 24%). At the municipal level, in 2018 only 33 (24%) of the 140 municipalities in the country achieved coverage of ≥95% for DTP3; only 1 in 5 children under 1-year old lives in a municipality with optimal coverage for DTP3.

Figure 12. DTP3 and DTP4 Vaccination Coverage in Haiti, 1981-2018



In Venezuela, the coverage for DTP3 in 2018 was the lowest in the last 10 years (60%), and there was a deterioration in coverage for DTP4 with respect to the previous year (2017: 38%; 2018: 31%). At the municipal level, in 2018 only 68 (20%) of the 335 municipalities in the country achieved coverage ≥95% for DTP3. Only 1 in every 11 children under 1 year of age lives in a municipality with optimal coverage for DTP3.

As a result of the low vaccination coverage in both countries over an extended period, there has been a significant accumulation of susceptible populations in all age groups. In the case of Haiti, this situation is aggravated by the non-inclusion of the TAG recommended booster doses in the national vaccination schedule.

Diphtheria Situation in the Remaining Countries of the Region

With respect to the other countries of the Region, there was a high incidence of diphtheria cases (≥10 cases per year, in ≥3 years of age, 1999-2018) in Brazil and the Dominican Republic. There was a low incidence (<10 cases per year, in ≥3 years of age, 1999-2018) in Bolivia, Canada, Chile, Colombia, the United States and Paraguay. Isolated cases were reported in Argentina, Ecuador, Guatemala and Peru. Only 22 of the 52 countries and territories report having implemented the third booster dose.

Recommendations

- TAG expresses concern over the current outbreaks and reminds countries that all diphtheria events should be reported. Countries with ongoing diphtheria transmission should accelerate immunization activities, identifying high-risk areas, and strengthen the existing routine immunization programs, surveillance and rapid response.
- TAG reiterates its previous recommendation of achieving high vaccination coverage levels with diphtheria-containing vaccines. In addition to the primary DTP series during infancy, countries must ensure that 3-booster doses of the diphtheria-containing vaccine are provided during childhood and adolescence in combination with the tetanus toxoid vaccine, using the same schedule and age-appropriate vaccine formulations (DTP among children 1-7 year(s) old; Td among children over 7 years old, adolescents and adults). All countries should closely monitor coverage with DTP3 and DTP4 at national and subnational levels.
- TAG recommends that all countries in the Region adopt the new WHO standards for the epidemiological surveillance of diphtheria.
- TAG recognizes the efforts made by Haiti and Venezuela to control the diphtheria outbreaks and calls on both countries to strengthen vaccination activities. Haiti should introduce the fifth and sixth booster dose in the national vaccination schedule and vaccinate health care workers.

Progress towards the Elimination of Hepatitis B in the Americas

Hepatitis B Burden

Hepatitis B virus (HBV) infection is a major global health problem causing acute and chronic infections that can lead to liver cirrhosis, hepatocellular carcinoma and death. The risk of chronic infection (defined as being hepatitis B surface antigen positive [HBsAg]) is inversely related to the age at infection. Up to 80-90% of infected infants develop chronic infection; 30-50% of children infected before the age of 6 years; and, <5% of older children, adolescents, and adults with infections acquired after that age. Between 20 and 30% of adults who are chronically infected will develop cirrhosis and/or liver cancer. Hepatitis B is a VPD. The vaccine is 95% effective in preventing infection and developing chronic disease and liver cancer due to HBV (it was the first vaccine to prevent cancer). TAG recommendations emphasize the importance of a birth dose of hepatitis B vaccine administered preferably within 24 hours followed by three doses during the first year of life, to reduce perinatal and early childhood transmission.

In the Americas, a model from Center for Disease Analysis (CDA) Foundation in 2016 estimated that 4.0 (2.8-6.5) million people are chronically infected, representing a prevalence among the general population of 0.4% (0.3%-0.6%) and among children under five years of age, less than 0.1%. Another model from the London School of Hygiene and Tropical Medicine (LSHTM) commissioned by WHO, in 2017 estimated that 3.2 (3.1-5.7) million people are chronically infected, representing a prevalence among the general population of 0.5% (0.3-0.7%) and among children under five years of age also less than 0.1%. The differences between these estimates are due to methodological differences in the estimation process. In both cases, most countries in the Region are considered as having low prevalence (<2%); however, there are some areas in the Caribbean and in the Amazon Basin (areas with a high concentration of indigenous populations) with intermediate (2-7%) to high (≥8%) prevalence of HBV infection. It is critical to note that the low incidence among children under 5 years of age at present can be attributed to the widespread use of the hepatitis B vaccine for more than two decades.

Global and Regional Hepatitis B Elimination Frameworks

In May 2016, the World Health Assembly adopted the first Global Health Sector Strategy on Viral Hepatitis, 2016-2021. This strategy has a vision of eliminating viral hepatitis as a public health threat (reducing the prevalence of chronic HBV in children to <0.1%, new viral hepatitis infections by 90% and reducing deaths due to viral hepatitis by 65%) by 2030. Its targets are aligned with those of the SDGs and the elimination of perinatal and early childhood horizontal transmission is considered a milestone on the road to HBV elimination as a public health threat.

In the Americas, in July 2015, TAG recommended that PAHO and countries should evaluate the status of hepatitis B control and the feasibility of elimination. In September 2015, the PAHO Regional Plan on Viral Hepatitis (2016-2019) and the PAHO RIAP (2016-2020) were presented to the Directing Council. Following it, a PAHO Hepatitis Technical Advisory Committee (TAC) and a PAHO Core Group on Hepatitis were established. In 2016, based on progress made by countries and a modelling exercise, the TAG assessed that perinatal and early childhood horizontal transmission elimination of hepatitis B was feasible in the Americas by 2020 by ensuring

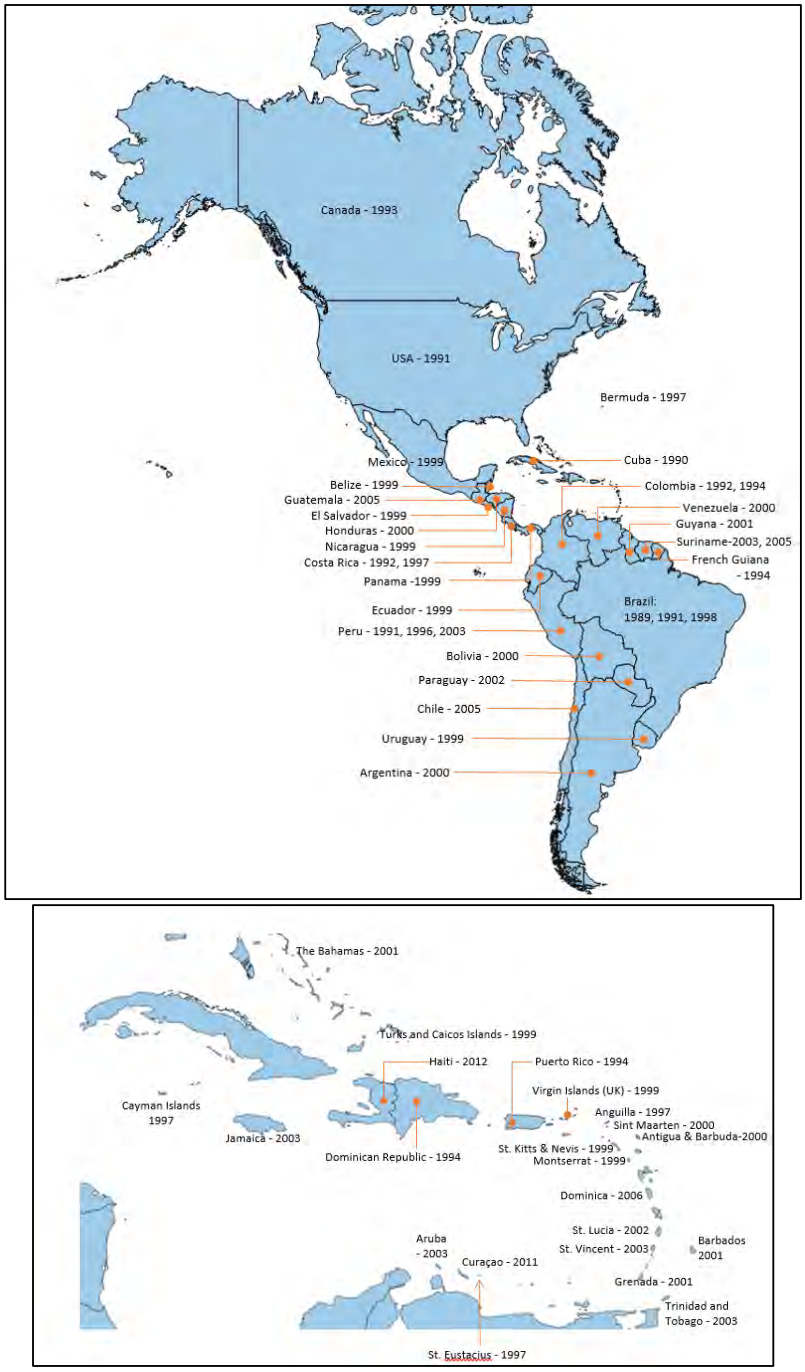
vaccination coverage equal to or greater than 95% with the first dose within 24 hours of birth and the third dose of the hepatitis B primary series among children less than one year of age.

Progress towards Elimination and Verification of Hepatitis B Perinatal and Early Childhood Horizontal Transmission

Following TAG recommendations, the Framework for Elimination of Mother-to-Child Transmission (EMTCT Plus) added in 2017 the elimination of HBV infection, as part of the approach for elimination of HIV, syphilis and Chagas. The framework included programmatic objectives related to immunization, HBsAg screening of pregnant women and administration of hepatitis B immunoglobulin (HBIG) in exposed infants and the impact target as ≤0.1% HBsAg prevalence in children at five years of age.

All 52 countries and territories in the Region have introduced hepatitis B vaccine (or hepatitis B containing vaccine) in their routine immunization schedules (**figure 13**), with 81% of regional coverage with three doses among children less than one year of age (reported in the 2018 JRF). Progress has also been made on birth dose introduction in the national infant immunization schedules from 18 countries in 2013 to 29 countries in 2019 (which represent more than 90% of the live birth cohort) with a regional coverage with the Hepatitis B birth dose of 72% in 2018. It is also important to strengthen the identification of persons chronically infected with hepatitis B through screening, including routine screening for HBsAg in pregnancy and follow-up interventions for exposed infants. As reported in the EMTCT 2018 progress report, in 2017, 24 out of 31 reporting countries in the Americas indicated having a policy for universal screening of pregnant women for HBV and 22 out of 28 reporting countries indicated that HBIG prophylaxis was made available to exposed newborns. According to WHO, nineteen countries in the Region might have already achieved the impact target for EMTCT and early childhood horizontal transmission in the Region (Argentina, Bahamas, Bolivia, Brazil, Chile, Colombia, Costa Rica, Cuba, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Panama, Peru, Saint Kitts and Nevis, Uruguay, United States and Venezuela) and according to the CDA model used by PAHO, thirteen countries (Argentina, Belize, Brazil, Canada, Chile, Colombia, Costa Rica, Cuba, Guatemala, Nicaragua, Mexico, Peru and United States) might have already achieved the same impact target.

Figure 13. Year of Introduction of Hepatitis B or Hepatitis B-containing Vaccine in the National Schedule



Note: Multiple years correspond to year of introduction in risk/selected areas.
Source: Ropero Alvarez AM, Pérez-Vilar S, Pacis-Tirso C, Contreras M, Omeiri N El, Ruiz-Matus C, et al. Progress in vaccination towards hepatitis B control and elimination in the Region of the Americas. BMC Public Health. 2017;17:325.

In line with the above, methods to assess the progress towards and achievement of the targets by countries are needed. In view of the low prevalence in the general population in the Region, approaches that are being considered:

a) Desk review of existing country data, including seroprevalence, surveillance and programmatic data.

b) HBsAg seroprevalence surveys, nationally representative surveys have been recommended by WHO for monitoring progress towards hepatitis B control targets but require large sample sizes in settings of low prevalence. Alternative approaches being considered include more focused surveys targeting high-risk areas or selected population groups. PAHO in coordination with the CDC assessed the feasibility and outcomes of a two-stage protocol in which a risk assessment conducted using existing data was followed by a focused serosurvey in identified high-risk areas. This approach was evaluated and implemented in collaboration with Colombia's ministry of health. This serosurvey was conducted among more than 3,000 children in identified high risk areas and no cases were detected suggesting that Colombia has achieved the impact target. The integration of HBsAg testing into other planned surveys (such as demographic, health, and nutritional) should also be considered. The establishment of systems to track the follow-up of infected women and monitoring outcomes among their infants could also provide relevant data to allow the verification of the elimination of perinatal and early childhood transmission.

c) Mathematical modelling exercises: Models leveraging existing in-country data and previously published literature may be useful to estimate the cumulative impact (cases and deaths averted) of hepatitis B vaccination programs, to assess the progress of countries towards the achievement of the perinatal and horizontal hepatitis B elimination impact target and to project the potential impact of additional preventive (including immunization) and treatment interventions for chronic HBV infections towards 2030 targets. This process has been recently conducted in Colombia and Cuba by an inter-programmatic team from PAHO in close collaboration with the ministries of health and with the assistance of modelers.

The lessons learned from these experiences, together with those of the verification of elimination of other VPDs and the elimination of MTCT of HIV and congenital syphilis, will guide the development of regional guidelines/guidance to countries and tools for verifying/validating the elimination of perinatal hepatitis B and early childhood horizontal transmission. PAHO will ensure the engagement of relevant stakeholders and partners. This process will benefit from ongoing discussions with other WHO Regional Offices (WPRO) that are advancing on the development of such a process and methodology and will closely relate to WHO's Immunizations and HIV/Hepatitis Units/Departments in Geneva that are also working on the development of global reference standards.

Recommendations

- TAG commends countries with regards to the progress made towards the elimination of mother-to-child and early childhood horizontal hepatitis B transmission and urges

countries to attain high vaccination coverage with hepatitis B birth dose and hepatitis B or hepatitis B-containing vaccines during the first year of life.

- TAG urges PAHO to develop guidance for the verification of mother-to-child and early childhood horizontal hepatitis B elimination in the Americas.

Immunization Agenda 2030

With just a year remaining on the GVAP 2011-2020, the development of the next 10-year strategy began in 2019 – one that sets a new vision for immunization by 2030 in alignment with global health priorities around PHC, UHC and SDGs. This new Immunization Agenda 2030 will be shared with Ministers of Health at the 73rd World Health Assembly in May 2020 for their endorsement.

Led by WHO with partners, a draft strategy was prepared and shared for public consultation. To ensure the inputs and voices of regions and countries are heard and reflected, various consultations have been organized, including with TAG Members.

An overview presentation was given to TAG members during the TAG meeting, describing the seven strategic priorities and key interventions proposed for the next decade of immunization. This was followed by a full day consultation with countries of the Americas on 12 July.

Recommendations

- TAG supports WHO's countries consultation process for the Immunization Agenda 2030 and encourages countries of the Americas to fully participate in the process and share the regional and national perspectives.

28th MEETING OF THE TECHNICAL ADVISORY GROUP ON IMMUNIZATION AND VACCINE-PREVENTABLE DISEASES IN THE WESTERN PACIFIC REGION

18-21 June 2019
Manila, Philippines

CONTENTS

SUMMARY

The 28th Meeting of the Technical Advisory Group (TAG) on Immunization and Vaccine-Preventable Diseases in the Western Pacific Region was held on 18-212 June 2019 in Manila, Philippines. The meeting was attended by six TAG members, four temporary advisors, 30 participants from 14 countries and areas, 53 representatives from partner organizations, and WHO staff from headquarters, the Regional Office for the Western Pacific and representative country offices.

The meeting participants discussed lessons learnt and the status of the measles and rubella elimination strategies and poliovirus (polio) eradication, the *Regional Guide for accelerated Control of Japanese Encephalitis in the Western Pacific* and the *Field Guide for Preparedness and Response to Diphtheria Outbreaks in the Western Pacific*. Discussions covered regional plans for surveillance, data management and laboratories and laboratory networks for vaccine-preventable disease control and elimination. Discussions also covered the goals for immunization and vaccine-preventable diseases during 2021-2030 for the 37 countries and areas that make up the Western Pacific Region. The TAG acknowledged that initiatives for vaccine-preventable disease control and elimination, and the introduction of new vaccines have led to strengthened immunization systems and programmes in the Region over the last four decades. The TAG offered full support to the WHO Secretariat to continue developing a post-2020 regional framework of action for immunization and vaccine-preventable diseases in the Western Pacific, working in collaboration with Member States and partners.

The TAG urged all Member States to continue to implement the Regional Committee resolution (WPR/RC68.R1) including, developing national strategies and plans, establishing a target year for rubella elimination, and ensuring adequate technical and financial resources for implementation. The TAG also urged all Member States to continue to introduce new vaccines that are recommended by WHO for inclusion in national immunization programmes. The TAG recommended all Member States to strengthen surveillance for diseases targeted by new vaccines and build capacity for laboratory diagnosis.

The TAG recommended the WHO Secretariat to continue providing technical support to Member States for investigation, causality assessment and response to vaccine and immunization safety events. The TAG also recommended the WHO Secretariat to continue technical support and capacity building to strengthen immunization services to reach under-served persons and achieve high immunization coverage across all population groups. The TAG requested the WHO Secretariat to advocate for an increased global commitment to achieving and sustaining measles and rubella elimination, continuous reduction and sustained prevention of measles deaths and congenital rubella syndrome in all WHO Regions. The TAG also requested the WHO Secretariat to support Member States to gather country-specific information on vaccine hesitancy and diagnosis of root causes and to develop strategies to overcome hesitancy and to build demand for vaccination. The TAG encouraged the WHO Secretariat to continue to work with all Member States to maintain polio-free status in the Region by addressing gaps in population immunity and AFP surveillance, and to expand environmental surveillance using WHO guidance. The TAG also encouraged WHO Secretariat to continue to support priority Member States in strengthening vaccine-preventable disease surveillance and improving data quality.

The TAG endorsed the *Regional Guide for Accelerated Control of Japanese Encephalitis in the Western Pacific* and the *Field Guide for Preparedness and Response to Diphtheria Outbreaks in the Western Pacific*. Finally, the TAG requested the WHO Secretariat to further develop the *Regional Strategic Framework for Vaccine-Preventable Diseases and Immunization in the Western Pacific, 2021-2030*, obtaining input from ministries of health, WHO country offices and headquarters, and other partners and stakeholders.

ABBREVIATIONS

ADB	Asian Development Bank
AEFI	adverse event following immunization
AFP	acute flaccid paralysis
APSED III	Asia Pacific Strategy for Emerging Diseases and Public Health Emergencies
bOPV	bivalent oral poliovirus vaccine
CCS	containment certification scheme
CDC	Centers for Disease Control and Prevention
cVDPV2	circulating vaccine-derived poliovirus type 2
DAT	diphtheria antitoxin
DoV	Decade of Vaccines
DTap or Tdap	diphtheria, tetanus, pertussis vaccine
DTP3	three doses of diphtheria-tetanus-pertussis vaccine
EC	Emergency Committee
eJRF	electronic Joint Reporting Form
EMT	emergency medical teams
EOC	Emergency Operations Centre
EPI	Expanded Programme on Immunization
FETP	Field Epidemiology Training Program
GAPIII	Global Action Plan, third edition
GBT	Global Benchmarking Tool
GID	Global Immunization Division
GPEI	Global Polio Eradication Initiative
GPS	global positioning system
GPW13	Thirteenth General Programme of Work
GRISP	Global Routine Immunization Strategies and Practices
GVAP	Global Vaccine Action Plan
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
Hib	*Haemophilus influenzae* type b
HKIA	Hong Kong International Airport
HPV	human papillomavirus
HQ	headquarters
HSE	Health Security and Emergency
ICT	information and communication technology
IDSC	Infectious Diseases Surveillance Center
IHR	International Health Regulations (2005)
IPV	inactivated poliovirus vaccine
IVI	International Vaccine Alliance
JE	Japanese encephalitis
MCV	measles-containing vaccine
MI4A	market information for access to vaccines
ML	maturity level
MMR	measles, mumps and rubella vaccine
MR	measles-rubella vaccine
MRCV	measles- and rubella-containing vaccine
MR-OPV	measles, rubella and oral polio vaccine
NAC	National Authority for Containment
NESVPD	National Epidemiological Surveillance of Vaccine-Preventable Diseases
NCD	non-communicable diseases
NCGM	National Center for Global Health and Medicine

NCIRS	National Centre for Immunisation Research and Surveillance
NIID	National Institute of Infectious Diseases
NIP	national immunization programme
NITAG	national immunization technical advisory group
OPV	oral poliovirus vaccine
PCV	pneumococcal conjugate vaccine
PEF	poliovirus-essential facility
PHEIC	Public Health Emergency of International Concern
PHC	primary health care
PICs	Pacific Island countries
PNG	Papua New Guinea
PV2	poliovirus type 2
QMS	quality management system
R_0	reproduction number
RF	Regional Framework
RI	routine immunization
RVC	Regional Verification Commission for Measles and Rubella Elimination
SAGE	Strategic Advisory Group of Experts
SDG	Sustainable Development Goal
SI	sub-indicators
SIA	supplementary immunization activity
TAG	Technical Advisory Group
TCV	typhoid conjugate vaccine
tOPV	trivalent oral poliovirus vaccine
UHC	universal health coverage
UNICEF	United Nations Children's Fund
VDPV	vaccine-derived poliovirus
VPD	vaccine-preventable disease
WHA	World Health Assembly
WHO	World Health Organization
WPR	Western Pacific Region
WPRO	WHO Regional Office for the Western Pacific
WPV	wild poliovirus
WUENIC	WHO/ UNICEF Estimates of National Immunization Coverage

1 INTRODUCTION

1.1 Meeting Organization

The 28th Meeting of the Technical Advisory Group (TAG) on Immunization and Vaccine-Preventable Diseases in the Western Pacific Region was held on 18-212 June 2019 in Manila, Philippines. The meeting was attended by six TAG members, four temporary advisors, 30 participants from 14 countries and areas, 53 representatives from partner organizations, and WHO staff from headquarters, the Regional Office for the Western Pacific and representative country offices. Annex 1 contains the list of participants, and Annex 2 contains the meeting programme.

1.2 Meeting Objectives

The objectives of the meeting were:

(1) to review progress, identify critical issues and determine key actions to achieve the regional immunization goals and strategic objectives specified by the GVAP;

(2) to identify opportunities to enhance coordination and collaboration among immunization-related initiatives, programmes and partners to support countries in achieving the regional immunization goals and GVAP strategic objectives; and

(3) to finalize the draft post-2020 regional framework for action on immunization and vaccine-preventable diseases in the Western Pacific to be widely shared with partners for extended consultation.

2 PROCEEDINGS

2.1 Opening Session

In his videotaped opening remarks, Dr Takeshi Kasai (Regional Director, WPRO) acknowledged that immunization programmes (IP) and the control and elimination of vaccine preventable diseases (VPD) are the most successful public health interventions in the last 50 years, particularly in the Western Pacific Region. Most notably, the Region has sustained its polio-free status since 2000 and achieved and sustained at least 95% coverage of the third dose of diphtheria-tetanus-pertussis vaccine (DTP3) since 2009. In 2018, the Expert Resource Panel verified 21 countries and areas in the Region as having achieved the goal of less than 1% hepatitis B surface antigen (HBsAg) prevalence among 5-year-old children. In the same year, the Regional Verification Commission (RVC) for Measles and Rubella Elimination confirmed nine

countries and areas as having achieved and sustained measles elimination. Presently, all countries and areas in the Region except one have achieved maternal and neonatal tetanus elimination.

Nevertheless, low vaccination coverage and sub-national pockets of unvaccinated children in some countries highlight the vulnerability of successes in public health intervention, which may reverse the progress in other countries in the future. Examples are the large-scale, nationwide resurgence of measles in the Philippines since last year and the largest outbreak of circulating vaccine-derived poliovirus (cVDPV) in Papua New Guinea in 2018. Other factors that pose a risk to IP in the Region include the continuing population growth, mass urbanization and migration, geopolitical uncertainty, natural disasters, and environmental disruptions.

Dr Kasai concluded that sustaining immunization gains will be challenging but, without constant vigilance, there is a risk for complacency, which can undermine national immunization programmes. Dr Kasai suggests establishing a long-term vision of a "desired future state" and work backwards to identify actions needed today towards achieving that state. Experiences and realities on the ground should guide actions; thereby, solutions always emerge from the "grounds up." Finally, Dr Kasai expects this 28th TAG meeting to continue providing practical recommendations for implementing the Global Vaccine Action Plan (GVAP) towards 2020 and also preparing new visions and strategic directions for immunization and VPD control and elimination in the Western Pacific in the coming decade.

2.2 Context and Perspectives

2.2.1 Global Overview - Implementation of GVAP and SAGE developing post-2020 global immunization vision

As the GVAP is coming to an end in 2020, a new vision and strategy for vaccines and immunization is needed to set a new direction for the next decade that engages and aligns stakeholders at all levels; addresses emerging issues; harnesses solutions for impact, and reiterates the importance of vaccinations in contributing to the broader health and development agenda. Although GVAP sparked attention and commitment, not all of its five goals and six strategic objectives will be met by 2020.

Immunization Agenda 2030 provides a dynamic way forward for the decade 2021–2030. This global strategy sets the priorities and worldwide goals for the next decade, complemented by an online resource that includes implementation plans and a Monitoring and Evaluation framework, which will evolve throughout the period. Because the benefits of immunization are

currently spread unevenly between and within countries, Immunization Agenda 2030 is intended to inspire and align the plans and activities of the country, region, and global audiences and stakeholders. Therefore, achieving the Immunization Agenda 2030 vision will ensure that everyone everywhere has access to immunization.

The Draft Zero document was being co-created in a wide stakeholder consultation concurrent with the 28th WPRO TAG Meeting. Draft One will be sent out on 3 July 2019 for input by WHO Member states until 5 August 2019 after which, the Immunization Agenda 2030 will be presented to the Strategic Advisory Group of Experts (SAGE) in October 2019, the WHO Executive Board in the first quarter of 2020 and finally, for endorsement at the World Health Assembly in May 2020.

2.2.2 Regional overview (1) - TAG reports to SAGE on implementation of GVAP in the Western Pacific Region

Since 2016, all WHO regions report to SAGE their regional progress on implementation of GVAP through the regional immunization TAGs. The report outlines the progress and achievements toward global and regional immunization goals on GVAP and the Regional Framework (RF) for the period of 2014 to mid-2019, in line with the five goals of Decade of Vaccines (DoV). The report also highlights the challenges, perspectives and country highlights. Professor Helen Oh May Lin, TAG vice-chair, presented the summary of the report.

Nearing the end of the DoV, the Western Pacific Region (WPR) is steadily making considerable progress towards achieving global and regional immunization goals, including implementing many Priority Actions proposed by the RF. Achieved and on-track are six out of eight regional immunization goals, while the other two goals of measles elimination and meeting regional vaccination coverage targets are in progress.

The potential risk for the resurgence of VPDs such as measles, polio, diphtheria and pertussis due to the population immunity gaps is a huge concern in the region. The reports particularly highlighted the emergence and outbreaks of cVDPVs and ongoing measles transmission in some countries. Sustainable domestic immunization financing and maintaining demand and acceptance of vaccines and immunization are important areas that the TAG stressed attention by countries. In short, the key factors to making continued progress and sustaining gains achieved in immunization and VPD eliminations are intensifying all available strategies to closing existing population immunization gaps, continued commitment by the governments, and partners support.

2.2.3 Regional overview (2) - Background and objectives of the 28th TAG

The regional overview summarized the context, challenges, and opportunities for VPDs in the WPR, which informed the objectives of the 28th TAG meeting. An evolutionary chart illustrated the progress of VPDs in the WPR during the last 50 years and highlighted the dramatic improvement of immunization programmes (IP), including in developing countries. Specific to the WPR is its polio-free status since 1997.

Following this was an update on progress towards the *Regional Framework for Implementation of the Global Vaccine Action Plan (GVAP) in the Western Pacific 2014-2020*, which had 8 immunization goals, 20 strategies, and 36 priority actions. Progress towards the goals included 1) sustaining polio-free status; 2) measles elimination in all high-income countries in the Region and Cambodia; 3) rubella elimination in Australia, Brunei Darussalam, Macao SAR, New Zealand, and the Republic of Korea; 4) maternal and neonatal tetanus elimination in Cambodia, China, the Lao PDR, the Philippines, and Viet Nam; 5) chronic hepatitis B (HBV) case reduction, and 6) introduction of new vaccines in a percentage of 27 countries and areas in the Region, such as *Haemophilus influenza*e type b (Hib) (96%), Human papillomavirus (HPV) (48%), and pneumococcal conjugate vaccine (PCV) (63%).

Challenges to progress include the resurgence and import-related measles outbreaks, circulating vaccine-derived poliovirus (cVDPV), and diphtheria outbreaks. Preparing for the next decade of implementation, the WHO Regional Office for the Western Pacific Expanded Programme on Immunization (WPRO/EPI) drafted the *Post-2020 Regional Framework for Action on Immunization and Vaccine-Preventable Diseases in the Western Pacific*, which takes into consideration the opportunities for innovation in addressing present and future challenges posed by the more diverse IP needs of each country and area in the Region.

2.3 Measles and Rubella Elimination

2.3.1 Global update on measles resurgence in multiple regions and progress towards establishment of global commitment to measles eradication

Is the global measles resurgence a Public Health Emergency of International Concern (PHEIC)? Under the International Health Regulations (IHR) 2005, PHEICs may be declared during public health events that have the potential to cross borders and threaten people worldwide and that require the coordinated mobilization of extraordinary resources for prevention and response by the international community. The IHR Emergency Committee (EC) has, so far, declared four

PHEICs: 1) Influenza A(H1N1) pandemic in 2009; 2) polio resurgence in 2014; 3) Ebola outbreak in West Africa in 2014, and 4) Zika virus outbreak in 2016. Of these, the polio declaration is the only one that continues.

WHO requires Member States to report a potential PHEIC when a public health event meets two of the following four criteria: 1) the impact of the public health event is serious; 2) the public health event is unusual or unexpected; 3) there is a risk for international spread, and 4) there is potential for restrictions on trade and travel. The current measles resurgence meets all four criteria. It is a serious event that resulted in a 22% increase in deaths in 2017; it is unexpected in that a global expert consultation in 2010 concluded that measles eradication is technically and programmatically achievable; its basic reproduction number (R_0) is 16, which is high-risk for international spread, and it has caused travel restrictions.

Should the EC declare the measles resurgence a PHEIC it could: 1) re-energize the global community to urgently strengthen health systems to ensure that every child born receives two potent doses of measles-containing vaccine; 2) stimulate innovations in communicating with migrants and travellers on the risks of measles and the benefits and safety of immunization; 3) refocus weary donors on the return on investment in measles immunization and accelerated elimination, and 4) release emergency funding from the Pandemic Emergency Financing Facility of the World Bank Group. Nevertheless, whether measles is declared a PHEIC or not, the global community should not give up its goal towards eradication because it makes sense epidemiologically, economically, and ethically.

2.3.2 Progress, achievements and challenges in (i) implementing the 2017 Regional Committee resolutions and (ii) operational targets by 2020 (including the 2017-2019 resurgence in the PHL)

The Western Pacific Region (WPR) faces many challenges in achieving measles and rubella elimination including, a large nationwide outbreak of measles in the Philippines due to chronically poor routine immunization coverage; multiple importation-related outbreaks in eliminated or low-incidence countries; insufficient capacity for rapid and effective outbreak response and prevention of healthcare-associated spread of measles and rubella in several countries and areas; insufficient case-based surveillance at the sub-national level; and insufficient surveillance capacity to detect congenital rubella syndrome (CRS) cases following rubella outbreaks in many countries.

However, although WPR is experiencing an increase in measles transmission during 2018 - 2019, including increased importation of the virus from endemic countries to many WPR Member States, WPR continues to make encouraging progress towards measles and rubella

elimination. All Member States except Vanuatu has introduced a second dose of measles-containing vaccine (MCV); the overall two-dose MCV coverage is 94% region-wide, but there is still wide variation in coverage among Member States. Thirteen countries conducted nationwide supplementary immunization activities (SIAs) during 2010 - 2019, including a measles rubella-oral polio vaccine (MR-OPV) campaign in Papua New Guinea in June to July 2019. WPRO developed the new *Regional Strategy and Plan of Action for Measles and Rubella Elimination* (2018) to guide the Region's response to newly identified challenges and incorporate lessons learned during the measles resurgence of 2013 - 2016; four countries have used this document to develop new final or draft national action plans for measles and rubella elimination. Finally, as of September 2018, the Regional Verification Commission (RVC) for Measles and Rubella Elimination verified nine countries and areas as having eliminated measles; and five have eliminated rubella.

2.3.3 Cambodia: Measles outbreaks and responses in 2018-2019

Since the RVC declared Cambodia free of endemic measles in 2015, the country has had multiple measles outbreak due to importation of the virus from endemic countries including, 66 cases in 2017, three cases in 2018, and 54 cases as of June 2019. Most of the cases in 2019 are from community transmission in Siem Reap Operational District (OD); however, nosocomial transmission in major hospitals in the OD also occurred. Outbreak investigation found that 75% of cases were unvaccinated and cases are occurring mostly among children aged at least five years. Also documented were multiple chains of transmission due to repeated importation.

Response to the outbreak has included 1) outbreak investigation and immunization response in affected villages; 2) measles and rubella (MR) immunization campaign in Siem Reap OD, which achieved 89% coverage; and 3) formal meetings with all major hospitals on infection prevention and control (IPC). Despite the response, challenges continue including 1) ongoing measles transmission; 2) immunization coverage remains low, with only 60% of ODs achieving ≥95% of MR1 and only 20% achieving ≥95% of MR2, and 3) global resurgence of measles and repeated importation due to endemic measles in neighbouring countries. To increase immunity against imported measles virus and sustain elimination, needed is a broader immunization response in Cambodia and, to reduce the burden of imported measles virus in Cambodia, also needed is a strengthened Regional commitment to measles elimination.

2.3.4 Hong Kong SAR, China: Measles outbreaks and responses in 2018-2019

The presentation described the upsurge of measles cases in Hong Kong in 2019, including a large outbreak at Hong Kong International Airport (HKIA). The characteristics of the outbreak include 1) multiple introductions with limited spread; 2) three generations of transmission; 3)

infection in adults aged at least 20 years, most of whom received at least two doses of the measles, mumps, and rubella (MMR) vaccine, and 4) modified measles presentation of milder symptoms without a fever. Enhanced outbreak response included serology testing to identify non-measles immune airport staff for subsequent vaccination and collaboration with the Airport Authority Hong Kong to implement environmental control measures that improve ventilation and air exchange. The outbreak epidemiology raised concerns that waning measles immunity in adults may have resulted in secondary vaccine failure with mild disease presentation.

2.3.5 New Zealand: Measles outbreaks and responses in 2018-2019

An increase in measles cases has occurred in New Zealand in 2019, including three major outbreaks in three regions. Outbreak investigations found that 1) all were imported cases; 2) most of the cases were unvaccinated individuals aged ≤15 months and ≥10 years, and 3) individuals born after 1985 had lower immunity than other cases. The presentation also described the national approach to outbreak management, using the Auckland outbreak as a case study. Each of four phases has different objectives, namely: 1) maintain high immunisation coverage with local elimination and prevention of transmission (Phase 0); 2) local elimination and prevention of transmission (Phase 1); 3) local elimination and preparation for outbreak management (Phase 2), and 4) reduce measles impact by improving MMR coverage (Phase 3). The challenges currently encountered include maintaining immunization coverage while managing vaccine shortages due to high demand and supporting regions that are overwhelmed by the surge in cases. Plans to move forward are to change the immunisation schedule to increase protection in infants; improve immunity in 10-29 year-olds who made up half of the cases and had the lowest immunity, and support regions to manage outbreaks.

2.3.6 Rubella outbreak and immunization strategy in Japan

An outbreak of rubella has occurred in Japan in 2019. The presentation summarized how the previous rubella control policy in Japan influenced the 2018-2019 outbreak and motivated changes in policy. The goal of the policy for rubella control in Japan was to achieve rubella and congenital rubella syndrome elimination before 2020. The policy recommended four strategies to accomplish the goal specifically, 1) routine vaccination at ages 1 and 6 years; 2) voluntary antibody testing and vaccination; 3) technical support for municipalities, and 4) evaluation of the policy by the national council meeting for measles and rubella control. Policy implementation brought about a decline in immunity in middle-aged men, due to a gap in rubella vaccination in men aged at least 40 years. The 2018 to 2019 rubella outbreak in Japan considerably affected more men aged 40 to 50 years than anyone else. In response to the

outbreak, and ahead of the Tokyo 2020 Olympics, Japan set new goals to raise seroconversion rates in men born between 1962 and 1979 to 85% by 2020 and 90% by 2022. The strategies are free rubella antibody testing for subsequent vaccination, routine immunization in men aged 40-57 years, and accessibility to free clinics to encourage uptake in middle-aged men.

2.3.7 Risk analysis of outbreaks/ resurgence of measles and rubella in the Western Pacific Region: How to achieve operational targets by 2020

The Regional Strategy and Plan of Action for Measles and Rubella Elimination in the Western Pacific describes several operational targets for 2020 including, 1) prevent the resurgence of endemic measles virus; 2) sustain interruption of measles virus in countries that have achieved elimination, and 3) prevent large-scale outbreaks after importation. Many issues and challenges in the WPR must be addressed in order to achieve the operational targets by 2020 including, 1) residual immunity gaps among children due to chronically poor routine measles- and rubella-containing vaccine (MRCV) coverage, such as in the Philippines; 2) outbreak risk due to "hidden" immunity gaps among subpopulations not adequately reached by current national strategies, such as among specific ethnic minorities in Lao PDR; 3) growing immunity gaps among young adults and adolescents in countries and areas achieving measles elimination; 4) risk of CRS cases due to rubella outbreaks affecting adults of childbearing age, such as in Japan and China; 5) cross-border, stateless, and migrant populations not adequately targeted by immunization or surveillance strategies, such as border communities in the Greater Mekong Delta Basin sub-region and in Sabah State, Malaysia; 6) health-care associated transmission, and 7) lack of a coordinated global or regional initiative, which places sustainability pressures on countries that have achieved elimination.

2.3.8 Measles and rubella elimination: regional goal 2030 and strategic direction

WPRO developed the *Regional Strategy and Plan of Action for Measles and Rubella Elimination in the Western Pacific* as a result of the new challenges and issues identified and analysed during the region-wide measles resurgence in 2013 to 2016. The document serves as guidance for individual Member States to develop national action plans for measles and rubella elimination. In addition to implementing the Regional Strategy through developing national action plans, WPRO proposes a new strategic direction for achieving measles and rubella elimination by 2030 while advancing WHO's broader agenda of health systems strengthening and equity. The new direction includes 1) strengthening and enhancing overall immunization systems through measles and rubella elimination strategies, such as school-based immunization initiatives, injection and immunization safety, and cold chain capacity building; 2) improving broader public health infrastructure and interventions through measles and rubella elimination strategies including, implementing the second year of life platform, strengthening overall

outbreak preparedness, establishing CRS surveillance, enhancing capacity to use epidemiological data for action, identifying individuals who are not reached by existing health services delivery strategies, and preventing nosocomial disease transmission, and 3) developing and implementing coordinated and synchronized cross-border initiatives to improve immunity among migrant and stateless populations and reduce cross-border importation.

2.4 Polio Eradication

2.4.1 Global overview from the perspective of current and anticipated developments and challenges

The presentation highlighted the status of the global polio eradication initiative. From 2017 to the present, two countries reported wild type poliovirus type 1 - Afghanistan and Pakistan. The risk for transmission in these countries is high, and the incidence of wild poliovirus-associated cases is already four times that of last year. In Afghanistan, access is the principal challenge. Particularly in the Southern Region, anti-government elements have restricted house-to-house vaccinations since May 2018, with hundreds of thousands of children unreached. In Pakistan, campaign quality and “silent refusals” are the primary obstacles.

Of most concern is the emergence of circulating vaccine-derived polioviruses type 2 (cVDPV2), following the withdrawal of Sabin type 2 poliovirus in April 2016. While outbreaks outside of Africa were brought under control, incidences in Sub-Saharan countries are of grave concern. In particular are the emergence and subsequent geographic spread of cVDPV2, and the “new” emergence of VDPV2 and cVDPV2 following supplemental immunization activities (SIAs). The eradication initiative developed a new strategic plan for 2019-2023, which addresses these challenges; fosters further integration with the routine immunization program, and attempts to eradicate poliovirus during this period.

2.4.2 Regional overview from the perspective of current and anticipated developments and challenges

The Western Pacific Region successfully maintains its polio-free status since 2000. Majority of Member States maintain over 90% coverage with three doses of polio vaccines. To cover immunity gaps China, Kiribati, Philippines, PNG and Viet Nam implemented multiple rounds of supplementary immunization activities (SIA) with polio vaccines. All countries and areas in the Region have successfully introduced one dose of IPV in their national schedules, following introduction in Viet Nam on September 2018 and in Mongolia on April 2019.

Majority of Member States in the Region maintain high quality, sensitive acute flaccid paralysis (AFP) surveillance. However, gaps in performance still exist in Lao PDR, Mongolia, Philippines, PICs and PNG. On March 2019, the WPRO/EPI conducted the first Regional polio outbreak simulation exercise to strengthen the outbreak preparedness and response capacity of Cambodia, China, Lao PDR and Viet Nam. Global Polio Eradication Initiative (GPEI) funding is being scaled down for non-endemic countries and regions, and support to the Member States in the Region is already affected, with a confirmed 25% decrease in 2020.

2.4.3 Regional overview of the implementation of poliovirus laboratory containment (GAPIII) in the Western Pacific

WHO developed the *Guidance to Minimize Risks for Facilities Collecting, Handling or Storing Materials Potentially Infectious for Polioviruses* to assist facilities to assess the risk of poliovirus potentially infectious materials in their possession, and to implement appropriate risk-reduction strategies consistent with GAPIII. Globally, there are 79 Poliovirus-essential Facilities (PEFs) in 27 countries. Five of these countries are in the Western Pacific Region - Australia, China, Japan, the Republic of Korea and Viet Nam - where PEFs handle and store WPV, VDPV, OPV, and Sabin PV2.

Member States endorsed the resolution on poliovirus laboratory containment at the World Health Assembly on May 2018, which urged Member States to complete inventories for type 2 polioviruses and report to WHO by 30 April 2019; destroy unneeded type 2 materials, and begin inventories and destruction of unneeded type 1 and 3 materials, in accordance with the latest available published WHO guidance. The resolution also urged all countries to request PEF to formally engage in the Containment Certification Scheme (CCS) as soon as possible and no later than 31 December 2019, by first submitting their applications for participation to their National Authority for Containment (NAC).

2.4.4 Update on outbreak of circulating vaccine-derived poliovirus (cVDPV) in Papua New Guinea

Papua New Guinea (PNG) authorities declared an outbreak of circulating vaccine-derived poliovirus type 1 (cVDPV1) on June 2018. Supported by partners and donors, the PNG government immediately initiated a comprehensive outbreak response, tasking the National Emergency Operations Center (EOC) with overall outbreak management and coordination. In addition, all 22 provinces established Provincial EOCs for more effective communication and coordination.

The outbreak response, which included implementing evidence-based and technically sound strategies, involved enormous financial and human resources but led to notable improvements

in AFP surveillance. Since the outbreak, more than 10 million children aged 15 years and below received polio, measles or rubella, and other vaccines. An external outbreak assessment in May 2019 concluded that cVDPV1 transmission has likely been interrupted in PNG. However, to declare the outbreak closed, it is important to further strengthen the current level of surveillance and routine immunization for the next six months, due to the remaining surveillance and population immunity gaps.

2.4.5 cVDPV in the Western Pacific Region: Lessons learned in the last 20 years

As the world approaches eradication of wild poliovirus transmission circulating vaccine-derived polioviruses (cVDPVs) continue to take on added significance. In 2018, the number of paralytic cases was three times higher due to cVDPVs than wild poliovirus. Although there are efforts to tackle risk factors, the surest way to prevent cVDPVs in the future is to stop oral polio vaccine (OPV) use rapidly. And, although the Western Pacific Region reported the last indigenous wild poliovirus case in 1997 and certified polio-free in 2000, outbreaks due to cVDPVs present a continuous risk for the region since certification.

Afghanistan and Pakistan are the only two countries in the world with ongoing transmission of the wild poliovirus, and the risk of exportation of the wild poliovirus to polio-free countries is now very low. The current biggest risk related to poliovirus in polio-free countries or regions that still use OPV in their routine immunization schedules is the emergence and circulation of vaccine-derived polioviruses. The Expanded Programme on Immunization of the WHO Regional Office for the Western Pacific (WPRO/EPI) is starting preparations for OPV use cessation in the Region and switch to IPV-only schedules to advance global eradication of polio.

2.4.6 Implication of long-term use of oral polio vaccine in polio-free countries

The presentation covered the rationale for the withdrawal of Sabin oral poliovirus vaccine (OPV); the experience with the shift from trivalent (tOPV) to bivalent oral poliovirus vaccine (bOPV), and the consideration of countries in polio-free regions for the switch to an all-inactivated poliovirus vaccine (IPV) schedule. Switching reduces the risks associated with OPV use, including vaccine-associated paralytic poliomyelitis (VAPP) and the emergence of circulating vaccine-derived poliovirus type 2 (cVDPV2). However, OPV induces intestinal mucosal immune responses that would be particularly important for countries in the Region that border the wild poliovirus type 1-endemic countries of Afghanistan and Pakistan. Therefore, the benefits of IPV need to be balanced with that of OPV, especially since the IPV supply does not support the large-scale expansion of IPV use. An intermediate approach could be the addition of a second IPV dose in routine immunization schedules. WHO/HQ/POL intends to bring this issue for discussion and eventual decision-making to the WHO Strategic Advisory

Group of Experts (SAGE), the principal technical advisory committee for immunization because the issue of all-IPV schedules has global implications.

2.4.7 Polio eradication: Regional goal 2030 and strategic direction

WPRO/EPI started development of the *Regional Strategic Framework for VPDs and Immunization in the Western Pacific 2021-2030*. One of its proposed goals is "no paralysis due to any type of poliovirus in the Western Pacific Region." However, despite past achievements, maintaining polio-free status in the Region faces several challenges including, 1) gaps remain in population immunity against poliovirus and surveillance for acute flaccid paralysis (AFP) at the national and sub-national levels; 2) continued use of OPV and limited global supply of IPV; 3) insufficient national capacity for outbreak preparedness and response and complacency in polio laboratories to accurately detect poliovirus, and 4) the need to timely implement polio laboratory containment activities. To address these challenges and achieve and maintain the goal, proposed implementation strategies include 1) sustain high level population immunity against poliovirus with routine and supplemental vaccination; 2) withdraw OPV use and immunize populations with IPV against possible re-emergence of any poliovirus; 3) sustain highly sensitive polio surveillance systems and regional polio laboratory network with skilled staff for accurate and timely detection of poliovirus; and 4) control or remove potential sources of poliovirus properly, in line with the GAPIII.

2.5 Vaccine-preventable Disease Surveillance, Laboratory Support and Data Management

2.5.1 WHO Immunization Information System (WIISE) for better access and use of data

WHO has a mandate to monitor and assess health trends, including those related to vaccine-preventable diseases, and has collected data from Member States since the inception of EPI. Over time, data have increased in quantity and complexity. These have created challenges such as fragmentation, duplication and inconsistencies in data collection, as well as inadequate governance over the data and sub-optimal access to and visualization of data. Therefore WHO (HQ and all Regional Offices) is developing the WHO Immunization Information System (WIISE), which is a collection of applications to collect, manage, analyze and disseminate immunization and VPD surveillance data reported to WHO worldwide. WIISE aims to improve the WHO data submission process for Member States through an electronic Joint Reporting Form (eJRF) and a module to submit measles and rubella surveillance data (XMart). In addition, the joint WHO/

UNICEF Estimates of National Immunization Coverage (WUENIC) will enable better access and visualization of data available in WHO while ensuring much-needed data protection and adherence to data sharing policies.

2.5.2 VPD seroprevalence surveillance system for developing and evaluating immunization strategies

In 1962, Japan established the National Epidemiological Surveillance of Vaccine-Preventable Diseases (NESVPD) as part of national surveillance systems for infectious diseases, to understand the actual situation of herd immunity against VPDs; search for causative factors of disease; promote the effective management of immunization programs, and predict the trends of diseases. Every year, prefectures voluntarily send remaining clinical sera to local laboratories, with consent from the selected individuals. Laboratory testing is conducted at the local level and results are analysed at the Infectious Disease Surveillance Center (IDSC) of the National Institute of Infectious Diseases (NIID), Japan. Results are disseminated through annual reports and in the NIID website.

In 2019, the diseases included in the serosurvey were polio, influenza, Japanese encephalitis, rubella, measles, HPV, varicella and hepatitis B. NESVPD has contributed and continues to identify immunity gaps and ascertain the impact of immunization intervention. For example, NESVPD data were used for measles elimination activity to guide the introduction of MCV2, to conduct catch-up MR vaccination in target age groups showing lower immunity levels.

2.5.3 Moving towards comprehensive VPD surveillance: documenting VPD surveillance status and best practices in the Western Pacific Region

Many surveillance systems in countries are fragmented or not functionally optimal across vaccine preventable diseases (VPDs) or both. WHO is developing a Global Comprehensive VPD Surveillance Strategy, which will be finalized by the end of 2019, to support the Immunization Agenda 2021-2030. Comprehensive VPD surveillance is defined as the country, regional and global systems required to meet the minimal recommended standards for surveillance of a comprehensive set of priority VPDs, with the integration of surveillance functions across other diseases where possible.

The U.S. Centers for Disease Control and Prevention (CDC) is collaborating with WHO/WPRO and WHO/HQ on a project to review the status of VPD surveillance in the Region and to document the challenges, enabling factors and innovations for integrating common functional components (e.g. personnel, logistics, and laboratory) for VPD surveillance systems in countries in the Western Pacific Region. As part of the process, surveillance focal points in countries will

be contacted about an online survey, and several countries will be asked to help to prepare case studies on specific aspects of their surveillance program. This work will help inform the next Regional Immunization and VPD Strategy.

2.5.4 VPD surveillance systems: regional goal 2030 and strategic direction

Based on findings from VPD surveillance reviews, observations during outbreak response, analysis of data reported to WHO, and a survey conducted in 2017 survey, all countries in the WPR have a surveillance system for measles, rubella and polio, but not all have systems for other VPDs. These systems are often non-compliant with the minimum requirements for quality surveillance, as defined by WHO guidelines. Therefore, while some countries are integrating surveillance for different diseases, VPD surveillance is often fragmented and vertically organized, which leads to excessive expenses and workload, as well as data discrepancies.

Overall, across countries in the WPR, there is a large variability of VPD surveillance maturity and performance; capacity for surveillance is often limited, and resources are inadequate. The strategic directions to address these challenges in 2021-2030 include to 1) expand quality surveillance to other VPDs (polio/AFP, measles, rubella, CRS, diphtheria; neonatal tetanus and Japanese encephalitis in all countries, and VPDs based on country context); 2) achieve for one or more surveillance functions the integration or optimization of the use of resources for VPD surveillance (i.e. specimen transportation, data management, surveillance review, etc.); 3) ensure adequate legal or regulatory frameworks and resources; 4) build capacity through effective pre-service and on-the-job training, including mentoring programs, distance learning, and Field Epidemiology Training Programs (FETP); 5) strengthen laboratory support capacity, particularly for bacterial diseases; 6) support the development of information and communication technology (ICT) solutions appropriate to the country context, and 7) ensure the availability, dissemination, and use of surveillance data for action at all levels.

2.5.5 VPD laboratories and networks: regional goal 2030 an strategic direction

WPRO/EPI coordinates five regional VPD laboratory networks consisting of 500 public health laboratories for polio (43) since 1992, measles and rubella (385) since 2001, Japanese encephalitis (20) since 2009, rotavirus (32) and invasive bacterial-vaccine preventable diseases (20) since 2010. These VPD laboratory networks are facing challenges including, still depending on WHO support; reduced funding that may affect elimination and eradication programmes; funds allocated for specific surveillance programmes; lack of integrated VPD surveillance systems; high workload during outbreaks (e.g., measles), and risk of complacency in polio laboratories due to the absence of poliovirus.

A regional strategy aims to maintain functional and sustainable laboratory surveillance for VPDs through (i) providing technical and financial support to VPD laboratories of priority countries; (ii) implementing Quality Management System (QMS) continuously; iii) promoting the shift of funding from specific diseases to integrated VPD surveillance to allow testing for differential diagnosis; and (iv) improving epidemiological and laboratory surveillance collaboration for VPDs in routine and outbreak situations; applying correct case definition criteria; collecting adequate specimens, and using appropriate laboratory resources.

2.6 Regional Technical Guidelines

2.6.1 Regional guide for accelerated control on Japanese encephalitis in the Western Pacific Region

The presentation outlined the rationale for accelerated Japanese encephalitis (JE) control in the Region and described the aims and targets of accelerated JE control and the contents of the draft technical guide for achieving accelerated control of JE in the Western Pacific Region. The draft includes three sections: 1) background, which discusses JE disease, surveillance, prevention and existing global guidance on JE control; 2) JE situation in the Western Pacific Region, which discusses strategies, progress and achievements in implementing strategies, and the rationale for accelerated control of JE, and 3) proposed regional guidance for accelerated control of JE, which describes the regional target, strategic areas, and strategic area activities for achieving accelerated JE control.

2.6.2 Field guide for preparedness and response to diphtheria outbreaks in the Western Pacific

The presentation provided an overview of diphtheria cases and vaccination schedules in routine immunization programmes in countries and areas in the Region. WHO recommends a three-dose primary vaccination series administered in the first year of life and three booster doses in early childhood through adolescence, preferably at age 12–23 months, 4–7 years, and 9-15 years. Also presented were 1) epidemiology of diphtheria outbreaks in the Lao People's Democratic Republic, Malaysia, the Philippines and Viet Nam; 2) methods and key milestones in developing the contents of the "Field guide for preparedness and response to diphtheria outbreaks in the Western Pacific Region"; 3) disease management and treatment with equine diphtheria antitoxin (DAT), and 4) DAT stockpiles and potential needs in the Region.

2.7 Vaccine Immunization Safety

2.7.1 Regional overview on routine immunization programme - progress, achievements and challenges

Presented were two immunization events in 2017-2018 that received regional attention. One was adverse events following immunization (AEFI) linked with the "Dengvaxia" programme in the Philippines, which described the response activities and the consequent negative impact on overall country immunization programmes. Who facilitated the causality assessment by an independent international team of experts to support the Department of Health; implement follow-up activities to improve dengue clinical management in 2018, and seek expert consultation in 2019 on re-building public confidence and encourage uptake of immunization in the Philippines.

The other was temporarily suspended immunizations by the government of Samoa, following two deaths linked to MMR vaccination on July 2018. WHO and other partners provided support for an investigation, which cited the cause as immunization errors related reactions. All vaccinations resumed on September 2018 except for MMR, which resumed on April 2019. MMR vaccinations followed intensified training and preparedness assessments conducted by the Ministry of Health, with the support of WHO and UNICEF. Nevertheless, overall immunization coverage in Samoa remained low during the period, and social media and other anti-vaccine groups actively carried out campaigns to attract public and political attention.

Reporting adverse events following immunization (AEFI) improved in the Region, but only 12 Member States have met the WHO reporting rate of 10 AEFI cases per 100,000 surviving infants. WHO continues to provide technical support for in-country capacity building, and conducted its first regional workshop for WHO staff on vaccine and immunization safety on April 2019.

2.7.2 Regional progress on vaccine regulatory and safety in the Western Pacific

WHO has conducted an assessment of vaccine regulatory systems in one vaccine producing country since the last TAG meeting - Viet Nam. Using the Global Benchmarking Tool (GBT, Revision V), WHO assessed Viet Nam's National Regulatory Authority on 283 sub-indicators (SI), and found that they had not met 21 out of 210 SI on maturity levels (ML) 1 to 3. Provided were 26 recommendations for corrective actions to meet ML 3. The WHO Regional Office for the Western Pacific recognizes the important contributions of Japan International Cooperation Agency (JICA), PATH, and other partners in the successful technology transfer of measles-rubella and seasonal influenza vaccines in Viet Nam, which paves the way towards expanding the global supply of quality-assured, affordable vaccines .

The WHO Regional Office for the Western Pacific (WPRO) convened the *Seventh Workshop for National Regulatory Authorities for Vaccines and Medicines in the Western Pacific* in Manila on August 2018, to update the strategic objectives and renew the composition of the steering committee. WPRO also convened a meeting of the Regional Alliance Steering Committee to discuss strategic plans for the next four years and agree on priority areas for technical working group activities.

As a way forward, WHO EPI teams, in collaboration with WHO emergency medical teams (EMT), will continue to support Member States in effectively responding to issues of public health concern including, immunization serious adverse events, and substandard and falsified vaccines.

2.8 Vaccine Acceptance and Demand

2.8.1 Vaccine acceptance and demand: global overview

The presentation offered an overall update on global acceptance and demand for immunization, considering the many drivers of vaccine uptake. It referenced specific examples that place a strong focus on currently available data, to illustrate the factors related to both access and acceptance that serve as enablers or barriers to vaccination, and it addressed possible misconceptions about the prevalence of vaccine hesitancy. The presentation also outlined a range of interventions that programmes could consider, to build and sustain vaccine demand and to manage the various risks associated with social media and misinformation. For example, programmes are encouraged to work at multiple levels (individual, community, and public), and to implement evidence-informed, multi-component strategies that target specific enablers and barriers to vaccination. Finally, the presentation emphasized the importance of investing in generating vaccine demand to avoid the spread of misinformation and committing to prevent vaccine-preventable diseases from re-emerging.

2.8.2 Country experience: promotion of vaccine acceptance and demand

The Republic of Korea National Immunization Programme (NIP) began in 1954. National and local (province, city) governments are responsible for its implementation, which they fund through the “health promotion fund subsidy program.” Meanwhile, the private sector leads the NIP service delivery, which covers 90% of the target population. At present, there are 20 vaccine types included in the NIP. To increase acceptance and demand for vaccines and immunization, the NIP has taken the following strategies: 1)

increase access to vaccination through free immunizations at public health centres and private clinics; 2) individualize immunization services through "Immunization Assistant," the website and mobile application that sends reminders, issues certificates of vaccination, and checks vaccination history online and via mobile phones; 3) mandatory vaccinations for children attending elementary and middle schools. Specifically, DTap, IPV, MMR and JE for those aged 4 to 6 years, and Tdap and HPV for those aged 12 years, and 4) implement vaccine safety management programmes, including transparent information sharing and public awareness. Nevertheless, the country faces challenges in maintaining high acceptance and demand for vaccine including, vaccine hesitancy, vaccinating migrant workers and multi-cultural families, and delay in vaccine supply, 70% of which the country imports.

2.8.3 Western Pacific Region guidance on generating acceptance and demand for vaccination

The 25th Meeting of the Technical Advisory Group (TAG) on Immunization and Vaccine Preventable Diseases in the Western Pacific recommended developing a guidance document to support countries in the Region to overcome vaccine hesitancy and generate and sustain acceptance and demand. The specific objectives of the regional guideline are to support Member States to 1) develop awareness of the main concepts related to vaccine demand, acceptance, and hesitancy; 2) understand the main interventions and steps to build and sustain acceptance and demand; 3) recognize vaccination barriers and enablers among specific populations, and 4) design and evaluate targeted strategies to address hesitancy and generate demand. The draft guideline, which is for the use of EPI staff and partners, has the following structure and content: 1) general background to vaccine issues and situations in the Western Pacific Region; 2) methods and survey tools for diagnosing under-vaccination and hesitancy, and 3) strategies to generate and sustain acceptance and demand. WPRO will continue working with relevant stakeholders to finalize the draft for Member State endorsement at the 29th TAG Meeting in 2020.

2.9 New Vaccines

2.9.1 Underutilized vaccines and new vaccines in 2021-2030: Global perspective

The presentation was an overview of available new vaccines, with a focus on 1) patterns of uptake and coverage including, cases studies on Hib, HPV, pneumococcal conjugate and

rotavirus vaccines; 2) factors influencing uptake and coverage, and 3) a look into the future for new vaccines.

Included were a discussion on the large increase in vaccine innovation since 2000; numbers of vaccines introduced in national immunization schedules in 2017 compared to 2000; proportion of countries globally that have introduced Hib (98%), HPV (50%), pneumococcal conjugate (74%) and rotavirus (52%) vaccines, and global coverage estimates during 1980-2017. Factors affecting new vaccine introduction include actual and perceived disease burden and impact; cost-effectiveness versus affordability; national decision-making capacity (e.g., NITAGs) and competing priorities; combination vaccines or "switches" (e.g., Hib/Penta), and global supply constraints (e.g., IPV, HPV and rotavirus vaccines). Finally discussed were market information for access to vaccines (MI4A) studies, which provide global analyses on vaccine supply and demand dynamics, and the future of new vaccines, focusing on HIV, malaria, TB, RSV and dengue vaccines.

2.9.2 Underutilized vaccines ad new vaccines 2021-2030 in the Western Pacific Region

The presentation gave an overview of available new vaccines and introduced new vaccines globally and in the Western Pacific Region. Also discussed was the progress towards achieving the GVAP new vaccine target that all low- and middle-income Member States introduce at least one new vaccine during 2010–2020. The vaccines considered as new are *Haemophilus influenzae* type b (Hib), human papillomavirus (HPV), Japanese encephalitis (JE), pneumococcal conjugate (PCV), and rotavirus (RV). Sixteen low- and middle-income countries had not introduced any of the new vaccines before 2010, 11 (69%) of which successfully introduced at least one vaccine between January 2010 and April 2019 - all nine lower-income countries, and two out of seven (29%) upper-middle-income countries. Countries in the Western Pacific Region continue to make progress in introducing new vaccines, though new vaccine introduction by upper-middle-income countries lags substantially behind that in lower-middle-income countries. Selected new vaccines are expected to be introduced in the Region during 2021-2030, including typhoid conjugate vaccine, respiratory syncytial virus, dengue, and malaria vaccines.

2.10 Immunization Service Delivery

2.10.1 Overview and future of immunization services throughout the life-course

Global initiatives on primary health care (PHC) and universal health coverage (UHC) highlight the need for a life-course approach to achieve SDG3: "Ensure healthy lives and promote well-

being for all at all ages." A life-course approach recognizes that the health outcomes of individuals and the community depend on the interaction of multiple protective and risk factors throughout people's lives. This comprehensive vision of health and its determinants calls for the development of health services that are more centred on the needs of people at each stage of their lives. Driving the impetus for a life-course approach to immunization are these external shifts, the epidemiological shifts (immunity gaps and waning in older age groups, outbreaks, etc.), and the programmatic introduction of new vaccines that follow schedules outside of the "traditional EPI" infant target group.

The concept of immunization service "delivery platforms" (including pregnant women, birth, 2nd year of life, child, adolescent, adult, and older persons) is a useful way to group vaccines according to life-stage The presentation focused on routine immunization (RI) evolution in the Western Pacific Region and the achievements, challenges, limitations, and needs for expanding RI service delivery through life-course immunization. The substantial contributions of country RI platforms to improving and strengthening overall immunization systems include 1) innovative policy and financing; 2) robust logistic and cold chain systems, and 3) skilled human resources, particularly in the areas of management, surveillance, and regulation. Closer to the end of the "Decade of Vaccines," the Region has made considerable progress towards achieving many of the Regional Framework (RF) goals. Examples include focused government leadership in Cambodia; stable service delivery system in China; sustainable domestic financing in the Republic of Korea, and sustainable vaccine supply in Malaysia. However, Regional diphtheria-tetanus-pertussis (DTP3) coverage for three doses is 93.4%, which is the first time since 2009 that the coverage is below 95%. Finally, the changing epidemiology of some VPDs, such as rising cases of diphtheria and measles among adolescents and adults, and the increasing need to immunize migrant populations and occupational groups (e.g., staff at points of entry and healthcare, day care, elderly, and food facilities) highlight the need for expanding RI platforms beyond childhood and across the life-course.

The priority in the Region beyond 2020 is to, therefore, strengthen and expand immunization services to close immunity gaps among the underserved and beyond childhood. The *Global Routine Immunization Strategies and Practices* (GRISP) document contains a comprehensive framework of strategies to transform immunization services and support life-course platforms. Strategies include maximizing reach, managing programmes, mobilizing people, and monitoring progress.

For many countries, adopting life-course vaccination requires policy changes, demand generation, and greater investment in booster doses to sustain long-term immunological

protection. These offer opportunities for integration, inter-sectoral collaboration, and increased coverage (i.e., catching up missing doses).

2.10.2 Regional overview on routine immunization programme: progress, achievements and challenges

The presentation focused on routine immunization (RI) evolution in the Western Pacific Region and the achievements, challenges, limitations, and needs for expanding RI service delivery through life-course immunization. The substantial contributions of country RI platforms to improving and strengthening overall immunization systems include 1) innovative policy and financing; 2) robust logistic and cold chain systems, and 3) skilled human resources, particularly in the areas of management, surveillance, and regulation. Closer to the end of the "Decade of Vaccines," the Region has made considerable progress towards achieving many of the Regional Framework (RF) goals. Examples include focused government leadership in Cambodia; stable service delivery system in China; sustainable domestic financing in the Republic of Korea, and sustainable vaccine supply in Malaysia. However, Regional diphtheria-tetanus-pertussis (DTP3) coverage for three doses is 93.4%, which is the first time since 2009 that the coverage is below 95%. Finally, the changing epidemiology of some VPDs, such as rising cases of diphtheria and measles among adolescents and adults, and the increasing need to immunize migrant populations and occupational groups (e.g., staff at points of entry and healthcare, day care, elderly, and food facilities) highlight the need for expanding RI platforms beyond childhood and across the life-course.

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2.10.3 Country experience: Improve delivery of immunization through a combination of different strategies (e.g., routine immunization, SIA, school-based immunization, etc.) - China

China's vaccination program has made notable progress towards targeting goals for vaccine-preventable diseases and improving vaccine coverage including, 1) maintaining polio-free status; 2) eliminating maternal and neonatal tetanus in 2012; 3) decreasing incidences of HBV infections to 0.32% in children aged under 5 years in 2014; 4) reducing VPD incidences to a

historically low level in 2018 (e.g., 3 per million population for measles), and 5) achieving over 95% national coverage for all vaccines used for infants in 2018.

China adopted a system-strengthening approach to vaccinate each child through enhancing registration and vaccination routinely, school entry vaccination checks, and supplementary immunization. Their strategies include 1) high-level political commitment to the Immunization Programme; 2) immunization knowledge popularization through social media; 3) investment from Central Government for vaccine procurement, subsidies, surveillance, and cold chain; 4) upgrading legislations and requirements on vaccine distribution and vaccination management, communicable diseases prevention, and school entry vaccination checks, and 5) vaccination service system with 176,000 deployed sites cross-country, and with efficient vaccine delivery, cold chains, information management, and disease surveillance.

China intends to continue efforts on the introduction of new vaccines (e.g., Hib, varicella vaccine, PCV, rotavirus, EV71), maintaining polio-free status and measles and rubella elimination, and improving the children's immunization information management system and the vaccine tracking and tracing system.

2.11 Draft Regional Strategic Framework for Vaccine-preventable Diseases and Immunization in the Western Pacific, 2021-2030

This meeting session comprised of 12 presentations on the zero draft of the *Regional Strategic Framework for Vaccine-preventable Diseases and Immunization in the Western Pacific, 2021-2030.* The EPI at WPRO developed the draft document for the next decade of implementation of GVAP. It takes into consideration the many opportunities for innovation including, combination vaccines; new vaccine delivery mechanisms, such as controlled temperature chain and micro-needle patches, and tracking using smartphones and global positioning system (GPS) mapping. It also considers the challenges that the next decade of implementation may bring, influenced globally by a growing population, rapid urbanization, expanding population movement, and increased migration and non-citizen states. Challenges anticipated include changes in financial and ideological commitment to global disease eradication initiatives; recurring outbreaks; increasing infections throughout the life course, and interruptions on vaccine services and supplies.

The vision of the framework document is a Western Pacific Region that is free from mortality, morbidity and disability due to vaccine-preventable diseases. In order to attain this vision, the

strategic goal is to achieve, accelerate, and sustain the control and elimination of more vaccine-preventable diseases. Using back-casting to work towards the vision and goal, the strategic objectives of the Regional framework are to 1) strengthen and expand immunization systems and programmes; 2) manage health intelligence on vaccine-preventable diseases and immunization, and 3) prepare for and respond to public health emergencies.

Strategic objective one (SO1) outlines how to strengthen each of the eight core components that include 1) governance and management; 2) financing; 3) health workforce; 4) vaccine regulation and safety; 5) vaccine and logistics; 6) advocacy and communication; 7) service delivery, and 8) programme review. Strategic objective two (SO2) has four core components, namely 1) VPD surveillance; 2) laboratory capacity and networks; 3) monitoring and evaluation, and 4) data for action. Finally, strategic objective three (SO3) has the following five core components 1) outbreaks and resurgence of VPDs; 2) vaccine and immunization safety events; 3) outbreaks requiring immunization responses (e.g., cholera and typhoid); 4) emergencies affecting immunization systems and programmes (e.g., smallpox virus release), and 5) other public health emergencies (e.g., pandemic influenza).

In line with the WHO White Paper, the draft framework also strongly encourages the implementation in the next decade of three areas that are synergistic with the White Paper thematic priorities including, 1) health system strengthening and universal health coverage; 2) preventing non-communicable diseases (NCD) and promoting the life-course approach, and 3) health security and emergency and environment and climate change.

2.12 Working with Immunization Partners

The Asian Development Bank (ADB) representative presented their goal to increase health investments in the Region from 2% to between 4% and 5% by 2030. The ADB committed USD 515 million to health investments in 2018, of which USD 29.6 million targets PCV, HPV and rotavirus vaccines in the Pacific Island countries (PICs) of Samoa, Tonga, Vanuatu and Tuvalu. The ADB focuses on the four PICs because 1) they are all middle-income countries that, therefore, cannot access initiatives for introducing newer vaccines, such as Gavi, the Vaccine Alliance; 2) they are small-island economies that have weak purchasing power, and that can benefit from economy of scale through pooled procurement measures, and 3) the ADB goal aligns with the Pacifica Health Island Monitoring framework to reduce VPDs.

The International Vaccine Institute (IVI, Republic of Korea) presenter gave a brief introduction of the IVI as an international organization with 160 partners, all of which are committed to global health. Also introduced were IVI capacities, which included laboratory science, field programs, and data and policy. Summarized was a list of several candidate vaccines that are under different stages of development. Finally, outlined were ongoing projects in the WPR including, 1) clinical phase trials of typhoid conjugate vaccine in the Philippines; 2) real-time tracking of neglected bacterial diseases and antimicrobial susceptibility patterns in Asia, and 3) data capture consortium on antimicrobial susceptibility patterns and trends in Asia.

The presenter from the National Center for Global Health and Medicine (NCGM, Japan) described their activities in providing international expert services, training and research. Examples of NCGM activities in the Region in 2019 include a nationwide serological survey in the Lao PDR, and the anti-MMR IgG and HBsAg survey in Viet Nam. The objectives of the Lao PDR survey are to 1) estimate the population immunity to measles and rubella, and compare the results to data from 2014; 2) estimate hepatitis B and hepatitis C prevalence, and 3) determine the socio-demographic factors affecting immunization in the country. Similarly, the Viet Nam survey collects data on immunity to measles, mumps, rubella and hepatitis B, in people aged one to 39 years. Included in the survey are four provinces with a total of 12 districts, 24 communes, and 48 villages.

The presenter from the National Centre for Immunisation Research and surveillance (NCIRS, Australia) reminded the TAG of their 21 years as independent technical specialists on immunization and vaccines for Australia. The key role of NCIRS is to support the Australian government on all key national data sets and peak national advisory committees. However, they also provide Regional assistance on NITAG support; all aspects of AEFI; vaccine acceptance, hesitancy and demand, and program monitoring and evaluation. Their recent regional projects include 1) a workshop for vaccine experts and policy and program managers on improving vaccine confidence, demand and uptake, and 2) the establishment of the Australian Regional Immunisation Alliance (ARIA), whose goal is to work collaboratively with governments, global immunisation partners, non-government organizations and other stakeholders to strengthen and expand immunization, and reduce the impact of VPDs in the WPR.

The presenter from the National Institute of Infectious Diseases (NIID, Japan) spoke of the roles of the NIID in immunization and VPD control in the WPR. The institute has six functions, namely 1) surveillance of infectious diseases and pathogens; 2) basic and applied research on infectious diseases; 3) reference laboratory activities; 4) quality assurance programs on vaccines; 5) international cooperation activities, and 6) technical staff training. The institute has three

virology laboratories - Virology I is the WPR JE specialized lab; Virology II is a WHO Polio laboratory, and Virology III is a laboratory specializing in measles, mumps, rubella and respiratory viruses (not including influenza). NIID Regional work includes an annual laboratory training course for the control of VPDs. In the next three years, their national and Regional goals are to 1) maintain their status in poliomyelitis eradication and measles elimination; 2) eliminate rubella by 2020, and 3) strengthen the monitoring and response to VPDs during mass gatherings including, the 2019 Rugby World Cup and the 2020 Tokyo Olympic and Paralympic Games.

The presenter from PATH outlined their Center for Vaccine Innovation and Access (CVIA); vaccine-related activities in the WPR for 2014-2019; upcoming vaccine-related activities; typhoid conjugate vaccine (TyVAC); and Japanese encephalitis vaccine activities close-out. The primary objectives of the CVIA are to 1) develop vaccines to prevent infectious diseases; 2) focus on vaccines that protect women and children; 3) technical assistance to developing country vaccine manufacturers, and 4) introduce public health vaccines to lower-income and lower-middle-income countries. Currently, the CVIA is developing two vaccines for 17 diseases, and has more than 30 projects to ensure effective vaccine uptake in Asia and Africa. PATH activities in the WPR include vaccines for Japanese encephalitis, typhoid, hepatitis B, influenza (seasonal, pandemic and avian), human papillomavirus and rotavirus. TyVac is the first licensed typhoid conjugate vaccine (TCV) that WHO included in its pre-qualified list in 2017, and one of its multi-disciplinary strategies to combat typhoid is to support countries in decision-making and preparing for sustainable typhoid conjugate vaccine introduction. Finally, after the many JE vaccine-related contributions in the Region, PATH has scheduled a close-out of its JE activities in December 2019, following the convening of global JE experts in August 2019 and the "Lessons Learnt Summit" in October 2019.

The presenter from UNICEF outlined the support they provide for children in 22 WPR countries and five South-East Asian Region countries. UNICEF support includes coverage and equity; demand generation; accelerate VPD control, and health system strengthening. For example, UNICEF supported Papua New Guinea through measles campaigns during earthquake emergencies; cVDPV outbreak response; MR-OPV campaign for measles elimination, and routine immunization and health system strengthening. Nevertheless, the continuing focus in the Region is on children disadvantaged by urbanization (e.g., children living in the slums). UNICEF support involves multi-sectoral engagement through social policy, child protection, education, and private engagement so that no child is overlooked.

The presenter from the U.S. Centers for Disease Control and Prevention (CDC) outlined their programmatic priorities and the work of the Global Immunization Division (GID) with Tier 2 countries in the Region. The CDC programmatic priorities are polio eradication; measles- and rubella-free world; ending VPDs in children aged less than five years; reducing chronic disease and cancer deaths from VPDs; improved VPD outbreak detection and response, and channeling or transitioning polio experiences and assets. Tier 2 countries are those with low immunization capacity and high numbers of unvaccinated children. For the WPR, these countries include Cambodia, China, Laos, Philippines and Viet Nam. GID work in some of these countries include 1) CRS surveillance development; 2) support for hepatitis B control; 3) support for the introduction of new vaccines for typhoid, HPV and influenza, and 4) support for VPD surveillance and data management. In addition, GID provided support to Papua New Guinea through polio outbreak response and polio SIAs.

3 Conclusions and Recommendations

3.1 Conclusions

Measles and rubella elimination

1. The TAG commends Member States of the Western Pacific Region for steady and encouraging progress toward the strategic objectives and operational targets established by the WHO Regional Committee for the Western Pacific in October 2017 through endorsement of the *Regional Strategy and Plan of Action for Measles and Rubella Elimination in the Western Pacific* (WPR/RC68.R1).

2. The TAG notes the encouraging overall epidemiological trend of measles in the Region and the sustained progress of the majority of countries in the Region towards measles and rubella elimination. The largest country, China, has made substantial progress and provides a noteworthy example of how to strengthen routine immunization delivery and target high-risk groups, including migrants, to minimize the risk of measles in the country.

3. The TAG congratulates the Western Pacific Region in preventing a broad resurgence of measles in the Region despite the global measles resurgence during 2018—2019. Endemic countries with large populations such as China and Malaysia have prevented large-scale measles transmission, and low-incidence countries and those that have eliminated measles have controlled spread of measles despite

experiencing multiple importation-related outbreaks.

4. The TAG notes that the epidemiology of both measles and rubella is changing, including increased transmission among adults and epidemiologically significant immunity gaps among specific groups who are not well targeted by existing strategies (e.g. specific ethnic groups, adults, and cross-border populations), which indicates that immunization strategies may need to be adjusted in response to signals in the epidemiology.

5. The TAG congratulates Singapore for achieving measles elimination; and congratulates Australia, Brunei Darussalam, and Macau SAR (China) for achieving rubella elimination during 2018.

6. The TAG congratulates Cambodia and Lao PDR for having finalized national plans of action for achieving and sustaining elimination of measles and rubella, and notes the progress of other Member States in preparing to achieve measles and rubella elimination and seek verification by the Regional Verification Commission.

7. The TAG commends Cambodia and Lao PDR for rapid and effective outbreak response immunization to prevent large-scale spread of import-related measles outbreaks.

8. The TAG notes that although WPR has sustained positive momentum towards Regional elimination of measles and rubella, numerous challenges and issues must be overcome in order to achieve these important goals:

    a. a global measles resurgence is ongoing, characterized by large-scale outbreaks, loss of long-held measles elimination status, cross-border spread with importation-related outbreaks, and vaccine hesitancy in some areas;
    b. a large, prolonged nationwide outbreak of measles is ongoing in Philippines during 2018—2019, highlighting both the risk of massive accumulation of susceptible individuals through unaddressed chronic weakness in routine immunization, as well as the challenges of achieving effective outbreak response in the face of emerging vaccination hesitancy and refusal;
    c. import-related outbreaks of measles and rubella in some countries and areas due to residual measles and/or rubella immunity gaps among adolescents and

adults, who are not targeted by routine childhood immunization and traditional mass vaccination campaigns; and

d. lack of coordinated global and regional actions to advance measles and rubella elimination.

Sustaining polio-free status and implementation of polio endgame strategies

9. The TAG appreciates the WHO Secretariat and Member States' successful efforts to maintain the Region polio-free for over 20 years. The TAG acknowledges that overall population immunity against poliovirus in the Region remains high, polio surveillance performance has exceeded regional targets for the main indicators, and the polio laboratory regional network has maintained high quality since its establishment.

10. The TAG congratulates Papua New Guinea on successful implementation of polio outbreak response activities that may have resulted in interruption of type 1 circulating vaccine-derived poliovirus (cVDPV1) circulation and efforts to establish environmental surveillance to monitor circulation of polioviruses. The TAG commends the Victorian Infectious Diseases Reference Laboratory (VIDRL), Australia; Research Institute for Tropical Medicine (RITM), Philippines; and National Institute of Infectious Diseases (NIID), Japan, for their support of the response to the cVDPV1 outbreak in Papua New Guinea with laboratory testing of acute flaccid paralysis (AFP) and environmental samples in 2018 and 2019.

11. The TAG notes that Mongolia and Viet Nam introduced inactivated polio vaccine (IPV) into routine immunization in April 2019 and September 2018, respectively.

12. Despite the achievements and progress made in sustaining polio-free status and implementing the polio endgame strategy in the Region, the TAG notes the following issues and challenges:

    a. risk of international spread of poliovirus remains a Public Health Emergency of International Concern, and the Western Pacific Region borders a region that has endemic transmission of wild-type poliovirus;
    b. vaccine-derived polioviruses (VDPV) intermittently circulate in the Region and there is a high risk of emergence and circulation of VDPV in oral polio vaccine

(OPV)-using countries with suboptimal population immunity against poliovirus and underperforming AFP surveillance;

c. need to maintain achievements from the response to polio outbreak in Papua New Guinea, and to monitor the outcomes of the response until the outbreak is declared closed;
d. immunity and/or surveillance gaps persist at subnational levels in China, Cambodia, Lao People's Democratic Republic, Malaysia, Mongolia, Pacific island countries, Papua New Guinea, Philippines and Viet Nam;
e. critical importance of continuing and expanding environmental surveillance to monitor the presence and circulation of polioviruses as the polio endgame reaches its final stages;
f. national inventories of all biomedical facilities that may contain poliovirus potentially infectious materials have not been completed in all countries in the Region;
g. final designation of polio essential facilities (PEFs) and establishment of fully functional National Authorities for Containment (NAC) in China and Viet Nam;
h. projected reduction of Global Polio Eradication Initiative (GPEI) financial support to maintain polio-essential functions in 2020 and beyond; and
i. continued tenuous global supply and high cost of IPV, challenges to use of fractional-dose IPV in the Region, very high cost of hexavalent vaccine and lack of a hexavalent combination product containing whole-cell pertussis vaccine (along with IPV, diphtheria and tetanus toxoids, hepatitis B vaccine and *Haemophilus influenzae* type b vaccine).

Surveillance and data management for vaccine-preventable disease control and elimination

13. The TAG acknowledges the Western Pacific Region for maintaining well-performing AFP, measles and rubella surveillance and establishing several sentinel sites to monitor the burden and changing epidemiology of diseases targeted by new or underutilized vaccines. The TAG also acknowledges the continued efforts made by Member States, WHO and partners to improve the quality of VPD surveillance data management by expanding the use of new tools (e.g. web-based reporting tools for AFP and acute fever and rash surveillance), conducting VPD surveillance reviews in priority countries (Cambodia, Lao People's Democratic Republic, Papua New Guinea and Viet Nam) and implementing new approaches (e.g. Immunization and Surveillance Data Specialist project in Lao People's Democratic Republic and Global Pediatric Diarrhea Surveillance

in Fiji, Lao People's Democratic Republic and Viet Nam).

14. Despite the achievements sustained and progress made in improving and strengthening VPD surveillance and data management in the Region, the TAG notes the following challenges to further progress toward well-performing VPD surveillance:

    a. inadequate surveillance system scope, in terms of geographical representativeness, use of recommended case definitions, reporting of cases on aggregate or case basis, as well as inclusion of all VPDs that should be under surveillance;
    b. insufficient training of human resources for detection and investigation of cases, surveillance data management and analysis;
    c. the need to maintain VPD surveillance key functions in integrated national surveillance systems (i.e., reporting of suspected cases and case classification following adequate investigation and laboratory testing);
    d. lack of surveillance and outbreak response guidance for various diseases in some countries;
    e. inadequate financial support and/or no plan for financial sustainability for VPD surveillance in some countries; and
    f. insufficient laboratory capacity for confirmation of diphtheria and pertussis in some countries, and for confirmation of measles and rubella in several Pacific island countries.

15. In addition, the TAG notes the following challenges to further progress toward well-performing immunization programme monitoring:

    a. inadequate quality and availability of expanded programme on immunization (EPI) data and indicators for monitoring and evaluation of the programme in some countries; and
    b. suboptimal use of data to guide decision-making, development of enhanced strategies, and preparedness and response to VPD outbreaks.

Laboratories and laboratory networks for vaccine-preventable disease control and elimination

16. The TAG acknowledges the substantial efforts made by the WHO Secretariat and Member States to maintain regional VPD laboratory networks with high-level performance in the Western Pacific, in order to provide accurate and timely data for elimination and eradication of VPDs and for introduction of new vaccines. The TAG notes the importance of maintaining high-quality VPD laboratories by providing technical and financial support to network laboratories of priority countries, particularly for polio laboratories facing low workload and complacency due to the long absence of poliovirus detection.

17. The TAG reaffirms the continuing challenge faced by many Member States in facilitating collaboration between epidemiological and laboratory surveillance for VPDs to ensure that case definition criteria are correctly applied, adequate specimens are collected, epidemiological and laboratory data are properly linked, and laboratory resources are adequately used, particularly during outbreaks.

18. The TAG acknowledges the ongoing work to develop a regional strategy to maintain functional and sustainable laboratory surveillance for VPDs (polio, measles, rubella, JE, invasive bacterial VPD and rotavirus) with skilled staff and high quality laboratory testing. Considering the reduction in donor financial support for laboratory surveillance, the TAG reaffirms the urgent need to promote national ownership of laboratory surveillance.

Accelerated Japanese encephalitis control

19. The TAG endorses the draft of *Regional Guide for Accelerated Control on Japanese Encephalitis in the Western Pacific*, taking into account the inputs provided during the TAG meeting.

Preparedness for and response to diphtheria outbreaks

20. The TAG endorses the draft of *Field Guide for Preparedness and Response to Diphtheria Outbreaks in the Western Pacific*, taking into account the inputs provided during the TAG meeting. The TAG further notes the challenges in ensuring availability of and access to diphtheria antitoxin (DAT) and the efforts of a WHO

headquarters ad hoc working group on DAT to ensure that any population experiencing cases of diphtheria has rapid and easy access to DAT.

Vaccine and immunization safety

21. The TAG commends Member States' continuous efforts to strengthen vaccine and immunization safety, particularly to improve reporting, investigation and rapid response to vaccine and immunization safety events. The TAG acknowledges the efforts of WHO to support the Philippines in responding to deaths among children who received dengue vaccine and to support Samoa for responding to infant deaths following measles, mumps and rubella (MMR) vaccination.

22. The TAG acknowledges the efforts of Member States and WHO to strengthen vaccine regulatory capacity to assure the quality, safety and effectiveness of vaccines. Specifically, Viet Nam undertook a WHO re-assessment of its vaccine regulatory system to extend WHO certification of functionality. China also initiated the re-assessment process with a revised benchmarking tool following decentralization of regulatory functions to provincial FDAs in 2018; decentralized functions include licensing of pharmaceutical manufacturers, suppliers and retailers; regulatory inspections including good manufacturing practices; clinical trial approval and oversight; and vaccine lot release and laboratory testing.

23. Despite progress towards vaccine and immunization safety, the TAG notes with concern that the following issues and challenges remain:

    a. continued under-reporting of vaccine and immunization safety events in some countries;
    b. gaps in timely and effective response and causality assessment following vaccine and immunization safety events in the Philippines and Samoa, resulting in decreases in overall immunization coverage;
    c. proper monitoring of national policy and standards implementation, and assurance of adherence, following decentralization of regulatory functions in China;
    d. critical regulatory gaps identified through re-benchmarking of Viet Nam’s regulatory processes, in particular, in the pharmacovigilance and laboratory testing systems: adverse events following immunizations (AEFI) data sharing,

investigation of severe adverse events, causality assessment, and animal health monitoring in the animal laboratory; and

e. self-benchmarking workshops and reports of EVM assessment found that middle-income vaccine importing countries need to strengthen the vaccine distribution chain quality management system.

Vaccine acceptance and demand

24. The TAG reaffirms the importance of public acceptance and demand for vaccination as critical components for increasing and sustaining the achievements of national immunization programmes. The TAG appreciates WHO efforts to develop the regional guide, *Generating acceptance and demand for vaccination: Strategies for building and sustaining vaccination uptake and addressing hesitancy*.

25. The TAG notes the challenges of vaccine hesitancy as described in the *SAGE 2018 Assessment Report of the Global Vaccine Action Plan* and the negative impact of hesitancy on immunization gains in the Western Pacific Region.

New vaccines introduction

26. The TAG notes the progress in introduction of new and underutilized vaccines in the Western Pacific Region. Of the 27 Member States in the Region, 18 introduced at least one of four new vaccines (Hib, HPV, pneumococcal conjugate, and rotavirus vaccines) since 2010 and an additional four Member States had introduced all of these vaccines before 2010. The TAG commends the progress in the introduction of new vaccines in low- and lower middle-income countries in the Region. Of the ten lower middle-income countries (LMICs) in the Region, one had introduced all four of these new vaccines before 2010, and all of the remaining nine LMICs have introduced at least one of these vaccines since 2010.

27. The TAG commends progress in the Region for developing and using evidence for making decisions on introduction of new vaccines and the continued support that WHO gives to governments on vaccination policy. Achievement of the Decade of Vaccines goals for introduction of new and underutilized vaccines requires that countries evaluate evidence on disease burden including surveillance, cost, the role of other disease prevention and control measures, vaccine characteristics, vaccine supply, and

strength of immunization programmes and health systems.

28. The TAG acknowledges challenges with new vaccine introduction, particularly the limited progress in upper middle-income countries, and the need to promote and facilitate new vaccine introduction in these countries. The TAG also notes the importance of laboratory-based surveillance for diseases prevented by new vaccines and the critical need to maintain surveillance and laboratory capacity in an era of declining resources.

29. Despite progress, the TAG notes the following issues and challenges:

    a. increasing introduction and sustaining vaccination programmes in middle-income countries, including those that will be graduating from eligibility for Gavi, the Vaccine Alliance (Gavi) support in the coming years;
    b. maintaining surveillance for diseases prevented by new vaccines and laboratory capacity in an era of declining resources; and
    c. determining the impact of new vaccine introductions and ensuring that they strengthen immunization delivery systems.

Immunization service delivery

30. The TAG congratulates Member States for the sustained high immunization coverage at the regional level and commends Member States' efforts to develop and implement strategies to improve coverage and strengthen routine immunization services to achieve regional and global immunization goals. The TAG congratulates China for impressive achievements in routine immunization coverage and historically low incidence of VPDs. The TAG appreciates WHO and partner efforts to support countries to strengthen routine immunization systems and to increase and sustain immunization coverage.

31. Despite progress in immunization coverage and routine immunization delivery, the TAG notes with concern the following challenges to further progress in coverage and to extending immunization delivery across the life course:
    a. decrease in regional diphtheria-tetanus-pertussis (DTP3) coverage to less than 95% for the first time since 2009 (in 2018 reported regional coverage for DTP3 is 93.4%);

b. uneven immunization coverage that results in pockets of susceptible person, favouring disease transmission and vaccine preventable disease (VPD) outbreaks;
c. changing epidemiology of VPDs including increases among older children, adolescents and adults, due to missed vaccination, lack of booster doses, waning immunity and other reasons;
d. limited platforms for immunization delivery beyond childhood to maximize the benefits of newer vaccines and schedules for adolescents, adults and the elderly; and to protect special at-risk groups including migrant workers, specific occupational groups and international travellers; and
e. insecure vaccine supply as the number of children receiving both traditional and newer vaccines increases.

Regional strategic framework for vaccine-preventable diseases and immunization in the Western Pacific, 2021-2030

32. The TAG appreciates the efforts of the WHO Secretariat in developing the draft *Regional Strategic Framework for Vaccine-Preventable Diseases and Immunization in the Western Pacific, 2021-2030* (hereafter, *Regional Strategic Framework*).

33. The TAG endorses the *Regional Strategic Framework*'s conceptual approach in which a strategic goal for the elimination and control of VPDs is achieved through three strategic objectives:

a. strengthening and expanding immunization system and programme;
b. managing health intelligence on vaccine-preventable diseases and immunization; and
c. preparing for and responding to public health emergencies related to VPDs, vaccines and immunization programmes.

34. These strategic objectives highlight the importance of data use to inform programme decisions and the linkages between immunization and health emergencies, while addressing the anticipated increased complexity of immunization programmes resulting from extending the benefits of vaccination through the life course, reaching additional population groups, and targeting newer vaccines that are indicated for specific at-risk groups or contexts.

3.2 Recommendations

3.2.1 Recommendations for Member States

Measles and rubella elimination

1. The TAG reiterates the recommendations of the 27th TAG meeting, including that Member States should implement the Regional Committee resolution, WPR/RC68.R1, which requests Member States to:

    a. develop or update national strategies and plans of action relating to measles and rubella elimination, including the establishment of a target year for rubella elimination; and
    b. ensure adequate technical and financial resources are available for the implementation of national strategies and plans of action for measles and rubella elimination.

2. The TAG urges all Member States to continue to implement the Regional Committee resolution, WPR/RC68.R1, including to:

    a. develop or update national strategies and plans of action relating to measles and rubella elimination, including the establishment of a target year for rubella elimination; and
    b. ensure adequate technical and financial resources are available for the implementation of national strategies and plans of action for measles and rubella elimination;

3. The TAG urges all Member States to use IHR mechanisms to notify outbreaks related to international travel or with risk of international spread.

4. The TAG urges all Member States to recognize the role that measles vaccination can play in improving routine immunization delivery, reducing equity gaps and strengthening primary health care, raise the need for a measles eradication goal at the World Health Assembly in 2020, to ensure maintenance of global commitment and achievement of elimination in all regions.

5. The TAG recommends each Member State to develop or update plans and procedures for preparedness and response to measles and rubella outbreaks, including establishing mechanisms to rapidly mobilize contingency resources and personnel for outbreak investigation, response, and post-outbreak root cause analysis to ensure immunization programmes are appropriately adjusted to address the underlying programme weaknesses; plans and procedures should be tailored to local context including programme and population size.

6. The TAG recommends each Member State to strengthen capacity for analysis of immunization coverage and surveillance data to identify subpopulations and geographic areas that are underserved by existing immunization strategies, and to guide programmatic changes and initiatives to prevent outbreaks.

7. The TAG recommends each Member State to address residual measles and/or rubella immunity gaps among adolescents and adults by planning and conducting targeted immunization initiatives, which may include school-based, university-based, occupationally-based, or travel-related immunization.

8. The TAG recommends each Member State to develop and implement national policies and procedures for hospital infection control for measles and rubella, to prevent healthcare-associated transmission and amplification of outbreaks, referring to WHO guidance (*Infection prevention and control of epidemic- and pandemic-prone acute respiratory infections in health care*, 2015).

9. The TAG recommends each Member State to continue to use investment in measles and rubella elimination activities as a means to strengthen immunization programmes and overall public health systems, including development of an immunization visit during the second year of life to achieve high coverage of the second dose of measles-containing vaccine.

10. The TAG recommends Member States that have achieved or are approaching elimination of measles or rubella to consider developing national policies to ensure that international students, workers, and others who are entering the country or area for an extended period, are appropriately vaccinated against measles and rubella.

11. The TAG recommends the Philippines to take all necessary actions to achieve measles outbreak control urgently, and to seek external assistance as needed to facilitate rapid control.

Sustaining polio-free status and implementation of polio endgame strategies

12. The TAG urges all Member States to achieve and maintain more than 90% coverage with three doses of polio vaccines at the national level and to address population immunity gaps, particularly in high-risk areas, by conducting supplementary immunization activities (SIAs) if needed.

13. The TAG urges all Member States to achieve and maintain regional targets for core AFP surveillance indicators and to conduct active surveillance in underperforming areas.

14. The TAG urges all Member States to consider initiation of poliovirus surveillance among patients with PIDs to detect immunodeficiency-related VDPV (iVDPV), following the GPEI Guidelines for Implementing Poliovirus Surveillance among Patients with Primary Immunodeficiency Disorders, and to consider establishment of a registry for patients with these disorders.

15. The TAG urges all Member States to ensure that national polio outbreak response plans are updated in accordance with the global guidance for timely and comprehensive response to any polio event or outbreak and tested by conducting polio outbreak simulation exercises.

16. The TAG urges all Member States to initiate the identification, followed by destruction, transfer or containment, of WPV1 and WPV3 infectious and potentially infectious materials and ensure completion of this task by the end of Phase II of GAPIII (at the time of global certification of poliomyelitis eradication).

17. The TAG urges all Member States to complete national inventories of all biomedical facilities that may contain poliovirus potentially infectious materials and submit reports (WHO PIM Form 2) to WHO by September 1 2019.

18. The TAG urges all Member States to intensify efforts to initiate environmental surveillance for polioviruses in line with the GPEI global expansion plan and as outlined in the WHO guidance on environmental surveillance, and to seek resources to sustain this surveillance as an integral part of routine surveillance systems; this step is indispensable for completion of global polio eradication.

19. The TAG urges Papua New Guinea to further strengthen the performance of surveillance and routine immunization for the next 6 months for the cVDPV1 outbreak to be declared closed.

20. The TAG urges the Philippines to proactively address gaps in population immunity against polio and AFP surveillance performance to reduce the likelihood of a VDPV outbreak.

21. The TAG urges Member States that are supported by international partners to maintain polio-essential functions to establish capacity and resources for sustaining polio-essential functions, as outlined in the Polio Post-Certification Strategy (e.g., polio immunization, surveillance and containment).

22. TAG urges Member States with Polio Essential Facilities (PEFs) [1] to establish and operationalize a NAC responsible for certifying PEFs (China and Viet Nam) at the earliest possible time, in line with GCC recommendations.

23. TAG urges Member States with Polio Essential Facilities (PEFs) to start the certification process as soon as possible and submit associated reports to the GCC for validation not later than December 31, 2019.

Surveillance and data management for vaccine-preventable disease control and elimination

24. The TAG reiterates the recommendations of the 26th TAG meeting, including:

    a. Member States that have not yet established a congenital rubella syndrome (CRS) monitoring system should do so as soon as possible;

[1] Australia, China, Japan, Republic of Korea and Viet Nam

b. countries with VPD surveillance of suboptimal representativeness and/or sensitivity should strengthen their surveillance systems;
c. countries should prioritize strengthening the systems that support surveillance of diseases targeted by elimination goals; and
d. countries are encouraged to continue strengthening rotavirus and invasive bacterial VPD surveillance with laboratory confirmation.

25. The TAG recommends all Member States to strengthen surveillance for diseases targeted by new vaccines (rotavirus and invasive bacterial VPDs) and build capacity for laboratory diagnosis through training workshops, introduction of new technologies and implementation of quality assurance programmes.

26. The TAG recommends all Member States to review their VPD surveillance systems and ensure compliance with minimum requirements as detailed in the new WHO VPD surveillance guidelines, specifically with reference to the VPDs included in the surveillance system, case definitions, scope of the surveillance (i.e. national or sentinel-based) and aggregate or case-based data collection, and ensure that those minimum requirements are also met when VPD surveillance is integrated into broader communicable diseases surveillance.

27. The TAG recommends all Member States to sustain high performing VPD surveillance systems, in the context of possible decreasing external funding from partners and donors.

28. The TAG recommends all Member States to strengthen immunization data quality and use through:

a. improvement of data standards, recording and reporting tools, SOPs and, in countries where applicable, ensuring quality integration of EPI data and indicators in broad health information management platforms;
b. strengthening health workforce capacity for data management and use, including through coordination with broader health workforce development efforts and implementation of ISDS-like approaches[1];

[1] Immunization and Surveillance Data Specialists (ISDS) is a project that envision deployment of STOP team at subnational level to provide training and mentoring of health facility and district/provincial level staff on management and use of EPI and VPD surveillance data

c. considering implementation of an electronic immunization registry upon evaluation of feasibility, sustainability and definition of suitable system requirements; and
d. conducting coverage surveys and serosurveys based on internationally recommended methodologies, as necessary to complement and validate data available through routine monitoring.

Laboratories and laboratory networks for vaccine-preventable disease control and elimination

29. The TAG reiterates the recommendations of the 27th TAG meeting for Member States to:

    a. improve collaboration between epidemiological and laboratory surveillance for VPDs through:

        i. promoting collaboration of epidemiologists and laboratory experts in routine surveillance as well as in outbreak situations;
        ii. engaging both immunization programme and laboratory experts in national expert committees (national certification and verification committees, etc.);
        iii. ensuring that interpretation and use of data for reporting and final classification are jointly assessed from clinical and laboratory perspectives; and
        iv. collecting adequate specimens from every case for virologic testing in countries achieving or having achieved measles and rubella elimination to ensure all virus transmission is properly monitored.

    b. develop plans to achieve sustainable laboratory surveillance for VPDs through:

        i. development of long-term plans for disease surveillance with clear objectives and realistic milestones;
        ii. conducting self-assessments to map existing capacities and to identify strengths, gaps and challenges; and
        iii. assessing financial sustainability of existing surveillance.

30. The TAG recommends the Philippines and Malaysia to consider establishing subnational laboratories for measles and rubella to support laboratory confirmation for these diseases.

31. The TAG encourages Cambodia to establish laboratory capacity for molecular detection and genotyping of measles and rubella viruses.

Accelerated Japanese encephalitis control

32. The TAG reiterates the recommendations of the 27th TAG meeting that:

    a. Member States that have not achieved effective control of JE disease should develop and implement national plans for accelerated control of JE, using the *Regional Guide for Accelerated Control on Japanese Encephalitis in the Western Pacific;* and
    b. Member States that use or are planning to use live attenuated JE vaccine should forecast the number of JE vaccine doses they will need to ensure that the vaccine doses are distributed in advance of when they are needed.

33. The TAG notes that the Philippines is JE endemic in all regions and urges the Philippines to continue implementation of JE vaccination and achieve high coverage in all areas of the country.

Preparedness for and response to diphtheria outbreaks

34. The TAG reiterates the recommendations of the 27th TAG meeting that:

    a. all Member States should update their national immunization schedules in line with the 2017 WHO position paper on diphtheria vaccines, to include:

        i. a primary series of three doses of diphtheria toxoid-containing vaccines, completed by 6 months of age, if possible; and
        ii. three booster doses in childhood and completed by adolescence with doses specifically recommended to be given at: 12–23 months of age; 4–7 years of age; and 9–15 years of age; and

b. Member States that have been frequently affected by diphtheria outbreaks to develop national guidelines for preparedness and response to diphtheria outbreaks, using the *Field Guide for Preparedness and Response to Diphtheria Outbreaks in the Western Pacific Region*.

Vaccine and Immunization Safety

35. The TAG reiterates the recommendations of the 27th TAG meeting, including that:

    a. Member States ensure that national regulatory authorities (NRA) function to meet WHO global benchmarks, supporting the availability of quality-assured vaccines; and
    b. Member States improve AEFI reporting, investigation and timely response capacity including risk communication.

36. The TAG urges Member States to share information and best practices to learn from each other's experience with response to vaccine and immunization safety events, including experience with addressing rumours and misinformation.

37. The TAG urges Member States to make continuous efforts to:

    a. strengthen reporting, investigation and causality assessment of immunization safety events; and
    b. provide timely and appropriate evidence-based responses to vaccine and immunization safety events.

38. The TAG urges Member States to strengthen the vaccine distribution chain quality management system.

39. The TAG urges Member States to adopt the new WHO benchmarking policy and tool to identify and address vaccine regulatory gaps.

Vaccine Acceptance & Demand

40. The TAG reiterates the recommendations of the 25th TAG meeting for Member States to work proactively on identifying and addressing country-specific vaccine hesitancy issues.

41. The TAG recommends each Member State to identify reasons for vaccine hesitancy in the local context, establish mechanisms to monitor vaccine acceptance and demand, and implement tailored strategies and activities to address barriers to vaccination.

New Vaccines

42. The TAG reiterates the recommendations of the 27th TAG meeting that Member States should:

    a. develop national plans for evidence-based introduction of new vaccines;
    b. monitor and improve surveillance implementation for diseases targeted by new vaccines;
    c. use recommended immunization schedules and should not add immunization visits solely for the purpose of preventing the administration of multiple injections during the same visit, as recommended by SAGE in April 2015; and
    d. continue to introduce new vaccines that are recommended by WHO for inclusion in national immunization programmes and sustain and enhance the vaccination programmes that have been established.

43. The TAG urges all Member States to continue to introduce new vaccines recommended by WHO for inclusion in national immunization programmes, and sustain and enhance established vaccination programmes.

Immunization Service Delivery

44. The TAG reiterates the recommendations of the 27th TAG meeting, including that Member States:

    a. secure sustainable domestic financing for immunization;

b. explore and implement immunization system strengthening strategies articulated in the Global Routine Immunization Strategies and Practices (GRISP) document; consider in particular strategies needed to reduce inequities in immunization coverage by reaching children of ethnic minorities and migrant groups and those living in dense urban areas and remote areas;
c. strengthen the functionality and effectiveness of NITAGs or equivalent immunization decision-making bodies to support formulation of evidence-based immunization policy; and
d. strengthen vaccine procurement processes for timely vaccine supply and effective vaccine management practices.

45. The TAG recommends each Member State to intensify the identification of barriers and use of tailored strategies to improve immunization coverage among underserved populations and to close immunity gaps.

46. The TAG recommends each Member State to identify and implement strategies to extend immunization across the life course and maximize the benefits of newer vaccines and schedules for adolescents, adults and the elderly; and to protect special at-risk groups including migrant workers, specific occupational groups and international travellers.

Regional Strategic Framework for Vaccine-Preventable Diseases and Immunization in the Western Pacific, 2021-2030

47. The TAG urges all Member States to consider their current immunization achievements and challenges, and appropriate objectives for the next decade, and to contribute to the *Regional Strategic Framework* as requested by the Secretariat.

48. The TAG urges all Member States to consider national financial and human resources and how they can contribute to the objectives of the *Regional Strategic Framework.*

3.2.2 Recommendations for WHO Secretariat

Measles and Rubella Elimination

1. The TAG requests WHO Secretariat to advocate to Member States and partners for an increased global commitment to achieving and sustaining measles and rubella elimination, continuous reduction and sustained prevention of measles deaths and CRS in all WHO Regions.

2. The TAG requests WHO Secretariat to provide technical support to the Philippines and other countries facing measles outbreaks to conduct effective outbreak investigation and response, and to strengthen their immunization and health systems to address the root causes of the outbreak.

3. The TAG requests WHO Secretariat to finalize the draft *Field Guide for the Surveillance of Congenital Rubella Syndrome (CRS) in the Western Pacific Region*.

4. The TAG requests WHO Secretariat to develop draft regional guidelines for preparedness and response to measles and rubella outbreaks through consultation with the TAG, NIPs, and partners.

5. The TAG requests WHO Secretariat to develop other regional technical guides as recommended during the 26th TAG meeting, including:

    a. field guidance for planning and implementing MRCV SIAs; and
    b. field guidance for measles and rubella surveillance.

6. The TAG requests WHO Secretariat to ask the Regional Verification Commission (RVC) to consider defining parameters to measure progress toward measles elimination in very large countries.

7. The TAG requests WHO Secretariat to request SAGE to consider the questions arising around the effects and the significance of possible waning immunity in adults fully immunized with two valid doses, as has been described in the recent Hong Kong outbreak.

8. The TAG recommends WHO Secretariat to continue to support Member States to:

    a. develop, update, and implement their national plans for measles and rubella elimination and set a national target date for rubella elimination;
    b. plan, prepare, and conduct high-quality SIAs to fill immunity gaps due to inadequate routine immunization;
    c. develop and implement quality CRS surveillance;
    d. strengthen measles and rubella case-based laboratory-supported surveillance; and
    e. strengthen outbreak preparedness and response capacity.

9. The TAG recommends WHO Secretariat to support Member States to identify opportunities and to develop and implement plans for cross-regional, sub-regional, and multi-country collaboration, coordination, and synchronization of strategies and activities for measles and rubella elimination.

10. The TAG recommends WHO Secretariat to continue to work with the Regional Verification Commission on Measles and Rubella Elimination in the Western Pacific in documenting, evaluating progress towards measles and rubella elimination.

11. The TAG recommends WHO Secretariat to support Member States to use International Health Regulation (IHR) mechanisms to notify outbreaks related to international travel or with risk of international spread.

12. The TAG recommends WHO Secretariat to recognize the role that measles vaccination can play in improving routine immunization delivery, reducing equity gaps and strengthening primary health care, facilitate the Member States to raise the need for a measles eradication goal at the World Health Assembly in 2020, to ensure maintenance of global commitment and achievement of elimination in all regions.

Sustaining Polio-free Status & Implementation of Polio Endgame Strategies

13. The TAG encourages WHO Secretariat to continue to work with all Member States to maintain polio-free status in the Region by addressing gaps in population immunity and AFP surveillance, particularly gaps in population immunity against type 2 poliovirus since the global cessation of OPV2 use in 2016, and to maintain

environmental surveillance where already established, using WHO guidance on environmental surveillance.

14. The TAG encourages WHO Secretariat to continue to support Papua New Guinea efforts to achieve and confirm closure of the outbreak of cVDPV1.

15. The TAG encourages WHO Secretariat to support the Philippines urgently to address immunity gaps to reduce the likelihood of a VDPV outbreak.

16. The TAG encourages WHO Secretariat to continue to support Member States, especially Cambodia, Lao People's Democratic Republic, Papua New Guinea, Philippines and Viet Nam, to establish or expand environmental surveillance, as outlined in WHO guidance on environmental surveillance.

17. The TAG encourages WHO Secretariat to continue to support Member States in implementing GAPIII and the certification process for PEFs.

18. The TAG encourages WHO Secretariat to continue to support Cambodia, China, Lao People's Democratic Republic, Mongolia, Pacific island countries, Papua New Guinea, Philippines and Viet Nam in identifying necessary resources for maintaining polio-essential functions as defined by the Polio Post-Certification Strategy.

19. The TAG encourages WHO Secretariat to support Member States that will initiate poliovirus surveillance among patients with primary immunodeficiency disorders (PIDs) or establish registries for patients with PIDs.

20. The TAG encourages WHO Secretariat to initiate expert consultation to guide preparation of Member States for OPV cessation prior to the global eradication of poliovirus.

Surveillance and data management for vaccine-preventable disease control and elimination

21. The TAG encourages WHO Secretariat to continue to provide support to priority Member States in strengthening VPD surveillance and improving data quality through:

a. development of national training materials on surveillance based on case studies and problem solving;
b. expanding the Immunization and Surveillance Data Specialist project or similar activities to other countries; and
c. strengthening linkages between epidemiological and laboratory data, including further expansion of WPRO web-based data management tools.

22. The TAG encourages WHO Secretariat to provide technical assistance to Member States in ensuring that national VPD surveillance systems, whether stand-alone or integrated with surveillance for other communicable diseases, are compliant with minimum requirements (i.e. number of VPDs under surveillance, national or sentinel surveillance, aggregate or case-based reporting, and case definitions) in accordance with the new WHO VPD surveillance guidelines.

23. The TAG encourages WHO Secretariat to support priority Member States (i.e. those relying on external funding to support surveillance functions) in conducting cost-benefit analyses of VPD surveillance, particularly AFP and acute fever and rash surveillance, to advocate for adequate domestic funding to sustain high quality surveillance systems.

24. The TAG encourages WHO Secretariat to support efforts of Member States to strengthen immunization data quality and use for action, through:

a. technical assistance to improve data standards and tools, and coordination and technical support to guide quality integration of EPI data in broad health information management platforms;
b. development of effective training materials, and identification and promoting effective capacity building strategies for health workforce capacity for data management and use.
c. supporting feasibility assessment for implementation of electronic immunization registry and development of suitable system requirements; and
d. supporting design and implementation of coverage surveys and serosurveys based on internationally recommended methodologies.

25. The TAG encourages WHO Secretariat to support development of the WHO Immunization Information System (WIISE) and reach to Member States to ensure

that WIISE fulfils their needs for the components relevant to them (eJRF, data visualization and access).

Laboratories and laboratory networks for vaccine-preventable disease control and elimination

26. The TAG reiterates the recommendations of the 27th TAG meeting to WHO Secretariat to:

    a. continue providing technical support to Member States to maintain high quality VPD laboratories;
    b. continue working on developing a regional strategy to maintain functional and sustainable laboratory surveillance for VPDs including:

        i. providing technical support to laboratories where needed to maintain technical skills and address gaps;
        ii. ensuring that all network laboratories receive timely updates and recommendations on new developments in laboratory testing;
        iii. addressing country-specific gaps and challenges; and
        iv. supporting countries in the polio transition period;

    c. work with Member States to promote collaboration between epidemiological and laboratory surveillance for VPDs through:

        i. organizing regular country-specific joint epidemiologic and laboratory workshops or meetings for advocacy purposes and exchange of experiences;
        ii. ensuring that interpretation and use of data for reporting and final classification are jointly assessed from clinical and laboratory perspectives; and
        iii. ensuring participation of both epidemiological and laboratory experts during country VPD surveillance reviews; and

    d. support Member States with insufficient capacity to manage increased laboratory workload during VPD outbreaks to consider establishing subnational laboratories.

27. The TAG requests the WHO Secretariat to continue to provide support to Pacific island countries without measles and rubella laboratory capacity, to ensure that they have access to accredited laboratories for measles and rubella confirmation.

Accelerated Japanese encephalitis control

28. The TAG requests WHO Secretariat to finalize and publish the *Regional Guide for Accelerated Control on Japanese encephalitis in the Western Pacific* based on inputs from TAG members during the 2019 TAG meeting.

29. The TAG requests WHO Secretariat to support Member States to develop or update their national plans for accelerated control of Japanese encephalitis, with consideration of country-specific context.

30. The TAG requests WHO Secretariat to collaborate with partners to mobilize resources to support Member States in implementing their national strategies and plans of action.

Preparedness for and response to diphtheria outbreaks

31. The TAG requests WHO Secretariat to finalize and publish the *Field Guide for Preparedness and Response to Diphtheria Outbreaks in the Western Pacific* based on inputs from TAG members during the 2019 TAG meeting.

32. The TAG requests WHO Secretariat to support Member States to develop or update their national guidelines for preparedness and response to diphtheria outbreaks, with consideration of country-specific context.

33. The TAG requests WHO Secretariat to collaborate with partners to mobilize resources to support Member States to implement their national strategies and plans of action.

34. The TAG requests WHO Secretariat to assess the need and feasibility of establishing a regional DAT stockpile to ensure immediate availability of DAT for diphtheria cases or outbreaks in the Region.

Vaccine and Immunization Safety

35. The TAG reiterates the recommendations of the 27th TAG meeting, including that:

    a. WHO continues providing technical support to Member States to conduct NRA assessments and to develop and implement institutional development plans; and
    b. WHO continues providing technical support to Member States for in-country AEFI training workshops.

36. The TAG recommends WHO Secretariat to continue providing technical support to Member States in staff capacity building for investigation, causality assessment and response to vaccine and immunization safety events.

37. The TAG recommends WHO Secretariat to support Member States to use the new WHO Global Benchmarking Tool Revision VI to identify vaccine regulatory gaps and address them.

38. The TAG recommends WHO Secretariat to consider compiling information and organizing a session in the next TAG meeting about compensation programmes for injury and disability following vaccination, related legislative frameworks, and innovations in AEFI monitoring.

Vaccine acceptance and demand

39. The TAG reiterates the recommendations of the 25th TAG meeting for WHO to develop a comprehensive regional guideline to support countries to overcome vaccine hesitancy.

40. The TAG requests WHO Secretariat to support Member States to gather country-specific information on vaccine hesitancy and diagnosis of root causes, and to develop strategies to overcome hesitancy and to build and sustain acceptance and demand for vaccination.

41. The TAG requests WHO Secretariat to finalize the draft regional guide, *Generating acceptance and demand for vaccination: strategies for building and sustaining vaccination uptake and addressing hesitancy*, through further consultation with the

TAG, NIPs and partners, and submit to the 29th TAG meeting in 2020 for review and possible endorsement.

New Vaccines

42. The TAG reiterates the recommendations of the 27th TAG meeting that WHO Regional Office for the Western Pacific should:

    a. continue to provide technical support and capacity building for the development of national plans for evidence-based introduction of new vaccines;
    b. continue to assess and improve the quality of surveillance implementation;
    c. provide technical support and capacity building to lower middle-income Member States to prepare for or implement introduction of new vaccines;
    d. provide technical support to upper middle-income countries to develop and implement an effective strategy that will promote increased introduction of new vaccines;
    e. support ministries of health in Pacific island countries in introduction of new vaccines funded by the Asian Development Bank during 2018-2021;
    f. continue to provide technical support for special studies focusing on strategies to increase the evidence base for introduction of new vaccines and new vaccination technologies; and
    g. use strategies and activities for introduction of new vaccines that further strengthen and enhance overall immunization systems and programmes.

43. The TAG recommends WHO Secretariat to support Lao People's Democratic Republic along with partners in:

    a. HPV vaccine introduction nationally in 2019;
    b. typhoid burden assessment in 2019; and
    c. rotavirus vaccine introduction nationally in 2020.

44. The TAG recommends WHO Secretariat to support Solomon Islands with Gavi and other partners in introducing:

    a. HPV vaccine nationally in 2019; and
    b. rotavirus vaccine nationally in 2020.

45. The TAG recommends WHO Secretariat to support Mongolia in:

    a. introducing PCV nationally during 2019; and
    b. conducting HPV vaccine cervical cancer costing studies in 2019, and
    c. introducing HPV sub-nationally in 2020.

46. The TAG recommends WHO Secretariat to support Viet Nam with intussusception surveillance in 2019 and 2020.

47. The TAG recommends WHO Secretariat to support Cambodia, Fiji, Mongolia, the Philippines and Viet Nam analyze their Invasive Bacterial Vaccine-Preventable Disease Surveillance Network data and write manuscripts summarizing the findings for submission to a special issue of *Vaccine* journal.

48. The TAG recommends WHO Secretariat to support ministries of health in four Pacific island countries (Samoa, Tonga, Tuvalu and Vanuatu) in Asian Development Bank-funded introduction of HPV vaccine, PCV and rotavirus vaccine during 2019-2021.

Immunization Service Delivery

49. The TAG recommends WHO Secretariat to continue technical support and capacity building to strengthen immunization services to reach underserved persons and achieve high immunization coverage across all population groups.

50. The TAG recommends WHO Secretariat to provide technical support to Member States for implementation of strategies to extend immunization across the life course, including for adolescents, adults and the elderly, and to achieve high coverage in these groups.

51. The TAG recommends WHO Secretariat to work with partners and ministries of health to mobilize resources for immunization systems strengthening and extension of immunization through the life course.

52. The TAG recommends WHO Secretariat to raise at the global level the importance of ensuring a secure increased vaccine supply to enable the coverage necessary to achieve the elimination and accelerated control goals.

Regional Strategic Framework for Vaccine-Preventable Diseases and Immunization in the Western Pacific, 2021-2030

53. The TAG requests WHO Secretariat to continue to develop the *Regional Strategic Framework*, obtaining input from immunization programme staff, ministries of health, WHO regional office staff working on topics that interface with immunization, WHO country offices and headquarters, and other partners and stakeholders.

54. The TAG requests WHO Secretariat to continue consulting and coordinating with Member States in identifying new VPDs for accelerated control or elimination during 2021-2030, and determining targets for these VPDs for 2030; hepatitis B, HPV, diphtheria and others may be good candidates for this purpose.

55. The TAG requests WHO Secretariat to continue to monitor progress in development of the global Immunization Agenda 2030, and ensure appropriate linkages between this global document's vision and resources and the more operational needs of the *Regional Strategic Framework*.

56. The TAG requests WHO Secretariat to analyse resource requirements for implementation of the *Regional Strategic Framework*, providing an evidence base for planning.

Tenth Meeting of the WHO South-East Asia Regional Immunization Technical Advisory Group (SEAR-ITAG)

New Delhi, India, 9 to 12 July 2019

Report

Contents

A. Introduction

The Tenth Meeting of the World Health Organization's (WHO's) South-East Asia Regional Immunization Technical Advisory Group (SEAR-ITAG) was held from 9 - 12 July 2019 in New Delhi, India. The SEAR-ITAG (referred to hereafter as the ITAG) is a regional technical expert group, established by WHO's Regional Director for South-East Asia to provide advice on all aspects of immunization, vaccines and vaccine-preventable-disease (VPD) prevention, control, elimination and eradication. It comprises experts from such disciplines as programme management, communicable disease and VPD control, virology, epidemiology and immunization. National Expanded Programme on Immunization (EPI) managers, national surveillance focal points, representatives of national immunization technical advisory groups (NITAGs) and partner agencies participate in the ITAG's annual meeting.

The terms of reference of the ITAG are to:

- review regional and Member State policies, strategies and plans for the control, elimination and/or eradication of VPDs, in particular polio eradication, measles elimination, rubella and congenital rubella syndrome (CRS) control, maternal and neonatal tetanus elimination (MNTE) and the acceleration of Japanese encephalitis (JE) and hepatitis B control;
- provide guidance on the setting of regional priorities for immunization and vaccines;
- make recommendations on the framework for development of national immunization policies as well as operational aspects of these policies' implementation; and provide a framework for and approaches to periodic evaluation and strengthening of routine immunization (RI) services and systems;
- advise Member States on appropriate choices of new vaccines, recommend optimal strategies and provide technical guidance for the introduction of these vaccines and for the monitoring and impact evaluation of new vaccines once they are introduced into national immunization programmes (NIPs);
- promote and provide technical guidance for the implementation of high-quality VPD surveillance, including high-quality laboratory networks to support VPD surveillance;
- advise Member States on regulatory requirements to ensure quality and safety of vaccines used in NIPs;
- provide guidance on public-private partnerships in immunization and vaccines; and
- identify and advise on appropriate implementation of research topics in immunization and vaccines and review the conduct and results of such research projects.

B. Objectives

The objectives of this meeting were to:

- review progress in performance of national immunization programmes relative to the strategic goals outlined in the South-East Asia Regional Vaccine Action Plan 2016-2020 (SEAR-VAP);
- review progress in implementation of recommendations of the Ninth meeting of the South-East Asia Regional Immunization Technical Advisory Group (SEAR-ITAG) held in July 2018; and
- seek guidance of SEAR-ITAG on priority actions that should be taken during 2019-2020 to achieve milestones and goals outlined in the SEAR-VAP.

C. Organization of the meeting

The meeting was organized over a period of four days and included six components:

1. Review progress of national immunization programme performance of each Member State of the Region relative to the goals outlined in the SEAR-VAP.
2. Review progress of implementation of recommendations of the Ninth meeting of the SEAR-ITAG.
3. Poster presentations by Member States on:
    a. innovations to improve immunization coverage and equity; and
    b. sharing a best practice on immunization.
4. Informational sessions on new vaccines on the horizon-dengue vaccine, malaria vaccine.
5. Cross-cutting session of special interest – data management, quality and coverage estimations.
6. Looking beyond 2020 – supporting co-creation of global vision and strategy and aligning global and regional priorities and goals.

The meeting began with an opening address by Dr Poonam Khetrapal Singh, WHO Regional Director for South-East Asia (see Annex 1 for the address of the Regional Director). The meeting was chaired by Professor Gagandeep Kang and co-chaired by Professor Mohammad Shahidullah. The meeting was attend by all ITAG members. The other meeting participants included:

- representatives from NITAGs from 11 countries of the South-East Asia (SEA) Region of WHO;
- national EPI managers and surveillance focal points from ministries of health of the 11 countries of the Region;
- the chairperson and two members of WHO's Strategic Advisory Group of Experts on Immunization (SAGE);
- the chairpersons of the SEA Regional Certification Commission for Polio Eradication (SEA-RCCPE) as well as Regional Verification Commission for measles elimination and rubella control;
- representatives and technical experts from the United Nations Children's Fund (UNICEF) headquarters and from UNICEF's Regional Office for South Asia (ROSA) and its East Asia and Pacific Regional Office (EAPRO), immunization focal points from UNICEF Country Offices;
- representatives from the United States Centers for Disease Control and Prevention (US CDC);
- immunization and VPD surveillance focal points from 11 WHO Country Offices in the Region;
- representatives and technical experts from WHO headquarters and the WHO Regional Office for SEA; and
- representatives of regional and global partners, donors and stakeholders in immunization and vaccines, including Gavi, the Vaccine Alliance (Gavi), PATH and Rotary International.

(see Annex 2 for the agenda of the meeting and Annex 5 for the full list of participants).

Methodology for the review of NITAG country progress reports

Both in preparation for and during the meeting, significant time and effort were dedicated to developing the methodology for the review of NITAG country progress reports, as these reviews were the major focus of the ITAG meeting.

Prior to the meeting:

- Eight weeks prior to the tenth ITAG meeting, a country-tailored template for annual reporting on progress in meeting SEAR-VAP goals was developed and shared with all NITAGs in the Region.

- The annual progress reports, based on the template mentioned above, were submitted to the ITAG (through WHO's Regional Office for South-East Asia) by all 11 NITAGs by the end of June 2019. The Regional Office and country offices provided technical support to all NITAGs as required.
- For each country report, two ITAG members were assigned as reviewers (Annex 3). The ITAG members were provided with a checklist to guide their review of countries' progress in implementing the recommendations from the ninth ITAG meeting and any newer initiatives and in achieving the SEAR-VAP goals.

During the meeting:

- The country progress reports and the reviewers' reports were provided to all ITAG members.
- Each NITAG representative presented their respective country progress report as per the template shared prior to the meeting.
- Comments on the progress report were provided by the ITAG members and partners.
- Country-specific discussions were conducted in the closed-door session and recommendations made accordingly.

D. Review of SEAR VAP goals-progress, conclusions and recommendations

The SEAR-VAP describes a set of goals and objectives for immunization and control of VPDs for the period 2016-2020. It has eight goals, as follows:

- 1: Routine immunization (RI) systems and services are strengthened.
- 2: Measles is eliminated, and rubella/congenital rubella syndrome (CRS) controlled.
- 3: Polio-free status is maintained.
- 4: Elimination of maternal and neonatal tetanus is sustained.
- 5: Control of JE is accelerated.
- 6: Control of hepatitis B is accelerated.
- 7: Introduction of new vaccines and related technologies is accelerated.
- 8: Access to high-quality vaccines is ensured.

Overall conclusions

Presentations on progress towards each SEAR-RVAP goal were made during the meeting. Based on the deliberations, the SEAR-ITAG appreciated the overall progress made in the Region to achieve the goals of the SEAR-VAP and commended the ministries of health of all 11 countries of the Region for their commitment to implement strategies targeted to achieve the goals of the SEAR-VAP as well as on the follow-up actions taken by countries towards the recommendations made by ITAG in its Ninth meeting in 2018.

The SEAR-ITAG noted that all countries in the Region have established NITAGs that provide technical support and monitoring oversight to the NIPs. The ITAG acknowledged the critical role of NITAGs in providing guidance to national programmes on policies and strategies related to vaccination, introduction of new vaccines and monitoring the NIP performance at national and sub-national levels. It acknowledged that NITAGs need more support to work with their NIPs and appreciated the efforts of the WHO Regional Office for South-East Asia (SEARO) to build NITAG capacity by conducting a workshop on strengthening the capacity of NITAGs.

The ITAG was pleased with the high quality of country reports submitted by NITAGs of all the 11 countries and fully endorsed the recommendations made by respective NITAGs.

The SEAR-ITAG:

- recognized the critical role of NITAGs in monitoring progress and guiding actions to overcome the various challenges at national and subnational levels in each country, and to achieve the goals of the SEAR-VAP;
- congratulated the partners for providing strategic support to countries of the Region; and
- noted that challenges and risks remain and that concerted efforts will be required to overcome these if all goals outlined in the SEAR-VAP are to be met.

Overall Recommendations

The SEAR-ITAG:

1. Emphasized the need for continued monitoring of implementation of its recommendations at national and sub-national levels by the national immunization programmes (NIPs) and the NITAGs;

2. Recommended that immunization partners should coordinate technical and financial support for monitoring the programme and meeting challenges both at national level and sub-national levels;

3. Re-iterated the need for the full implementation of the ITAG 2018 recommendations and their monitoring by NITAGs;

4. NIPs and NITAGs should implement the recommendations of the NITAGs capacity building workshop' (March 2019), including a review of current ToRs, to formalize processes and declarations of interest and for capacity building of NITAG members; and

5. WHO-SEARO should conduct an external evaluation of the NITAGs in the Region.

Goal 1. RI systems and services are strengthened

Progress

Strengthening the RI systems and services is the overarching goal of the SEAR-VAP 2016-2020. The key targets to achieve are that:

- by 2015 all countries have ⩾90% national coverage and ⩾80% coverage in every district or equivalent with three doses of DPT containing vaccine (***DTP3***); and
- by 2020 all countries have ⩾90% national coverage and ⩾80% coverage in every district or equivalent ***for all vaccines*** in national programmes, unless otherwise recommended.

As per the WHO/UNICEF estimates, Bangladesh, Bhutan, DPR Korea, Maldives, Myanmar, Nepal, Sri Lanka and Thailand have achieved 90% or more national coverage with DPT3 in 2018. India has achieved 89%, Timor-Leste 83% and Indonesia 79% DPT3 coverage. Bangladesh, Bhutan, DPR Korea, Maldives, Sri Lanka and Thailand have achieved 90% coverage for all vaccines provided during infancy. As per the 2018 national reports, all districts have achieved more than 80% DPT3 coverage in Bangladesh, DPR Korea, Maldives and Sri Lanka. 95% districts in Bhutan and 90% districts in Thailand have reported more than 80% coverage. From 2000 to 2017, the overall DPT3 coverage in the SEA Region has increased from 64% to 88%.

India has reported 5 293 diphtheria cases, 23 766 pertussis cases and 12 032 measles cases in 2018 while Indonesia has reported 954 diphtheria cases, 1 043 pertussis cases and 9 035 measles cases during the same period. Myanmar has reported 68 diphtheria cases and 1 293 measles cases and Nepal has reported 232 diphtheria cases and 4 153 pertussis cases, in 2018. The occurrence of diphtheria outbreaks demonstrates a vulnerability of populations to diseases for which vaccines have been available for a long time, due to sub-optimal coverage with these vaccines as well as policy barriers.

All Member States in the Region have committed to immunization through legislation or a legal framework that upholds immunization as a priority. National immunization plans are integrated into national health plans, and countries are demonstrating good stewardship in implementation of their national plans. All countries are implementing their national comprehensive national multi-year immunization plans.

Countries in the Region are involved with assessing coverage at district and sub-district levels to identify pockets of low coverage and taking appropriate actions to improve coverage and reach the un-immunized. EPI and VPD surveillance reviews and EPI coverage evaluation surveys (CES) have been conducted in the Region to identify areas of low coverage, barriers for immunization and to take appropriate actions. Bangladesh, DPR Korea, Indonesia, Nepal and Timor-Leste have recently conducted EPI coverage evaluations surveys. India continues to conduct evaluation surveys in phases. Bhutan Maldives, Myanmar and Nepal have relied on demographic and health surveys. Bangladesh, Indonesia and Timor-Leste conducted coverage evaluation surveys using new WHO methodology in 2018 and Myanmar is planning to do a similar survey in 2019.

Countries have developed innovative approaches such as mapping hard-to-reach areas using GIS mapping tools, electronic registration of beneficiaries and an urban immunization strategy in Bangladesh; installing solar direct drive (SDD) refrigerators at rural Ri levels and tracking and immunization of missed children by household doctors in DPR Korea; the Intensified Mission Indradhanush followed by Gram Swaraj Abhiyan in India; declaring 2018 as the "immunization acceleration year" in Indonesia; verification of completion of childhood vaccine doses at the time of entry into school in Maldives; prioritization of townships for service delivery improvement in Myanmar; fully immunized district initiative in Nepal; nationwide adult vaccine programme in Thailand; and community registration and additional outreach clinics in Timor-Leste. These approaches have not only strengthened RI services but have also increased the access of the general population to the health system.

On promoting vaccination demand

In South-East Asia – as elsewhere in the world – there is a substantial need to improve confidence in immunization. Phrased more positively, there is an opportunity to promote resilient demand for vaccines. Vaccine demand and refusal is not a binary issue. There is a spectrum from outright refusal, through to hesitancy, to passive acceptance, to resilient demand. Parents' decisions about whether to vaccinate their children or not are based on multiple factors. Communication plays a key part in addressing concerns and promoting the benefits of vaccination. But communication alone is insufficient. Action to strengthen vaccine demand needs to be multi-faceted, to: i) reduce barriers – using data and evidence to make vaccination the easiest action for parents to take; ii) build trust – cultivating and sustaining trust in vaccines and services through social and political will, and ensuring resilience and preparedness for challenges to trust; iii) tailoring services – involving communities to improve the quality and accountability of services; iv) activating intentions – using motivation to overcome the gap between intentions and action, through community engagement.

Countries in the Region engage communities in effective discussions on their knowledge, attitudes, and practices as they relate to immunization and health services in general. Countries in the Region are implementing and evaluating strategies to increase community demand for immunization. All countries are building capacity by training front-line health workers in effective communication techniques and recruiting new voices to champion immunization. As a part of the EPI coverage evaluation survey (CES) knowledge of care takers on immunization, sources of immunization and reasons for not vaccinating or partial vaccination are evaluated. The CES in Bhutan and DPR Korea had found no vaccine hesitancy in these countries. However, CES in Bangladesh and Nepal has demonstrated an emerging hesitancy in these countries. There are potential issues of vaccine hesitancy in some areas of India. At the onset of the second phase of the measles rubella (MR) immunization campaign in 2018 in Indonesia, there was resistance to vaccination with MR vaccine.

To assist and support countries in the development of multi-year immunization demand promotion strategies and plans (or the review of existing plans), the UNICEF Regional Office for South Asia (ROSA), in partnership with the WHO Regional Office for South-East Asia (SEARO) and the UNICEF East Asia and Pacific Regional Office (EAPRO), is developing regional programme guidance on the promotion of resilient vaccination demand in South and South- East Asia. The first part of this guidance was presented to the ITAG for input. Over the next year, the full guidance will be developed, piloted in two countries, and presented to the ITAG.

Conclusions

The ITAG:

- observed that countries have initiated implementation of 2018 ITAG recommendations on improving coverage and recognized that improving coverage requires ongoing efforts.

- noted that financial sustainability is essential to maintain equity and coverage achievements, even in countries with high coverage, and that this is an indicator of sustainable immunization programmes.

- took note of the diphtheria outbreaks in some countries of the Region.

- was concerned that some recommendations from the 2018 ITAG, such as introducing booster doses, shifting from TT to Td and initiating case-based surveillance supported by laboratories, were not been fully implemented in many countries.

- acknowledged the multifactorial determinants of NIP performance, including the strength of health systems in addition to the social factors that influence vaccine delivery, demand and acceptance.

- supported the direction being taken by UNICEF to develop practical and user-friendly guidance on demand generation for use by national and sub-national programmes.

Recommendations

The ITAG recommended that:

1. In-country financing for immunization should increase in countries that are currently not fully self-funding their immunization programmes.
2. NIPs should continue to:
    a. identify and prioritize districts for interventions to strengthen immunization services;
    b. identify gaps and reasons for why children are not fully vaccinated;
    c. improve micro-plans for immunization;
    d. track and reach missed children with vaccination;
    e. improve data quality for immunization and surveillance;
    f. monitor progress and provide supportive supervision to immunization programme; and
    g. strengthen laboratory-supported surveillance for vaccine preventable diseases.

On Diphtheria, the ITAG re-iterated the following recommendations:

1. Strengthening laboratory supported case-based surveillance for diphtheria.
2. Achieving high coverage with DPT3 and minimizing DPT1-DPT3 drop-outs in all areas in all countries.
3. Ensuring three booster doses of diphtheria vaccination, at appropriate times of the life cycle, based on epidemiological evidence, as recommended by ITAG in 2018.
4. Implementing timely and appropriate outbreak response, that includes immunization of close contacts and chemoprophylaxis, as specified in the Regional surveillance guidelines.

On Demand generation, the ITAG recommended that

1. Demand generation should be a standing agenda item at future ITAG meetings.
2. Practical guidance for demand generation should be urgently finalized and shared with countries.

3. Strategies should be developed, implemented and evaluated to improve communication skills of immunization providers to better inform patients/parents/guardians about vaccine benefits and safety.
4. NIPs should work closely with NRAs and other key stakeholders on the development of risk communication strategies in the case of AEFI or other events to mitigate the risk of public loss of confidence in vaccinations.

Bangladesh

1. Adequate government funds should be allocated for the NIP and vacancies filled at the earliest.
2. The urban immunization strategy should be urgently implemented.

Bhutan

1. AEFI surveillance should be strengthened

India

1. An evaluation of Mission Indradhanush (MI) and Intensified MI should be conducted, and the findings presented at the next ITAG meeting.
2. Lessons learned from urban immunization strengthening pilots and best practices in other urban settings should be identified and expanded.

Indonesia

1. Tailored sub-national plans, supported by partners, should be developed and monitored to improve coverage and equity.
2. Sufficient sub-national resources should be ensured to address un- and under-immunized populations.
3. NITAG training needs should be addressed to ensure highly functional NITAG.

Maldives

1. A clear policy and plan should be developed to recruit NIP staff.

Myanmar

1. Strategies should be developed and implemented to improve immunization for urban, hardship areas and migrants.

Nepal

1. Quality information systems should be built that integrate data across platforms to guide programme actions.
2. Consideration should be given to appropriately relocate cold chain facilities following federalization.

Thailand

1. The utility of the immunization registry should be improved to enable accurate coverage estimation, identification and reminder/recall of children who are due or late for immunization, targeting of public health interventions, operational research to assess vaccine impact (particularly for new vaccines) and other programme priorities. Plans should be developed to expand the registry nationwide.

Goal 2. Measles is eliminated, and rubella/CRS controlled

Progress

The WHO Regional Committee for South-East Asia, during its Sixty-sixth session in September 2013, adopted resolution SEA/RC66/R5 to eliminate measles and control rubella/CRS in the Region by 2020. To ensure adequate technical guidance to accelerate progress towards the goal, a Strategic Plan for Measles Elimination and Rubella and Congenital Rubella Syndrome Control 2014-2020 was developed.

Five countries in the South-East Asia Region – Bhutan, DPR Korea, Maldives, Sri Lanka and Timor-Leste – have been verified by the South-East Asia Regional Verification Commission for measles elimination and rubella/CRS control (SEA-RVC) as having eliminated endemic measles. Six countries of the Region – Bangladesh, Bhutan, Maldives, Nepal, Sri Lanka and Timor-Leste – have been verified as having controlled rubella and CRS. An estimated 75% reduction in mortality due to measles has occurred in the Region in 2017 compared with 2000. And a nearly 23% decline in mortality is estimated during the period 2014-2017.

As of end-2018, all countries in the Region are administering two doses of measles-containing vaccine (MCV) under their routine immunization programmes and 10 countries have introduced rubella-containing vaccine (RCV) in their programme. DPR Korea, the only remaining country, has plans to introduce RCV before the end of 2019. The regional coverage of first dose of measles-containing vaccine (MCV1) was 89% in 2018 compared with 63% in 2000 and six countries have reported coverage of more than 95% at national level in 2018. The regional coverage of the second dose of measles containing vaccine (MCV2) has increased to 80% in 2018 compared with 59% in 2014. The coverage of RCV delivered through RI was reported at 83% for the Region in 2018 compared to 13% in 2014. An estimated 400 million children are likely to be reached

through mass vaccination campaigns with a measles-rubella (MR) vaccine in the Region between 2017 and 2019. Of these, nearly 305 million children have already been reached in India and 60 million in Indonesia.

All countries in the Region are conducting laboratory supported case-based surveillance for measles and rubella, with India and Indonesia expected to complete the expansion by end-2019. Seven out of 11 countries in the Region have achieved the desired target for the non-measles and non-rubella discard rate (as a proxy of sensitivity of surveillance). CRS surveillance has been initiated in all 11 countries, either as sentinel surveillance or as part of the case-based surveillance system. All countries in the Region have at least one proficient national laboratory to support measles and rubella case-based surveillance. The measles-rubella laboratory network has expanded from 23 laboratories in 2013 to 50 in 2018 with 41 laboratories accredited as "proficient" for measles and rubella testing.

A mid-term review, conducted in 2017, of the Strategic Plan for Measles Elimination and Rubella and Congenital Rubella Syndrome Control in the South-East Asia Region (2014-2020) concluded that the goal of achieving measles elimination and rubella/congenital rubella syndrome (CRS) control by 2020 is unlikely to be achieved in the Region due to suboptimal implementation of the strategies in some countries. Financial insufficiency to accelerate implementation of activities for measles elimination and rubella/CRS control remains a challenge in the way of achieving the 2020 target.

The Regional Office conducted a high-level consultation in March 2019 on the feasibility of adopting the goal of rubella elimination and harmonizing the goal of measles elimination with that of rubella elimination. The consultation discussed a position paper on "Establishing a rubella elimination goal and aligning measles and rubella elimination goals in the WHO South-East Asia Region". Representatives from countries, technical experts and professional bodies proposed the revision of the goal of 'rubella control by 2020' to 'rubella elimination by 2023' and the harmonization of the goal of measles elimination with that of rubella elimination.

A draft Strategic Plan for Measles and Rubella Elimination: 2020-2024 has been developed for achieving and sustaining measles and rubella elimination in the South-East Asia Region. The key elements of the plan are to:

(1) strengthen immunization systems for increasing and sustaining high level of population immunity against measles and rubella at both the national and subnational levels through well laid-out subnational plans and their optimal implementation;

(2) enhance and ensure highly sensitive laboratory-supported case-based surveillance systems so that high-quality epidemiological assessments of population susceptibility to measles and rubella are conducted to inform policy and better plan strategies to increase population immunity levels uniformly at the national as well as subnational levels;

(3) ensure preparedness for response activities for measles and rubella outbreaks through development and effective implementation of outbreak preparedness and response plans for measles and rubella;

(4) develop national measles and rubella elimination policy strategies addressing subnational variations using evidence-based data in line with the Regional Strategic Plan; and

(5) mobilize political, societal and financial support to ensure interruption of transmission of indigenous measles and rubella virus by 2023.

Conclusions

The ITAG acknowledged the significant progress and momentum created towards measles elimination and rubella/CRS control in the Region; however, it noted that the regional target of measles elimination and rubella control will not be met by 2020.

The ITAG endorsed the recommendations of the high-level consultation meeting (March 2019) on revising the current goal to 'measles and rubella elimination by 2023' and appreciated efforts of WHO to present the revised goal to the Seventy-second session of the Regional Committee for South-East Asia for consideration by Member States as well as the draft 'Strategy for Achieving and Sustaining Measles and Rubella Elimination:2020-2024' in the WHO South-East Asia Region.

The ITAG also endorsed the conclusions and recommendations of the fourth meeting of the Regional Verification Commission for measles and rubella and congratulated:

a. Sri Lanka for eliminating endemic measles;

b. Bhutan, DPR Korea, Maldives and Timor-Leste for sustaining measles elimination; and

c. Bangladesh, Bhutan, Maldives, Nepal, Sri Lanka and Timor-Leste for sustaining rubella control.

The ITAG appreciated efforts made by the Region for putting together a MR Laboratory Quality Management System to ensure sustained proficiency status of the MR laboratory network.

Recommendations

1. The ITAG recommended that WHO-SEARO should: work closely with the MR SAGE working group to ensure that Regional priorities are included in the SAGE agenda.
2. identify research priorities on measles and rubella and work with key partners and stakeholders for implementation.
3. report back on the progress towards implementation of the Measles and Rubella Laboratory Quality Management Systems at the next ITAG meeting.
4. Measles rubella laboratory network in SEAR should develop a quality assurance plan that is aligned with the new Regional Strategy 2020-2024.
5. Countries should genotype all viral chains of transmission and share data through MeaNS and RubNS database, including for sporadic cases in countries that have eliminated or are close to achieving elimination status.

The ITAG also made country-specific recommendations:

Bangladesh

1. Considering the occurrence of measles cases in infants less than nine months of age a zero-dose of MR vaccine at six months of age should be considered based on an epidemiological review.
2. The upcoming MR SIA should be planned and implemented to achieve high coverage and RI strengthening activities should be implemented during and after the SIA and presented at the next ITAG meeting.

Bhutan

1. Vaccination should be considered for migrant workers.
2. MCV2 district-level coverage should be reviewed for appropriate action to ensure high coverage.

DPR Korea

1. The MR SIA planned for this year should be implemented with high coverage and used to improve and sustain high routine immunization coverage.

India

1. MR-IEAG recommendations should be fully implemented and progress shared at the next ITAG meeting.
2. Multi-antigen sero-surveys should be considered to help with:

- identification of rubella immunity gaps in women of child-bearing age;
- decision-making and vaccine scheduling of Td booster doses; and
- monitoring the progress for achieving the hepatitis B control goal.

Maldives

1. Consideration should be given to vaccination of migrant workers.
2. The post-elimination sustainability plan for measles should be revised with a focus on strengthening surveillance for both measles and rubella.

Myanmar

1. The MR SIAs planned later this year should be of high quality and used to strengthen routine immunization.

Nepal

1. The recommendations made by the recent measles and rubella programme review should be fully implemented and progress reported in the next meeting.

Sri Lanka

1. A post-elimination sustainability plan for measles and rubella should be developed with a focus on:
    - closing the immunity gap in birth cohorts between 1994-1997; and
    - outbreak preparedness and response.
2. An in-depth independent external review of the MR laboratory should be conducted to ensure adequate laboratory support post- elimination of measles and rubella.

Thailand

1. Measles outbreaks should be used to identify and improve areas with sub-optimal immunization programme performance, and used to advocate for programme resources.
2. High quality MCV SIA should be conducted to strengthen routine immunization delivery and target appropriate age groups.
3. Vaccination policies should be considered in high-risk occupational groups like health care workers.

Timor-Leste

1. A detailed desk review should be conducted to identify activities to enhance coverage of MCV1 and MCV2 and to reduce the drop-out rate.

Goal 3. Polio-free status is maintained

Progress

The SEA Region has achieved the goal of polio eradication and maintained its polio-free status for the past eight years. However, the Region continues to be at risk of importation of wild poliovirus (WPV) from countries with current poliovirus transmission and any outbreak due to circulating vaccine-derived poliovirus (cVDPV).

Acute flaccid paralysis (AFP) and environmental surveillance (ES)

The overall non-polio AFP rate in the Region in 2018 was 6.55 (data as on 3 June 2019) per 100000 population under 15 years of age which exceeds the globally recommended operational target of 2 per 100000. The non-polio rate was above 2, in 2018, in seven countries of the region, namely Bangladesh, Bhutan, India, Indonesia, Maldives, Myanmar and Nepal, while it was between 1 and 2 (which meets certification standards) in three countries, namely DPR Korea, Sri Lanka and Thailand. No AFP case was reported from Timor-Leste in 2018.

In 2018, two stool samples were collected at least 24 hours apart and within 14 days of onset from 85% of the reported AFP cases in the Region, as against the globally recommended target of at least 80%. Nationally, the target was achieved in 2018 by eight countries, namely Bangladesh, Bhutan, DPR Korea, India, Indonesia, Myanmar, Nepal and Sri Lanka. For both performance indicators there is considerable subnational variance in several countries.

In 2018, Environmental Surveillance (ES) is being conducted through 81 sites in six countries – namely Bangladesh, India, Indonesia, Myanmar, Nepal and Thailand. Bangladesh is operating four temporary sites in Cox's Bazaar following the influx of migrants from Myanmar in 2017-18. Indonesia has initiated ES in Papua Province recently following the recent detection of a cVDPV outbreak.

In February 2019, a circulating vaccine-derived poliovirus type 1 (cVDPV1) was confirmed in Papua province of Indonesia. An aggressive outbreak response has been carried out comprising of an immediate district level bivalent oral poliovirus vaccine (bOPV) campaign followed by two mass vaccination campaigns, in Papua and Papua Barat provinces, targeting 1.5 million children less than 15 years of age.

Population immunity

Eight SEAR countries – namely Bangladesh, Bhutan, DPR Korea, Maldives, Myanmar, Nepal, Sri Lanka and Thailand – have reported OPV3 coverage above 90% while India, Indonesia and Timor-Leste have coverage between 80-90% in 2018. To close immunity gaps against polio, SIAs with bivalent OPV (bOPV) were conducted in 2018 in India. All countries in the Region, have access to IPV supplies for their routine immunization programme. Four SEAR countries – Bhutan, Maldives, Sri Lanka and Thailand – have reported IPV coverage above 90%, while two – Myanmar and Timor-Leste – have coverage between 80-90% and three – Bangladesh, DPR Korea and Indonesia – have coverage between 60-80%. India reported a coverage of 50% and Nepal 16% with IPV in 2018. Bhutan carried out a catch-up campaign to reach children missed during the IPV stockout period.

Poliovirus laboratory containment

Activities to contain type 2 polioviruses in facilities under GAPIII requirements are progressing in the Region. Two poliovirus essential facilities (PEF) have been identified to store/handle type 2 polioviruses in two countries of the Region, namely India (research facility) and Indonesia (vaccine manufacturer). National authorities for containment (NAC) have been established in both countries. The Global Certification Commission (GCC) has endorsed the certificate of participation (CP) submitted by the vaccine manufacturer in Indonesia as designated poliovirus essential facility (PEF) through the Indonesia national authority for containment (I-NAC). As of March 2019, only four CPs had been granted worldwide making Indonesia a frontrunner in GAPIII implementation and poliovirus facility containment. From India, submission of certificate of participation (CP) is expected in mid-2019 and future PEFs are expected to be identified among vaccine manufacturers.

The Regional Polio Laboratory Network (RPLN) has conducted several bio-risk management capacity building activities and network laboratories are conducting self-assessments against GAPIII requirements. GAPIII update implementation training for national containment taskforces (NCTF), PEFs, NAC and vaccine manufacturers, was conducted at Bandung, Indonesia in February 2019. An advance auditors training and mock audit exercise was conducted at Pune, India in March 2019.

All countries are completing new surveys of biomedical laboratories and facilities to meet requirements outlined in GAPIII. While WPV type 2 (WPV2) and VDPV type 2 (VDPV2) inventories have been completed by all countries inventories for Sabin2 potentially infectious materials are likely to have been completed in six countries and in process in four; Indonesia has yet to start. One of the challenges in GAPIII implementation is the involvement of facilities that collect, handle and store clinical and environmental samples for purposes other than polio research. To support such laboratories, WHO has developed 'Guidance for non-poliovirus facilities to minimize risk of

sample collections potentially infectious for polioviruses (PIM)' which were pilot tested in Bangladesh in December 2017 in a workshop with high risk laboratories. All materials identified in Bangladesh can be stored outside a PEF as per the PIM guidance. Work for poliovirus type 2 inventories provides a good platform for inventories for type 1 and type 3 polioviruses. WHO is supporting countries in preparation of a national response framework for use in the event of a breach of poliovirus containment.

Certification of maintaining polio-free status

The Regional Certification Commission for Polio Eradication (RCCPE) and National Certification Committees for Polio Eradication (NCCPEs) in all 11 countries remain functional and continue to provide oversight and guidance for polio eradication activities. The 11th RCCPE meeting took place in November 2018 in Paro, Bhutan. The RCCPE reviewed progress in each country in the Region and concluded that the Region has remained polio-free. The RCCPE, however, was concerned about continued WPV1 transmission and the ongoing and new outbreaks of circulating vaccine-derived polioviruses.

Transition planning

The Global Polio Eradication Initiative (GPEI) has begun to ramp down its funding and will eventually end in the post-eradication era. However, certain critical functions as mentioned in polio Post-Certification Strategy (PCS) would still be required to be maintained after global certification.

Over the past two decades, polio-funded assets that include human workforce, infrastructure, equipment and systems have been established in five countries of the Region, namely Bangladesh, India, Indonesia, Myanmar and Nepal. These assets have not only contributed to the elimination of polio and the implementation of the polio endgame strategies but have also been increasingly involved with other health activities in the Region.

Polio transition efforts are being considered as a critical opportunity to strengthen immunization systems, strategies for elimination of measles, vaccine-preventable disease surveillance and strengthen capacity for implementation of the IHR (2005). The status of transition in priority countries of the Region is summarized below:

1. Government of Bangladesh has endorsed the national polio transition plan and is on track with the implementation in three phases, as planned.
2. Recent endorsement of the national plan in India by the government and transfer of domestic resources to cover the gaps reflects its commitment to priorities outlined in the plan.

3. Government of Indonesia has initiated actions to self-fund a large proportion of the surveillance, laboratory and immunization costs, previously funded by GPEI.
4. The national transition plan of Myanmar is under consideration for endorsement by the government.
5. Due to ongoing federalization, there has been a delay in endorsement of the national transition plan by the Government of Nepal.

Global Polio Eradication Initiative (GPEI) Polio Endgame Strategy 2019-2023

The four objectives of "The Global Polio Eradication and Endgame Strategic Plan: 2013-2018" have proven effective around the world. However, to guide the programme in its last mile towards eradication, GPEI recently finalized the Polio Endgame Strategy 2019-2023. The key elements of the strategy are:

1. Eradication
2. Integration
3. Certification and containment

Conclusions

The ITAG commended the Region for remaining polio-free for over eight years but recognized that risk of poliovirus resurgence remained. The ITAG noted with concern the recent detection of cVDPV1 in Indonesia and a VDPV1 in Myanmar in areas with pockets of low routine immunization coverage of OPV and IPV.

While the ITAG noted progress with GAPIII implementation, it continued to be concerned about the complexity of requirements for poliovirus essential facilities, as well as the identification and proper handling of potentially infectious materials.

Recommendations

The ITAG recommended:

1. Outbreak response plans for the detection of any wild or vaccine-derived polioviruses should be updated as per recent global guidelines. An outbreak response assessment should be conducted following response to all WPV or cVDPV outbreaks.
2. Polio transition plans should be operationalized in five polio priority countries (Bangladesh, India, Indonesia, Myanmar and Nepal) and NITAGs should provide a progress report to the ITAG.

   The following country-specific recommendations were also made:

Indonesia

1. AFP surveillance should be improved, and consideration given to expansion of environmental surveillance.

Myanmar

1. Appropriate measures should be taken in response to the recently detected VDPV1.

Goal 4. Elimination of maternal and neonatal tetanus is sustained

Progress

All countries follow the WHO recommendation on vaccinating pregnant women with tetanus toxoid containing vaccine (TTCV). Five countries have reported ⩾90% coverage with two or more doses of TTCV in pregnant women (TT2+) for several years as reported through the WHO/UNICEF Joint Reporting Form (JRF). However, lower coverage does not necessarily indicate weak programme performance. After accumulating repeated vaccine doses during multiple pregnancies and SIAs, women of childbearing age (WCBA) eventually become non-eligible for further vaccination during pregnancy while still contributing to the target denominator for calculation of TT2+ coverage. Field surveys conducted during validation exercises have indicated much higher protection at birth than reported TT2+ coverage suggested.

Infant immunization against tetanus (DTP and Penta) rose from 56% in 2000 to 88% in 2017 according to JRF country official estimates. Several countries give booster doses in early childhood or have integrated TTCV vaccination into their school health programmes. Five countries have six doses TTCV in their national schedule; however, coverage rates are not available beyond the primary series. Five countries offer only short-term protection and continue to create protection gaps between early childhood and child bearing age for females and after early childhood for males.

The number of reported NT cases declined to 252 in 2018 in six countries. None of the countries exceeded the "elimination" definition of <1 NT case per 1000 LB in each district (3rd administrative level of a country). The total number of reported tetanus cases continued to increase but it is not known if due to better reporting. Analysis of tetanus cases reported in JRF remains limited and no module is yet available for tetanus surveillance.

Conclusions

The ITAG noted that no country exceeded the "elimination" definition of <1 NT case per 1000 LB in each district in 2018 although quality of surveillance data is limited. The ITAG noted that TT2+

coverage remains <90% in several countries while no protection at birth data are available. However, ITAG appreciated that countries have begun reporting subnational TT2+ data to SEARO.

The ITAG noted that TTCV booster doses are being provided in several countries and plans for introduction exist in others. The ITAG also noted the planned post- validation assessments in Bangladesh and Indonesia.

Recommendations

The ITAG recommended:

1. A full implementation of the recommendations of the 2017 WHO position paper on tetanus vaccines as appropriate in countries;
2. Countries should review and implement the 2019 WHO guidelines "Protecting All Against Tetanus: Guide to sustaining maternal and neonatal tetanus elimination (MNTE) and broadening tetanus protection for all populations"; and
3. WHO-SEARO should review with priority countries, data on immunization, disease reporting and reporting systems for NT surveillance.

Goal 5. Control of JE is accelerated

Progress

Currently, 10 of 11 countries in the SEA Region are endemic for JE, with the exception being Maldives. Vaccination is the most cost-effective strategy to prevent and control JE and WHO recommends that JE vaccination be integrated into national immunization schedules in all areas where JE is recognized as a public health priority. Four countries - Myanmar, Nepal, Sri Lanka and Thailand - have introduced JE vaccination nationwide while India has introduced JE vaccine in nationally-defined high-risk areas and Indonesia in one province. The estimated coverage in 2018 for these five countries are: India (69%), Myanmar (88%), Nepal (81%), Sri Lanka (99%) and Thailand (95%). All JE endemic countries in the Region are conducting JE and acute encephalitis syndrome (AES) surveillance with varying levels of intensity: nationally in six countries (Bangladesh, Myanmar, Nepal, Sri Lanka, Thailand and Timor-Leste), in all high-risk areas in India and at sentinel sites in Bhutan, DPR Korea, and Indonesia. JE/AES surveillance is supported by 14 laboratories in the Region and one regional reference laboratory (RRL) in Bangalore, India. In 2017, 10 laboratories were accredited while four laboratories are provisionally accredited. In April 2019, a regional workshop to strengthen the capacity of JE laboratory network in the region was organized at RRL Bangalore, India.

Due to the variability of type of surveillance in the countries, there is a wide variation in the number of confirmed cases reported in each country. In 2018, around 22 000 cases of suspected JE were reported in the Region of which India reported around 17 000 cases and Myanmar about 2000 cases. Around 338 cases were laboratory confirmed as JE in the Region of which 126 were in Myanmar and 96 in Bangladesh.

Conclusions

The ITAG noted that five countries are providing JE vaccine nationally or in endemic sub-national areas. It acknowledged that there were opportunities to improve protection against JE remains in countries that have already introduced the vaccine.

Recommendations

The ITAG recommended that:

1. A JE expert panel should be convened at the regional level to address issues related to case definition of AES and the adequacy of number and type of vaccine doses required for protection.
2. Case-based surveillance for AES should be strengthened by:
    a. following up on regional workshop recommendations on strengthening the capacity of the JE laboratory network;
    b. linking laboratory and epi surveillance data; and
    c. sharing case-based data with WHO-SEARO monthly.

There were country-specific recommendations as well:

Bangladesh

1. A JE disease burden analysis should be completed to consider the introduction of JE vaccine with Gavi support.

India

1. Reasons for outbreaks in areas that have introduced JE vaccination should be identified and corrective actions taken.

Goal 6. Control of hepatitis B is accelerated

Progress

In 2018, all 11 countries in the Region continued to have hepatitis B vaccine (HepB) in their routine immunization schedules as part of combination vaccines, and eight countries (Bhutan, DPR Korea, India, Indonesia, Maldives, Myanmar, Thailand, Timor-Leste) had a universal HepB birth dose (HepB BD) (WHO Monitoring System 2018).

A South-East Asia Regional Expert Panel (SEA-REP) has been formed in 2019 to make recommendations to the Regional Director on whether the target of reducing chronic hepatitis B prevalence to less than 1% among children at least five years old has been achieved. The SEA - REP finalized draft 'Guidelines for verification of achievement of hepatitis B control target through immunization in the WHO South-East Asia Region' and reviewed progress made by Bangladesh, Bhutan, Nepal and Thailand and verified that these countries have achieved the target of reducing chronic hepatitis B prevalence to less than 1% among children.

The overall HepB3 coverage with three doses HepB (HepB3) in the Region increased from 54% in 2010 to 88% in 2017 (Source: WUENIC best estimates in JRF 2017). As per draft WHO/UNICEF best estimates in 2018 the HepB3 coverage was reported to be >90% in eight countries (Bangladesh, Bhutan, DPR Korea, Maldives, Myanmar, Nepal, Sri Lanka, Thailand). India reported 89%, Indonesia 79% and Timor-Leste 83%. Among the eight countries that included HepB BD in their vaccination schedule in 2018, coverage was >90% in four (Bhutan, DPR Korea, Maldives, Thailand). India and Indonesia reported 54% and Myanmar and Timor-Leste where the HepB-BD was introduced in 2016 reported 14% and 61%, respectively. Several countries have sustained high HepB BD and HepB3 coverage for at least five years and likely achieved the target of reducing chronic hepatitis B prevalence to less than 1% among children.

Nationally representative sero surveys among children at least 5 years of age are available in Bangladesh, Bhutan, Nepal and Thailand and indicate low post-vaccination infection rates in the surveyed cohorts. Maldives is planning a national school-based survey among Grade 1 children while DPR Korea is planning to conduct a national household-based survey among children aged over 5 years.

Conclusions

The ITAG appreciated the establishment of the South-East Asia Regional Expert Panel (SEA-REP) for Verification of Hepatitis B Control and noted the report of its first consultation. It endorsed the draft 'Guidelines for verification of achievement of hepatitis B control target through immunization in the WHO South-East Asia Region'.

Recommendations

The ITAG recommended that:

1. WHO-SEARO should:
    a. distribute the final version of the "Guidelines for verification of achievement of hepatitis B control target through immunization in the WHO South-East Asia Region" to all stakeholders.
    b. convene a specific technical consultation on hepatitis B control through immunization and report on the outcomes at subsequent ITAG meetings.
2. In countries that have been verified to have achieved the control target, NITAGs should assess whether hepatitis B control status has been maintained and report their conclusions at subsequent ITAG meetings.
3. NIPs should enhance the dialogue and coordination with other programmes concerned, especially to increase birth dose coverage.

There were country-specific recommendations as well:

DPR Korea

1. A seroprevalence survey should be conducted to support verification of Hep B control.

Indonesia

1. Hepatitis B birth dose coverage is improved, and monitoring strengthened.

Goal 7. Introduction of new vaccines and related technologies is accelerated

Progress

New vaccines have become available in the last decade for diseases that were previously not included in the national Immunization programmes (NIPs). As a result, all countries in the Region have added two or more new vaccines to the national immunization schedule during the last decade and have strengthened their NIPs in the process. The SEA-RVAP 2016-2020 has identified the acceleration of introduction of new vaccines as a goal. Each country is expected to introduce at least two additional new or underutilized vaccines from 2016 to 2020. Table 1 highlights the progress in new and underutilized vaccine introduction in the Region.

Table 1: Introduction of new and underutilized vaccines in the SEA Region, 2016-2019

Country	National	Subnational	Planned introductions
Bangladesh		HPV vaccine (1 district)	Rotavirus vaccine (2020)
Bhutan	MMR, PCV		Influenza vaccine
India	MR	Rotavirus vaccine (11 States), PCV (6 states) HPV (2 States),	
Indonesia	IPV, MR	HPV (1 province and 4 districts), PCV (3 districts), JE (1 province)	
Maldives	MR, HPV		
Myanmar	MR, PCV, JE Influenza		Rotavirus vaccine (2020) HPV (2020)
Nepal		HPV (2 districts)	Rotavirus vaccine (2019)
Sri Lanka	HPV		
Thailand	HPV, Hib	Rotavirus vaccine (1 province)	Rotavirus vaccine nationally (2019)
Timor-Leste	IPV		Rotavirus (2019), HPV (2020), PCV (2021)

Priority vaccines for consideration are rubella-containing vaccine (RCV), pneumococcal conjugate vaccine (PCV), human papilloma virus (HPV) vaccine, JE vaccine and rotavirus vaccine (RV). In addition, cholera, mumps, seasonal influenza and typhoid vaccines could be considered for specific geographical areas and age groups.

In the South-East Asia Region, Bhutan introduced HPV vaccine nationally in 2011 while Sri Lanka and Thailand introduced the vaccine nationwide in 2017. Maldives is the most recent country in the Region to have introduced HPV vaccine (March 2019). In India, HPV vaccine was introduced in Sikkim state in 2018 while in Indonesia, HPV vaccine has been introduced in all districts of Jakarta province in 2016, two districts of Jogjakarta in 2017 and in Surabaya city in 2018. Nepal and Bangladesh have successfully completed demonstration projects with HPV vaccine in one district each and are now planning to submit applications to Gavi, The Vaccine Alliance (Gavi) for national introduction. Myanmar has successfully submitted its application to Gavi for HPV introduction and is planning for national introduction of the vaccine in June 2020. A regional meeting on prevention of cervical cancer through HPV vaccination was conducted in India in June 2018 with the overall objective of strengthening the capacity of countries for prevention of cervical cancer through HPV vaccination and other strategies.

India has initiated a phased introduction of indigenous Rotavirus Vaccine (RV) and has already introduced the vaccine in 11 states. Bangladesh and Nepal are likely to introduce RV nationwide, with Gavi support, in 2019 while Myanmar is likely to introduce RV in 2020. Thailand has conducted a pilot project of RV introduction in one province and plans for national introduction in 2019. Non-availability of RV is a challenge that may delay introduction of the vaccine in countries of the Region.

Bangladesh, Nepal, Myanmar, five states of India and, more recently, Bhutan, have introduced PCV while Indonesia has introduced PCV in three districts and one city. Sentinel surveillance data from invasive bacterial disease surveillance sites in these countries has supported decision making for the introduction of PCV, which have been supported by Gavi. Post-introduction evaluations conducted in Bangladesh and Nepal and subsequent follow-up of recommendations confirmed that PCV3 coverage has reached coverage equivalent to DPT3 coverage, the vaccine is acceptable to the communities and poses no concerns related to injection safety.

Conclusions

The ITAG noted the introduction of HPV in four countries and PCV in one country since its last meeting.

The ITAG noted that introduction of Rotavirus vaccine is planned in five countries, HPV vaccine in two countries and influenza vaccine in high-risk populations of two countries over the next two years.

The ITAG recognized that conducting a cost effectiveness analysis of HPV vaccination would help with advocacy – making the case for securing internal and external financial resources, selecting the right mix of interventions to optimize the healthcare budget, and facilitating tender evaluation between purchasers and vaccine manufacturers.

Recommendations

The ITAG recommended that:

1. NITAGs and NIPs should work together to prioritize introduction of new and under-utilized vaccines based on the country context and SAGE recommendations.
2. Pre-readiness assessments and post-introduction evaluations should be conducted when new vaccines are introduced to help identify and correct programmatic gaps.
3. All countries should consider sharing their data with the Global Invasive Bacterial Surveillance Network (GIBSN) and the Global Rotavirus Surveillance Network (GRSN) through WHO-SEARO.

4. All countries should consider implementing recommendations for vaccination against HPV, as part of cervical cancer elimination, as recommended at the Regional Consultation (June 2019).

There was a country specific recommendation as well:

Sri Lanka

All evidence (research, clinical data, socio-demographic, disease trend, disease burden, co-morbidity/mortality reduction) should be considered when deciding on the introduction of new vaccines.

Goal 8. Access to high-quality vaccines is ensured

Progress

Recognizing that access to affordable vaccines of assured quality is central to the performance of immunization programmes, the SEAR-VAP 2016-2020 has identified ensuring access to high-quality vaccines as one of its eight goals.

The National Vaccine Institute (NVI), Thailand in collaboration with the Association of Southeast Asian Nations (ASEAN) Member States and the ASEAN secretariat has identified key areas for regional collaboration and prioritization including (1) system development for vaccine security, (2) human resource development, (3) ASEAN price policy for vaccines and pooled procurement, and (4) communication and coordination plan. These identified areas are expected to be Incorporated into a regional strategic action plan which is to be developed following the anticipated endorsement of an ASEAN Leaders Declaration on ASEAN Vaccine Security and Self Reliance (AVSSR) at the 3rd ASEAN Health Cluster Meeting and the 35th ASEAN Summit in 2019. The NVI will be hosting the Eastern Asian Sub-Regional Vaccine Procurement Exchange Forum (VPPEF) in partnership with UNICEF and Learning Network for Countries in Transition (LNCT) in September 2019 in Yangon, Myanmar. Participating countries include Indonesia, Myanmar, Philippines, Papua New Guinea, Thailand, Timor-Leste, Mongolia and Vietnam.

In 2019, all SEAR countries in the Region reported to WHO's Vaccine Product, Price and Procurement (V3P) web-based platform through the WHO/UNICEF Joint Reporting Form (JRF). The Regional Office provided additional inputs collected through other monitoring activities to finalize analysis with the WHO Market Information for Access to Vaccines (MI4A) team. It is estimated that the size of the vaccine market in the Region is 35% of the global market by volume but about 8% by value.

Vaccine procurement policy in the Region is split between self-procuring in three of the 11 Member States (27%); group procurement through UNICEF in six countries (55%) and mix procurement in two countries (18%). Among the five countries self-procuring vaccine; three are ranked by the World Bank as low middle-income countries (MIC), one is a low-income country (LIC) and one is upper MIC. In 2019, no supply shortages for the primary series vaccines were reported among countries in the Region. MICs however, have reported price as a major barrier to introduce RV, HPV, PCV and MMR and the uncertainty about vaccine availability contributed to delay in their introduction into the NIPs.

IPV supply situation has gradually improved since 2016 and no shortages of BCG and DPT vaccine are reported. However, the global production for recently introduced vaccines, such as HPV, PCV and Rota, is below current requirements.

WHO will conduct a workshop on Good Distribution Practices for National Regulatory Authority (NRA) inspectors in countries of the Region and from other WHO regions. These trained regulators will be collaborating with national EPI mangers and the MoHs to enforced good distribution practices (GDP) standards within the cold chain system in the national immunization programme as part of their regulatory inspection plans for pharmaceutical products.

In the South-East Asia Region, more than a billion doses of vaccine are administered annually, with the introduction of new vaccines and combinations of antigens growing steadily. In 2016-2018 countries in the Region reported 1.5 billion doses of bOPV administrated representing 57% of all antigens provided during this period. During the same period, half a billion individuals received MR vaccine in the routine and SIAs representing 16% of all vaccine doses administered. Pentavalent is the third most administered vaccine with more than 300 million doses (11%) during 2016-2018.

Conclusions

The ITAG acknowledged current regional initiatives on vaccine procurement and vaccine price sharing platforms, including the proposed pooled procurement initiative by the ASEAN Vaccine Security and Self-Reliance (AVSSR) working group.

Recommendations

The ITAG recommended that:

1. WHO-SEARO should report to ITAG on good practices for vaccine pool procurement.

2. WHO-SEARO should review existing initiatives on vaccine products, procurement and prices information exchange initiatives to identify suitable mechanisms to share procurement experience and engage with manufacturers on vaccine demand and supply.
3. NIP managers should engage with regulatory inspectors of NRAs to elaborate standards for benchmarking on good distribution practices within the cold chain infrastructure.

Countries should continue to meet regularly to review AEFI cases and publish vaccine safety data collected through the AEFI monitoring system as reviewed by national AEFI causality committees.

E. Posters on Innovations to improve immunization coverage and equity

All countries made poster presentations on innovative approaches adopted by them to improve immunization coverage and equity. The summary of each country poster is presented below.

BANGLADESH: Piloting online registration for vaccination

Bangladesh has initiated several innovations to improve immunization coverage to overcome immunization gaps in low coverage areas and populations. The country piloted online registration of children for vaccination in three city corporations and a rural area with the support of the government and city corporations. The online registration helps to track children for vaccination, defaulters and drop-outs. Messages are generated and sent to parents one day before the day of vaccination to remind them of vaccination. Reports are generated automatically, and vaccination certificates are generated and issued to parents after completion of full vaccination. Bangladesh has also initiated a GIS mapping tool to map all high-risk populations in city corporations and districts to reduce gaps in immunization. The information is used for better micro planning and to reschedule vaccination centres as per need.

BHUTAN: Initiative to improve immunization coverage

Bhutan has a robust immunization system that is delivered through a network of national referral hospital, district hospitals, basic health units and through outreach and satellite clinics. The immunization programme has maintained high coverage over 95% for most vaccines consistently for many years. Significant progress has been made and several vaccine-preventable diseases eliminated. However, there are certain pockets especially in the remote areas where coverage is lower than 90%. Also, there are challenges in providing immunization services to the nomadic population residing mostly in the difficult northern terrain of the Himalayas.

Annual review meetings are conducted to monitor the coverage and supply chain system and to discuss the way forward for increasing coverage in areas that have less than 90% coverage. Catch-up vaccination campaigns are conducted to fill the coverage gaps. As an example, a catch-up campaign with MR vaccine and OPV was conducted in five districts in 2018.

Riding on the good immunization system, Bhutan is striving to be at the forefront of introducing new vaccines. The country introduced PCV in routine immunization schedule in 2019 and is planning to introduce flu vaccine in October 2019 for key priority groups as recommended by WHO.

DPR KOREA: High Immunization coverage has been sustained

DPR Korea has sustained high coverage for RI during the past several years.

There is a strong commitment by the government and a sound policy for immunization in the country. In DPR Korea, under the wise leadership of the government, universal and free health care and immunization services are guaranteed under the Constitution, the law on upbringing of children as well as the public health law on prevention of communicable diseases.

There is a well-organized health system from the central down to the peripheral level. The quality of health care and immunization services also contribute to high vaccination coverage.

Primary health care units are available everywhere in the country regardless of mountainous or remote areas and these PHC units are supported by a section doctor system through which one household doctor takes care of 100-120 families.

The Central Hygiene and Anti-Epidemic Institute (CHAEI) conducts various activities to maintain high vaccination coverage by organizing routine technical training on both vaccination planning and practices under the guidance of National Hygiene Control Board, Ministry of Public Health.

The national EPI team and NITAG continue to strengthen supportive supervision of the immunization programme activities while strengthening surveillance of diseases prevented by routine immunization and other VPDs according to the Global Vaccine Action Plan of WHO.

Improved community awareness on vaccine effectiveness has also contributed to high vaccination coverage. The household doctors conduct various IEC activities in their catchment areas to encourage voluntary participation in the routine immunization programme.

INDIA: Boosting and sustaining routine immunization coverage- addressing inequities through Mission Indradhanush

India's immunization programme (one of the largest in the world) caters to a birth cohort of around 26.7 million infants and 29 million pregnant women every year through 12 million sessions. Despite being operational for over 30 years, immunization coverage among children aged 12-23 months in the country increased at a slow pace of almost 1% each year (from 35% in 1992-93 to 62% in 2015-16). There was also a significant disparity in immunization coverage of urban areas with only 6.3% improvement from NFHS 3 to NFHS 4 as compared to 22.7% in rural areas.

Receiving commitment from the highest political level for an aggressive action plan to achieve 90% full immunization coverage in the country, the Ministry of Health & Family Welfare launched a massive routine immunization (RI) intensification campaign called Mission Indradhanush (MI) in December 2014. This was further intensified as initiated under the Prime Minister's vision to accelerate progress and bolstered focus on 190 districts in the lowest quintile of identified FIC (fully immunized child) as Intensified Mission Indradhanush (IMI). MI / IMI was rolled out in phases through an amplified demand generation and communication approach. It successfully reached 33.9 million children and 8.7 million pregnant women in 680 districts across the country during Mission Indradhanush.

Ensuring that the gains made under MI are integrated into RI, a roadmap has been drawn to guide states in fast-pacing their efforts and ensure sustainability thereafter. Emphasis is given on adopting different actions for three categories of districts in the country based on their FIC status as summarized below:

Category 1: Sustaining gains, incorporating MI areas in RI micro-plans.

Category 2: Prioritizing and focusing on poor performing areas, urban and tribal areas, improving RI plans.

Category 3: Mission Indradhanush in districts with less than 50% FIC.

The categorization is based on latest IMI survey (2018) for 120 IMI districts conducted by UNDP and 70 districts by WHO and NFHS-4 data for remaining districts.

The roadmap is complemented by other key reforms-introduction of new vaccines, greater investments in research and innovation to bolster coverage (especially in urban and tribal areas), enhanced use of data, increased focus on adolescent immunization and robust surveillance to detect & counter AEFIs.

Sustained high level political support, advocacy and supervision is required for achieving the goal. Communication and counselling skills are to be tailored to deal with vaccination-centered barriers.

INDONESIA: Strengthening routine immunization in pockets of low coverage areas

Indonesia has made several innovations in strengthening routine immunization in pockets of low coverage areas. These include the newly introduced defaulter tracking system using ''my village and my home'' approach during immunization session, empowerment of volunteer/kaders for family-based approach to increase access to health services, drop-out follow-up and sweeping immunization, sustainable outreach sessions 3-4 times per year in hard-to-reach areas, communication strategy using immunization and MCH flash card and technical assistance for routine immunization training.

The Ministry of Health has identified EPI as one of the three national priority programmes and declared 2018 as the "immunization acceleration year". Eighty districts are being targeted for intensification of RI through various strategies such as sustained outreach strategy and drop-out follow-up as well as immunization sweeps. Five major urban areas with many immunization drop-outs are being supported through a Rapid Pro programme. Remote islands and hard-to-reach areas were identified and supported to improve immunization coverage; additional operational costs were provided for these areas; additional new cold chain equipment was provided. Due to challenges during the second phase of the MR immunization campaign a communication strategy for immunization that includes directives from religious leaders in support of the immunization programme was developed. Additional IEC materials including messages from religious leaders have been prepared and disseminated. Defaulter-tracking guidelines for health centres have been revised for better tracking of partially vaccinated children. Private sector reporting is being intensified, and a web-based electronic routine reporting pilot is being developed. Meanwhile, a vaccine management improvement plan has been developed and implemented. The national immunization technical advisory group is independent and functioning well.

However, there are challenges like VPD outbreaks, rapid urbanization, vaccine hesitancy due to religious issues, limited integration of the private sector and lack of province-or island-specific effective commination strategy and non-implementation of mandatory vaccination policy.

As a way forward, the programme has included indicators such as second dose of MR and Pentavalent 4 vaccine coverage, high quality micro plans development, defaulter tracking tool implementation. The programme has also included additional technical assistance at subnational level and advocacy to gain more political commitment and development of province-or island-specific communication plan with engagement of local leaders.

MALDIVES: Initiatives to improve immunization coverage; innovations to overcome immunization gaps in low coverage areas

The Maldives spends 9.5% of GDP on health and health care is free for all citizens. The expanded programme on immunization was officially launched in 1976. Since then the country has maintained decades of high immunization coverage. Polio, neonatal tetanus and measles have been eliminated and rubella and CRS controlled. MR, DPT booster, and HPV vaccines have been introduced in the last two years. National immunization policy was developed in 2018. Vaccine-preventable diseases are rare.

In order to improve immunization coverage, verification of completion of immunization at school entry is ongoing for decades. Several partners are actively engaged in the programme ranging from Islamic Ministry, Ministry of Education, the private sector, academic institutions, telecommunication sector, NGOs etc. Mass vaccination campaigns have been conducted to bridge immunity gaps e.g. MR vaccination campaign, HPV campaign. Sermons related to immunization in Friday prayers and involvement of MTAGI in supportive supervision and monitoring trips is a part of efforts to improve immunization coverage. Panel discussions (experts) in mass media during introduction of new vaccines or campaigns, reaching out to people using social media platforms (facebook, twitter, viber) to monitor and respond to queries and concerns including vaccine hesitancy have contributed to achievement of high coverage.

The country maintains a vaccine refusal database to monitor, track and address issues of vaccine hesitancy. Development of a communication plan is underway to improve acceptance of vaccine and tackle vaccine hesitancy.

MYANMAR: Use of GIS in EPI microplanning and monitoring

Routine immunization in Myanmar is a building block of strong primary health care and universal health coverage as it provides a point of contact for health care at the beginning of life. The Ministry of Health and Sports (MoHS) is constantly identifying possible ways to improve routine immunization coverage by reaching the unreached population of geographically and socially hard-to-reach areas through innovative approaches, such as hospital-based immunization clinics and urban immunization strategy. Myanmar highlighted the need for identification of reliable target for EPI and is currently piloting GIS-based microplanning as one among the many innovative ways to strengthen efficiency of immunization service delivery and logistics for outreach immunization.

GIS map-based microplanning strategy is built on the development of a micro-plan based on population information in the catchment areas of health workers and is mainly intended to identify missed villages through satellite imagery followed by strengthened delivery of health services for geographically hard-to-reach areas.

The project encourages accountability of health workers and supervisors to ensure every eligible child is included in the plan and all efforts are made to reach them on time.

The project will allow health workers to review, edit and update the micro-plan electronically. A national roll-out of this project is planned in 2019-2020.

NEPAL: Fully immunized declaration initiative

In December 2012, Nepal started a unique initiative known as 'Full Immunization Declaration (FID) Initiative'. With the aim to reach every child through immunization services and reduce child morbidity and mortality associated with vaccine-preventable diseases, the initiative's slogan is 'With local participation, ownership, and local resources mobilization; Our commitment is to ensure full immunization'. The initiative is deeply grounded in the cultural-political ethos of Nepal where local communities have traditionally taken ownership and continue to do so. Full immunization declaration initiative is often integrated with other health and beyond-health initiatives such as open defecation-free, full literacy, domestic smoke free, nutrition, and menstrual taboo-free programmes.

The objective of the initiative is to have all eligible children fully immunized with all vaccine doses as per the national immunization programme. A rigorous method is followed as laid out in national FID guidelines. The local health workers first search and line list all eligible children by visiting every house-hold and vaccinate any unvaccinated children found in their area. The health facility then invites the district to run a cross-check in its catchment area based on a sample survey. If no unimmunized children are found, the health facility area is declared to have achieved full immunization with local community celebration. Once all health facility areas in a district are declared as fully immunized, the district is declared FID.

This initiative addresses issues of inequities in immunization as the FID declaration is done in a bottom-up manner starting at the lowest level. Further, every child regardless of socio-economic, geographical, or cultural aspect within an administrative boundary is to be fully immunized under this programme. To declare any administrative area as fully immunized, all stake-holders should ensure that 100% of the eligible children in that area have received complete vaccination as well as ensure sustainability following guidelines jointly endorsed by the Ministry of Health and Population and Ministry of Federal Affairs and Local Development.

Over the years, Nepal has witnessed participation of all stakeholders at all levels to achieve full immunization. This has ensured ownership of the immunization programme not only by policy makers and service providers, but also by the communities. As of June 2019, 56 out of 77 districts, and one out of seven provinces have been declared fully immunized.

SRI LANKA: Sustaining high immunization coverage: Addressing Challenges

Sri Lanka has a strong public health infrastructure for immunization service delivery and is coordinated through district level regional epidemiologists and divisional level medical officers of health staff (MOH staff).

Immunization is provided at various stages of the life cycle. All divisional level geographic areas are divided into smaller areas and a public health midwife (PHM) and a public health inspector (PHI) are allocated to each area to ensure ownership and accountability for immunization and communicable disease prevention. Field level public health staff routinely create demand for vaccination through regular home visits which are well accepted. During home visits, appointments are given for vaccination and missed and newly arrived children to the area are identified for vaccination.

Immunization services are provided as an integrated service at the community level with other public health services by the same public health staff. As the same system is existing throughout the country, there is no difference observed for urban and rural immunization service provisions. Vaccination services are made available on weekends (Saturdays) for client convenience and for providing an opportunity for missed children for vaccination. Further, missed opportunities for vaccination are well addressed during other service seeking opportunities such as when individuals come for curative care to institutions, or are accompanying parents during antenatal, well-women clinic services and during Grade 1 school enrolment.

Good public-private partnership exists in providing EPI vaccines free by the private health sector and coverage data and AEFI data is shared by the private sector with the government. There are enabling factors in assuring public trust in providing quality vaccines controlled through NRA. A well-functioning AEFI system and staff competency in addressing AEFI emergencies have built public confidence to accept vaccines. Regular supervision, regular reviews and feed-back by national EPI staff enable the programme to identify gaps and help in taking measures for improvement. Sri Lanka plans to take further measures to sustain high coverage and establish a legal framework for immunization based on the national immunization policy.

THAILAND: Improvement in immunization coverage

A national immunization coverage survey among children under 5 years and pregnant women has been conducted annually since 1980. After survey results showed high immunization coverage in 1999, the survey frequency was changed to every 3-5 years. School children were included in the survey in 2013 and survey sites were expanded to cover Bangkok and deep-south provinces in 2018.

There are two immunization coverage estimation techniques in the country. A conventional maternal and child health handbook which is a paper-based system that is used to record type and date of vaccination, as well as making an appointment. An electronic-based system was developed to collect 43 categories of health data from healthcare facilities, including demographic data and vaccination-related variables.

The latest national immunization coverage survey was conducted in 2018. The results showed high coverage in general provinces. However, low coverage was marked in the deep-south for all vaccines except birth doses. And under-target of vaccine coverage among late years children were shown in Bangkok.

A gap analysis was conducted, and the way forward proposed to solve the identified issues. 1) In the deep-south where vaccine hesitancy is causing low coverage, communication and social mobilization will be promoted to encourage parents to get their children vaccinated. 2) Seeking extra sources for funds for migrant vaccination is ongoing to reduce obstacles to access vaccination services. 3) In the urban areas coordination with the private sector is to be strengthened. 4) An immunization recording platform and gathering individual vaccination history from all health facilities is planned to be put in place.

TIMOR-LESTE: Reaching the unreached- path to achieving GVAP goals

The government and partners in Timor-Leste have worked together to improve the immunization coverage and control vaccine-preventable disease. The key activities conducted to reach the un-immunized and partially immunized children were prioritization of districts for interventions, regular micro planning and following the plans to identify and map areas with low coverage, identification of partners support including logistic and other related needs, encouragement of community leaders and local authorities to fully participate in developing micro planning which will help in advocacy and encourage mothers to seek health services, including immunization.

National reviews were conducted with local authorities to find solutions to address the gaps and monthly immunization coverage reviews were conducted at national level to identify low coverage areas and the action taken to bridge the gap. Mothers' support groups were engaged to advocate for the immunization programme by using local media and local languages. To track and reach missed children, the routine immunization programme was strengthened in all government health facilities and some private clinics by providing daily immunization services. Screening of mother's card was intensified to identify the eligible age for different antigens and outreach and mobile clinics were conducted in areas with low coverage.

EPI data quality audit was conducted in 2018 and recommendations are under implementation. Timor-Leste has already implemented the DHIS 2 online platform to report EPI data integrated with data from other public health programmes. The country has implemented unique information technology platform, "Saude na Familia" to capture all health-related information including immunization and plans are in place to develop an electronic national immunization register

Dili municipality is the main urban centre with 30 % of the national population. Since 2015, *Stop Transmission of Polio* (STOP) consultant has been continuously assigned to the municipality for direct international technical assistance and many strategies were instituted to improve the immunization coverage, such as: involving community /political leadership in advocacy and the establishment of cold chain and immunization services in all health posts and the private sector, strengthening of immunization services in the National Hospital to minimise miss-opportunities, involving the highest political leadership and NITAG chairperson and members in advocacy through TV and radio and regular quarterly EPI and VPD reviews as well as in-service training with STOP consultant support.

With these efforts WHO UNICEF has estimated that DPT3 coverage has increased from 72% in 2010 to 83% in 2018.

F. Poster Café- Best practices in immunization in countries

Each country presented one theme to showcase a best practice in immunization. A summary of the presentations is provided below:

BANGLADESH: MR SIA planning and preparedness

Bangladesh is planning to conduct MR follow-up campaign targeting children between 9 months to 9 years (34 million children). Gavi has agreed to support vaccine and operation cost up to five years. The vaccine operation cost to cover children 5-9 years will be funded by the government. Bangladesh has the highest level of political commitment and would like to ensure the campaign reaches at least 95% of children especially those that were missed by previous campaigns and routine immunization. The programme will use innovative approaches such as real-time data monitoring, flexible opening and closing hours, use of supervision app, use of invitation card and household sticker and mapping of hard-to-reach areas using GIS mapping tool.

Bangladesh is piloting selective vaccination in two districts: one high-performing and one poor-performing. In these districts, all children of eligible age will be line-listed and their MR vaccination status recorded. A child already vaccinated with 2 doses of MR vaccine, documented

by card, will not receive vaccination during the campaign. The approach will be evaluated after the campaign.

Several pre-campaign readiness assessments will be conducted both at national and sub-national levels using the WHO prescribed checklist.

BHUTAN: Introduction of PCV 13 - a cost utility analysis

In September 2015, the National Committee on Immunization Practice (NCIP) made a recommendation to the MoH to introduce the PCV vaccine. With support from WHO and the Health Intervention and the Technology Assessment Programme (HITAP) a cost utility study was conducted in early 2017 and this was presented to MoH and a policy brief recommending introduction of vaccine was issued in July 2017.

The vaccine was launched on Her Majesty's birthday on 4th June 2018 and was introduced into the routine EPI programme from January 2019.

The essential medicines and technology department (EMTD) conducted a cost utility study comparing no vaccination to PCV 10 and PCV 13 looking at only the government perspective of the cost of vaccine. The Markov model with a one-year cycle was used and both the cost and outcomes were discounted at 3% per annum. The results were presented using an ICER (incremental cost effectiveness ratio) in US$ per quality-adjusted life year (QALY) gained. The disease incidence rates of meningitis, bacteremia, pneumonia, and acute otitis media were derived from the Annual Health Bulletin 2016. The incidence rates of pneumococcal bacteremia and sequelae were transferred from Thai studies as these data were not available in Bhutan. Mortality rates and probability of developing sequelae were derived from literature reviews.

A cost-effectiveness threshold of 1xGPD per capita or US$ 2708 per QALY gained was deemed to be appropriate for this study. With indirect effects of vaccination, the ICERs of PCV10 and PCV13 were US$ 36 and US$ 40 per QALY gained, respectively. The ICER of PCV13 versus PCV10 was found to be US$ 92 per QALY gained. Without indirect vaccine effects, the ICERs per QALY gained of PCV10 and PCV13 were US$ 175 and US$ 205, respectively, compared to no vaccination. PCV 13 was found to prevent more episodes of illness and deaths compared to PCV 10 in both the vaccinated and unvaccinated population.

The study also looked at the impact on human resources on health and it was found that if PCV vaccine is introduced into the routine immunization programme the work of the health assistant would increase by 2 full time equivalent (FTE) per year while the FTE of other health workers would decrease, particularly for specialists (from 0.6 to 1.1 FTE) and nurses (from 1 to 1.6 FTE).

The findings of the study indicated that both PCV 10 and PCV 13 were cost-effective at the current price of US$ 3.05 and US$ 3.55 respectively. The study also showed that the maximum prices for these two vaccines to be cost-effective are US$ 7.95 and US$ 8.65 for PCV 10 and PCV 13 respectively. The budget impact analysis revealed that the total budgetary requirement will increase by approximately US$ 3.77 million for PCV10 and US$ 3.75 million for PCV13.

Limitations:

a) Data on sequelae and health utility estimates were transferred from Thailand studies and the data on herd protection was adapted from the USA.

b) The incidence of OPD visits was based on the data collected between January and March and this may not capture seasonal variations if they exist.

c) The direct non-medical costs borne by households including traveling costs for seeking care, and productivity loss of caregivers was not considered.

DPR KOREA: EPI and VPD surveillance review - recommendations and follow-up actions

The recommendations of the EPI and VPD surveillance review have been followed by the programme and the key actions taken are summarized below:

- A software for logistics drug management inventory system (LMIS) has been developed and LMIS has been established at the national and provincial level.
- A plan for vaccine distribution and supervision on implementation of EPI and VPD surveillance activities according to the monthly immunization clinic plan in each province and estimate for the vehicle requirement has been developed and is being implemented.
- Heating systems were installed in a few immunization clinics with support from GAVI and using local funding to improve the quality of immunization services.
- Session schedule was reviewed, and different vaccination days were set for different immunization posts at peripheral level within counties to improve transport of immunization supplies and supportive supervision.
- A standardized checklist for field supportive supervision and monitoring was developed and is being used.
- The progress of the programme is being reviewed regularly through national committees.
- A national cold chain equipment (CCE) deployment and comprehensive national CCE repair/maintenance plan has been developed for further strengthening of the cold chain.
- Polio and measles/rubella outbreak response plans have been developed.

- VPD surveillance guidelines have been updated in line with WHO regional guidelines.
- AEDs (Anti-Epidemic doctors) at county hygiene and anti-epidemic station (HAES) were increased and training on HHDS for timely case investigation and sample collection was planned.
- For computerized surveillance data management of county hygiene anti-epidemic stations, a software is being developed for county/province/national-level. Hardware and training will be conducted first in Pyongyang city and in a few provinces located in the north-eastern part of the country.
- According to the updated guideline all AEFI data by minimum core variables is analyzed, detailed information is collected and causality assessment for severe AEFIs is being conducted with involvement of a strengthened national AEFI committee.
- National/provincial joint supportive supervision and monitoring of HAES/sentinel hospitals is being strengthened with a log system for supervisory notes.

INDIA: Rotavirus introduction - key lessons learnt

India introduced the rotavirus vaccine (RVV) in phases starting from 2016. Currently, there are four Rotavirus vaccine products available in the Indian market: Rotavac®, Rotasiil®, Rotarix® and RotaTeq®. All four products are technically interchangeable under the routine immunization programme but vaccine handling, dose and administration differs. India has introduced two types of RVV- the oral liquid RVV (Rotavac®) and the oral lyophilized RVV (Rotasiil®). Separate trainings were conducted, and a separate training package was developed for the two types of RVV. Various innovations tried during the trainings were the station approach - a small group interactive session, online pre- and post-test, query process using the sticky pad and a vaccine administration film for the participants

Nearly 50 million doses of RVV have been administered since the introduction of the vaccine in 2016. Only three cases of intussusception have been confirmed and all of them recovered. The preliminary findings of the impact study being done in different sentinel sites shows a decrease in rotavirus positivity rate in the post-vaccination period.

The key product-related challenges faced during the introduction of the two types of RVV include the large cold chain and dry storage space requirement for Rotasiil®, logistic mismatch if bundling is not meticulously followed and the increased time required for vaccine reconstitution and administration for Rotasiil®. During the introduction process, the key lessons learned were that the preparedness assessment with cold chain and dry storage space requirement and focused training of cold chain handlers on bundling ensures smooth logistic management after the

vaccine introduction, hands-on training at all levels is required for smooth programme implementation. Strengthening AEFI surveillance is essential for immunization safety and the interchangeability of the RVV products to decrease drop-outs and improve coverage.

INDONESIA: Interrupting cVDPV1 transmission - enhancing surveillance, boosting immunity and strengthening routine immunization

On 12 February 2019, Indonesia reported an outbreak of circulating vaccine-derived poliovirus type 1 (cVDPV1) in Yahukimo district, Papua province. Laboratory data confirmed that VDPV1 was isolated from a 31-month-old male child with date of onset of paralysis on 27 November 2018. Evidence of virus circulation was confirmed through the detection of genetically related VDPV1 in stool from two healthy children, living in the same district, collected on 24 January 2019 and 13 February 2019. The cVDPV1 outbreak has been graded as emergency grade 1. The country has mounted an aggressive outbreak response to control the outbreak. The cVDPV1 case count remains one and localized to Yahukimo district. The salient features of the outbreak response activities are summarized below:

- Immunization response: Two mass scale vaccination campaigns were conducted using bivalent oral polio vaccine (bOPV), targeting 1.26 million children under 15 years, in provinces of Papua and Papua Barat.
- Coordination and partnership: Weekly coordination meetings were held among partners, consultants were deployed to support the response activities. Emergency operations centres were established at national and provincial levels for coordination of outbreak response activities.
- Surveillance: Actions were taken to enhance active surveillance by measures such as; hospital record reviews, collection of stool specimens from community contacts and expansion of environmental surveillance.
- Risk communication and community engagement: Local religious leaders have been engaged, tools have been revised to cater to populations with low literacy level and local communication channels are being utilized.
- Managing vaccines and logistics: Adequate vaccine and marker pens were procured and provided to all teams in a timely manner, monitoring tools were simplified and new cold chain equipment was provided to the province.

The priority actions undertaken are monitoring and supervision of high-risk districts including real time monitoring, social and behavioural change communication, including involvement of religious leaders, surveillance trainings for district, hospital, health centre focal points in 12 high-

risk provinces, and applying lessons learnt from Yahukimo special operations to reach hard-to-reach children. An assessment of outbreak response will be undertaken to determine the end of outbreak or any need for additional mass vaccination campaigns.

MALDIVES: Planning hepatitis B seroprevalence survey

Planning for hepatitis B seroprevalence survey started through a consultative process involving the health protection agency (HPA), Maldives Technical Advisory Group on Immunization (MTAGI), WHO and UNICEF. The objectives of the survey are to measure the prevalence of hepatitis B surface antigen among Grade 1 school children and to collect immunization coverage data and calculate the effectiveness that hepatitis B vaccine has on preventing chronic infection. The survey population proposed for inclusion is children enrolled in Grade 1 (~ 6 years of age). The proposed sample size is 2121 students. A total of six schools in the Greater Male' region, nine from atoll capital schools and 48 from other peripheral islands are proposed to be selected for the purpose. The training and piloting of the survey is planned for September-October 2019 and survey implementation is expected to be completed by December 2019 with the availability of the report in early 2020.

MYANMAR: Post-introduction evaluation of JE vaccine -Key recommendations and follow-up

JE vaccine has been introduced into RI at 9 months of age since January 2018 following a nationwide catch-up campaign (9m-15 yrs. age group). A post-introduction evaluation (PIE) was conducted with the main objectives to assess the impact of JE vaccine introduction on the EPI programme performance; to use the findings to correct identified problems and to improve planning for introduction of additional vaccine in the future.

The methodology included a desk review and adaptation of tools, a field assessment at different health administrative levels by assessment teams (MoHS, WHO, UNICEF, PATH). The main findings of the PIE indicated that JE vaccination coverage was high (>90% in most of the townships) and the reported AES and JE positive cases had declined significantly after introduction of JE vaccine in 2018.

PIE also identified strengths and weaknesses on areas of planning, cold chain and vaccine management and storage, logistics, AEFI management and highlighted suggestions for improvements in areas such as distribution of training materials, funds, availability of reporting forms, capacity building of cold chain handlers and adherence to the multi-dose vial policy to reduce vaccine wastage as well as needs for specific plans for AEFI crisis communication. On waste management, the PIE indicated that all health facilities use safety boxes, but incinerators are available only at a few hospitals. It also noted the unsafe waste disposal practices at some

facilities and recommended the need for standard operating procedures and further trainings on waste management.

NEPAL: Concurrent routine immunization monitoring – processes, outputs and challenges – Data triangulation to improve immunization programme performance.

The goal of the national immunization programme (NIP) is to immunize every child with all vaccines included in the NIP. Immunization is mandated as a right of every child in the National Immunization Act.

To operationalize this concept, the NIP needs real time, reliable and actionable data to inform decisions. The health management information system (HMIS) is a nation-wide passive aggregate data collection system with granularity down to the health facility level. Data from vaccine-preventable diseases surveillance system including case-based laboratory supported measles surveillance system (supported by a nationwide network of programme for immunization-preventable diseases at WHO also known as WHO-IPD) is also available. Measles case and outbreak data could serve as the proverbial 'canary in the coal mine' to identify areas with suboptimal immunization programme performance.

However, a system of granular data which would also identify actionable intervention points for the local programme manager at health facility or municipality levels was lacking. Furthermore, information available from different sources was not triangulated systematically to inform programmatic decisions.

The NIP in collaboration with immunization partners (WHO and UNICEF) established an immunization programme core group (IPCG) to triangulate information from different sources to improve access and equity for NIP. The IPCG holds periodic meetings with immunization partners and other sections of the department of health services' divisions (like logistics) to solve problems promptly.

To fill the gap of granular data which would also identify actionable intervention points for local programme managers, WHO-IPD spearheaded a system of concurrent routine immunization monitoring (with support from Gavi, the vaccine alliance). IPCG endorsed the methodology and standardized data collection tools. Under this system, specially trained independent monitors hired by WHO-IPD and surveillance medical officers (SMO) of WHO-IPD monitor immunization programme performance at district, health facility, and immunization session levels as well as conduct quick immunization assessments in areas selected through purposive selection. In 2018, more than 5000 children have been assessed in 460 communities across Nepal. The monitors share the data immediately at local level so that corrective actions can be taken.

Information from measles surveillance has been used to vaccinate more than 10000 persons in different age groups with measles-rubella vaccine as part of outbreak response immunization.

HMIS data is analyzed at least every quarter and WHO-IPD SMO follows up with local health authorities for any gaps identified. IPCG examines and triangulates all available information holistically to improve immunization coverage with access and equity in the country.

SRI LANKA: HPV vaccine introduction and scale-up-lessons learnt

The estimated girl cohort in Grade 6 in schools (10 years completed) is 175000 for HPV vaccination. The age-specific school enrolment ratio (grade 1-9) was high and 96.3 % in 2017. The NIP has experience of school-based vaccination for aTd booster in Grade 7 and rubella vaccination until 2012.

HPV vaccination was introduced as an evidence-based new vaccine introduction by assessing country-specific HPV prevalence among normal women, incidence of cervical cancers, genotype risk attribution for cervical cancer development, government cost incurred for cervical cancer screening, costs being incurred for cervical cancer management at each stage, including radiotherapy and chemotherapy. These cost implications were used for different case scenarios such as costs on investing in screening in preventing country cervical cancer burden, costs required for total case burden management and comparing with costs required to vaccinate for preventing vaccine preventable cervical cancers.

The decision of national introduction of the HPV-quadrivalent vaccine through existing public health infrastructure of *school medical inspection programme* was taken based on results of an implementation feasibility study.

The government assured sustainable funding, with some Gavi support, for implementation and assured access to vaccines at Gavi price. All partner organizations (Gavi, UNICEF, WHO) supported the preparatory work including advocacy and training conducted by the NIP, in line with the programme requirements. Consistency of advocacy messages was maintained for different categories (health staff, teachers, students, parents) and this helped to achieve public trust and to create demand. Shared resources for refresher training on AEFI also helped to build confidence among health staff to handle anxiety-related issues in schools. All this contributed to achieve high coverage within a short period of time after the introduction of the HPV vaccine in October 2017.

The key lessons for scale-up include the need for organizing carefully and targeting consistent messages on the benefit of vaccine to gain confidence of parents, children and school authorities. Trainings should be targeted to build confidence of health care staff to address emergency AEFI

and anxiety-related issues. There should be a proper mechanism for 2nd dose follow-up and mechanism for opportunistic screening to vaccinate any missed children. Sri Lanka is practicing opportunistic screening of girls at Grade 7 school medical inspection and combines missed HPV doses, if any, with the due aTd booster dose.

THAILAND: Closing immunity gap for measles - action taken, planned

Thailand started the measles elimination programme in 2012. Immunization, surveillance and laboratory strategies are being implemented. Measles cases declined during 2014-2015. However, a large outbreak occurred in 2018 with a high number of measles cases in the deep-south, along the Thai-Myanmar border, in urban and industrial areas, with spread to other parts of the country.

Epidemiological data shows that most cases in the deep-south provinces are in children under 5 years caused due to vaccine hesitancy. In the rest of Thailand cases are mostly between 20-40 years and one-tenth of these are among migrants.

A MCV immunization campaign was conducted in the deep-south to contain outbreaks in late 2018. Around 250000 doses of vaccine were administered from routine stockpile. Non-health sectors such as religious leaders, community leaders, media and local administrative offices were involved to encourage vaccination acceptance among hesitant parents. The number of cases is showing a decline in early 2019.

Three population groups were classified as high risk; children in the deep-south, migrant children and adults living in crowded conditions.

A national immunization campaign with MR vaccine is planned in September 2019. The target beneficiaries will be children between 1 - 12 years in the entire country who have missed MCV regardless of nationality. In 2020 an adult immunization campaign is proposed to raise immunity among adult risk groups such as military personnel, prisoners, factory workers, tourism staff and health personnel in the 10 highest-risk provinces and Bangkok.

TIMOR-LESTE: Coverage evaluation survey - overcoming challenges of denominator

Timor-Leste is an island at the eastern end of the Indonesian archipelago with an estimated total population of 1.2 million. The population census (2010) gave a projected birth cohort of 40351 for 2016. But the cohort size was found to be 33710 in 2016 based on the population census conducted in 2015. This reduction in the birth cohort causes a sudden rise in the coverage estimates for the first two years of life based on data reported routinely. Hence, a vaccine coverage evaluation survey was planned according to the new guidance published by WHO in

2018 with the objective to estimate the vaccine coverage in the first and second years of life as per the national schedule

Children who were 12-23 months and 24-35 months old at the time of the survey were studied as separate cohorts for their first and second year of life vaccinations respectively. The new vaccine coverage survey methodology used probability sampling.

The primary sampling unit was the census enumeration area. Assumed non-response rate and design effect were 5% and 1.45% respectively. The final sample size was 301 per cohort. Three children were expected to be enrolled from each cluster per cohort and it was expected to find one eligible child in every 8th household from the 26 selected per cluster. A nationally representative sample of 101 clusters was selected based on probability proportional to the size of the population.

Data were collected using an interviewer-administered questionnaire. The home-based records and health facility records were referred to extract date of vaccinations.

The selected households were identified on the field using paper maps and Global Positioning System (GPS) receivers. An independent group of external supervisors verified the survey protocol adherence.

In the first year of life cohort, the estimated highest crude dose coverage was 94.7% (95%CI,91.7-97.0) for BCG. The lowest crude dose coverage was reported for hepatitis birth dose, 66.2% (95%CI,58.5-73.0). Among the infants, 4.8% (95%CI, 2.9-8.0) had never been vaccinated. DTP 4th and the MR 2nd doses in the second year of life were also low at 54.8% (95% CI, 46.5-63.0) and 54.4% (95% CI, 46.1-62.0) respectively. The estimated design effect was 1.74.

The new methodology is technically more robust and feasible. However, training of surveyors is challenging when compared to 30x7 cluster survey practiced earlier. The sample size calculation depends on reliable data for birth rate, infant mortality rate and average household size. Hence, current methodology is relatively difficult to be practiced in a country where the civil registration system is not functioning. Similarly, considerable resources need to be invested when the required maps, GPS are not readily available.

The immunization coverage estimates derived from EPI coverage survey was much lower than the over 100% administrative immunization coverage derived when using 2015 census-based population estimates and this led the Ministry of Health to revisit the 2015 census-based population estimates and adjust accordingly.

G. Informational session on two new vaccines

Dengue vaccine

CYD-TDV (Dengvaxia®) is a live attenuated, recombinant tetravalent vaccine employing the attenuated Yellow fever (YF) virus 17D strain as the replication backbone. Two large Phase-3 trials involving over 30 000 participants aged 2-16 years indicated that a 3-dose regimen of this vaccine was associated with 65.6%, 93% and 81% reduction in virologically-confirmed dengue, severe dengue and dengue hospitalizations, respectively, over a 25-month period from the first dose, in the 9-16-year age group. These data led to licensure of the vaccine with an indication of 9 to 45 years.

In April 2016, SAGE recommended the use of dengue vaccine, while suggesting that the public health benefits of vaccination could be maximized if dengue seropositive was high (70% or greater) in the targeted age group. SAGE noted the limited safety data in seronegative populations and recommended further safety studies, particularly in vaccinated seronegative persons.

Additional data that became available in 2017 showed that the vaccine performs differently in seropositive and seronegative individuals. Vaccine efficacy against virologically-confirmed symptomatic dengue in the 25 months after the first vaccine dose was higher among those aged ⩾9 years who were seropositive at baseline (76%; 95% CI: 63.9 – 84.0%) than those seronegative at baseline (38.8%; – 0.9 – 62.9%). Also, there was an increased risk of hospitalized dengue and severe dengue in seronegative individuals from year 3 onwards during the 66-month observation period. Thus, in high prevalence settings, the vaccine provides overall population benefit but an increased risk for seronegative individuals.

SAGE, in April 2018, considered these data and discussed two vaccination scenarios for countries considering the use of the dengue vaccine as part of their dengue control programme: (i) screening individuals for seropositivity prior to vaccination and vaccinating only those who were seropositive, and (ii) using the vaccine only in populations with high seroprevalence (>80%) in those 9-45 years of age. It concluded that the former, i.e. a pre-vaccination screening strategy in which only dengue-seropositive persons are vaccinated, is the preferred option. This requires a validated screening test with the highest specificity to identify persons who have had a previous dengue infection, to minimize inadvertent vaccination of seronegative persons; however, currently, point-of-care screening tests with high accuracy are not available. The alternative strategy of introduction of CYD-TDV dengue vaccine in disease-endemic areas (e.g. those with frequent dengue outbreaks) based on population seroprevalence criterion without individual

screening requires identification of areas with documented seroprevalence rates of at least 80% at age 9 years using population sero-surveys at district and sub-district levels.

SAGE also emphasized that important research and implementation questions remain concerning CYD-TDV, in particular the need to develop a highly sensitive and specific rapid diagnostic test to determine serostatus, simplified immunization schedules, and assessment of the need for booster doses.

An updated dengue vaccine WHO position paper on CYD-TDV was published on September 2018 and is available online at https://apps.who.int/iris/bitstream/handle/10665/274315/WER9336.pdf?ua=1.

Malaria vaccine

The ITAG was provided an update on the RTS, S/AS01 malaria vaccine implementation programme (MVIP), a synopsis of the vaccine development pathway, the main results of the phase-3 clinical trial and the considerations that led to the WHO recommendation in 2016 for pilot-testing of RTS, S/AS01. The MVIP was established by WHO to coordinate and support national immunization programmes in Ghana, Kenya and Malawi in introducing the vaccine in selected areas and to ensure rigorous evaluation of the programmatic feasibility of administering the required four doses, the impact on mortality and the safety of the vaccine. The main aim of the programme is to answer the questions identified in 2015 by SAGE and the Malaria Policy Advisory Committee (MPAC) as a basis for WHO recommendations on wider use of the vaccine.

H. Data management, quality and coverage estimations

Improving data quality and use in the Region:

A number of actions were identified and discussed to improve the quality and use of data on surveillance and immunization in the SEA Region. These are summarized below:

- Timely, complete and accurate data should be ensured through WHO/UNICEF Joint Reporting Form (JRF) and SEAR Annual EPI Reporting Form (AERF) as these are critical documents for tracking progress of RVAP and GVAP indicators, monitoring the health situation and assessing health trends and contribute to WHO/UNICEF estimate for national immunization coverage;
- Mechanism to validate/estimate sub-national level immunization coverage data should be strengthened;
- Data should be used for action at national and subnational level;
- Methods to improve target population estimates for programmatic use- including a bottom-up strategy and the use of alternative sources of data should be explored to derive better estimates of targets;
- Inbuilt data validation mechanisms should be developed to ensure quality of data, and provide regular feedback to sub-national levels on core variable data omissions, inconsistencies or discrepancies;
- Communication between the laboratory and surveillance units should be strengthened for linking the laboratory and surveillance data;
- Periodic in-depth data review/assessment (e.g., data quality review should be conducted and plans for improvement developed;
- Regional office should continue to provide feedback to the NIPs on the quality of surveillance data and share data omissions, inconsistencies and errors.

WIISE-A new tool on data management for improving data capture, analysis and dissemination

A brief overview of WIISE (WHO Immunization Information System) was presented. WIISE is a collection of applications to collect, manage, analyze and disseminate immunization and VPD surveillance data reported to WHO worldwide. WIISE is not a replacement for countries' information systems.

WHO uses immunization and surveillance data to develop strategies and implement activities to reduce the morbidity and mortality of vaccine preventable diseases as well as assess their impact at the country level. Immunization is key to achieving several of the SDG goals and targets. The

ability to collect and analyze accurate, up-to-date data is critical for the activities of the Organization. For example, data on children's immunization coverage helps identify gaps in national vaccination programmes and trigger information to ensure that every child is vaccinated, punctually and adequately, no matter where he or she lives.

WHO currently relies on fragmented data collection and analysis systems in which WHO Regional Offices and HQ have their own processes, workflows, and storage system to manage country-level and subnational data. These systems work in silos, may contain slightly different data, and have limited analytical capabilities, preventing WHO from having the consolidated view of information that is needed for decision-making and to best support its Member States.

In order to mitigate these constraints, the Organization is developing a common platform that will simplify and harmonize immunization data management while ensuring the autonomy of regional offices. WIISE will streamline processes and workflows and improve the overall governance of immunization data across the Organization.

Estimating coverage using survey and reported data

Countries measure immunization coverage by administrative reports and through coverage surveys. The two methods are complementary and can be used in combination to better interpret time trends in immunization coverage data. A similar approach, used by WHO and UNICEF to estimate national immunization coverage and methodology, has been published and available. It is important that immunization programmes get involved with household surveys measuring immunization coverage in an early state to provide necessary information on vaccination schedules and recording practices. WHO recently published a white paper on harmonizing vaccination measures in household surveys https://www.who.int/immunization/monitoring_surveillance/Surveys_White_Paper_immunization_2019.pdf?ua=1 to ensure results are useful for immunization programmes.

In addition, it is essential to use data for action at all levels of the immunization programme, including at the service delivery level. To better understand programme performance and identify pockets with un- and under-vaccinated children it is important to review data from different sources, such as vaccination histories from surveillance data, SIA post-campaign data, immunization session monitoring data and vaccine stock data.

I. Looking beyond 2020

Immunization Agenda 2030 consultation at the SEARO TAG in July 2019

The vision and strategy for the immunization programme in WHO South-East Asia Region is guided by the South-East Asia Regional Vaccine Action Plan 2016-2020 (SEARVAP) which describes the regional goals and targets for immunization and control of vaccine-preventable diseases in the Region. In the development of SEARVAP, global strategic documents such as the Global Vaccine Action Plan 2011-2020 (GVAP), WHO's Twelfth General Programme of Work 2014-2019 and the relevant United Nations (UN) Sustainable Development Goals were taken into consideration.

With SEARVAP coming to an end in 2020, development of a new regional strategic document to guide the programme was identified as an immediate priority for the Region. To align the future strategies and direction for the Region with the global post-2020 vision that is currently being documented in the 'Immunization Agenda 2030", a regional consultation was held at the Tenth meeting of the SEAR ITAG (July 2019) to review the global strategy for leaving no one behind, and to provide a perspective based on priority needs and emerging challenges in the countries of the Region.

Much like the SEARVAP, the Global Vaccine Action Plan will also end in 2020 and a new global strategy is needed for the next decade 2021-2030, a strategy that engages and aligns stakeholders for immunization and beyond at all levels, addressing emerging issues, and to harness new solutions for impact while reiterating the importance of vaccinations in contributing to the broader health and development agendas. This strategy has been envisioned in the Immunization Agenda 2030 (IA 2030) through a wide stakeholder consultation. The final IA 2030 will be presented to the SAGE in October 2019, then presented to the Executive Board in Q1 2020 and finally for endorsement at the World Health Assembly in May 2020.

IA 2030 is intended to inspire and align the plans and activities of country, regional and global audiences, including immunization, health and development stakeholders. Achieving the IA 2030 vision will ensure that everyone, everywhere has access to immunization. The benefits of immunization are currently spread unevenly, both between and within countries. IA 2030 will set the strategic priorities and world-wide goals for the decade 2021-2030 and is expected to provide a dynamic way forward until 2030. Further, IA 2030 will be complemented by a living online resource, including technical guidance, implementation plans in regions and a monitoring & evaluation framework, which will evolve throughout the decade.

The regional review of the IA 2030 at the SEAR ITAG was led and facilitated by WHO-HQ and Unicef-HQ. Participants from each of the 11 SEAR Member States of the Region brainstormed within the country-specific groups, including other partners/stakeholders, to review at least two pre-assigned strategic priorities to provide a collective country-group feedback on:

a) 'Key focus areas' described for the strategic priority

b) 'Objectives' and 'Core Principles' for the strategic priority

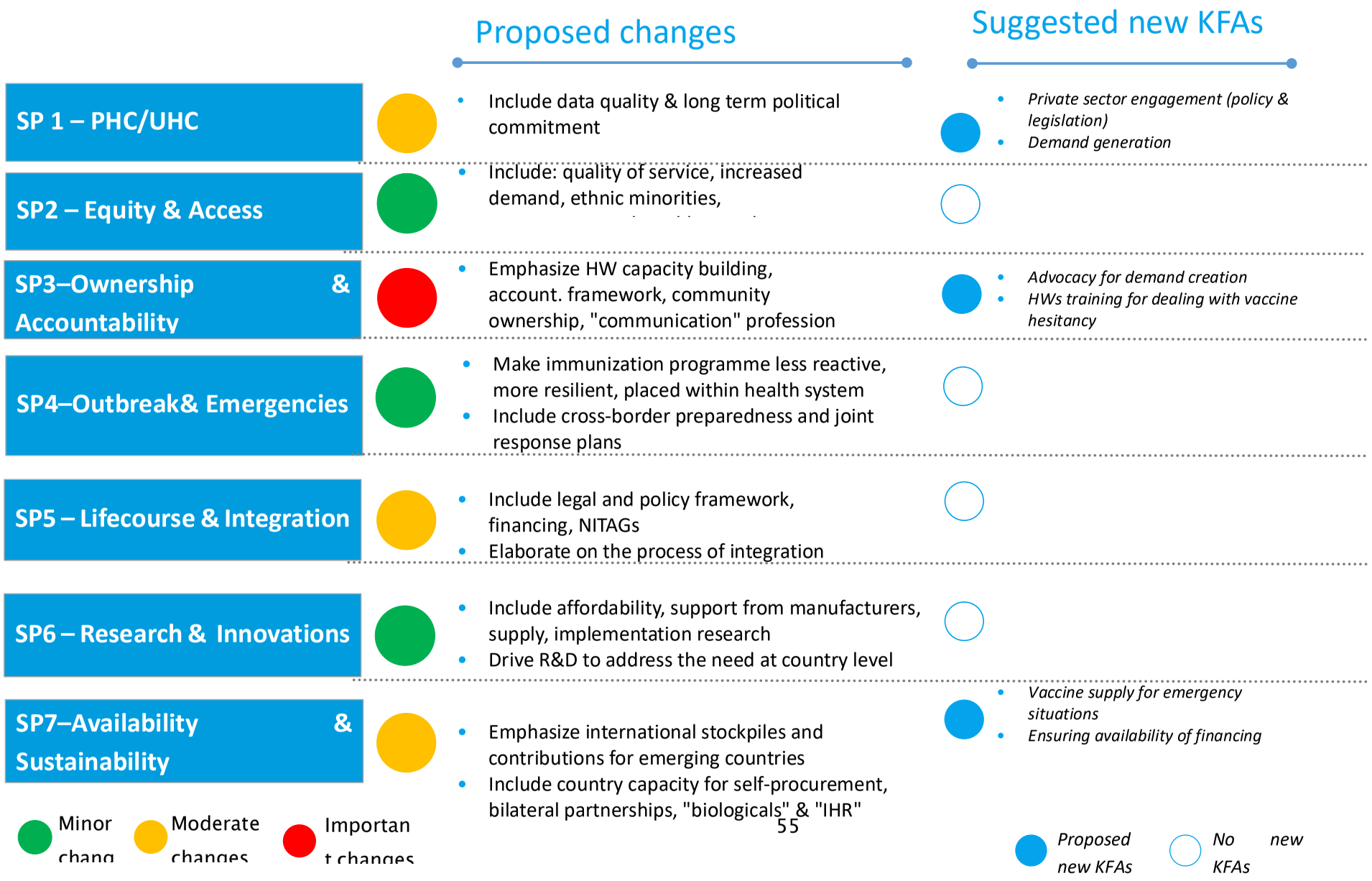
(with specific focus to get feedback on how the core principles - people centered, country owned, partnership and data-driven – could be applied to implement the strategic priority proposed in the IA 2030)

c) 'Goals and Targets' set for the strategic priority

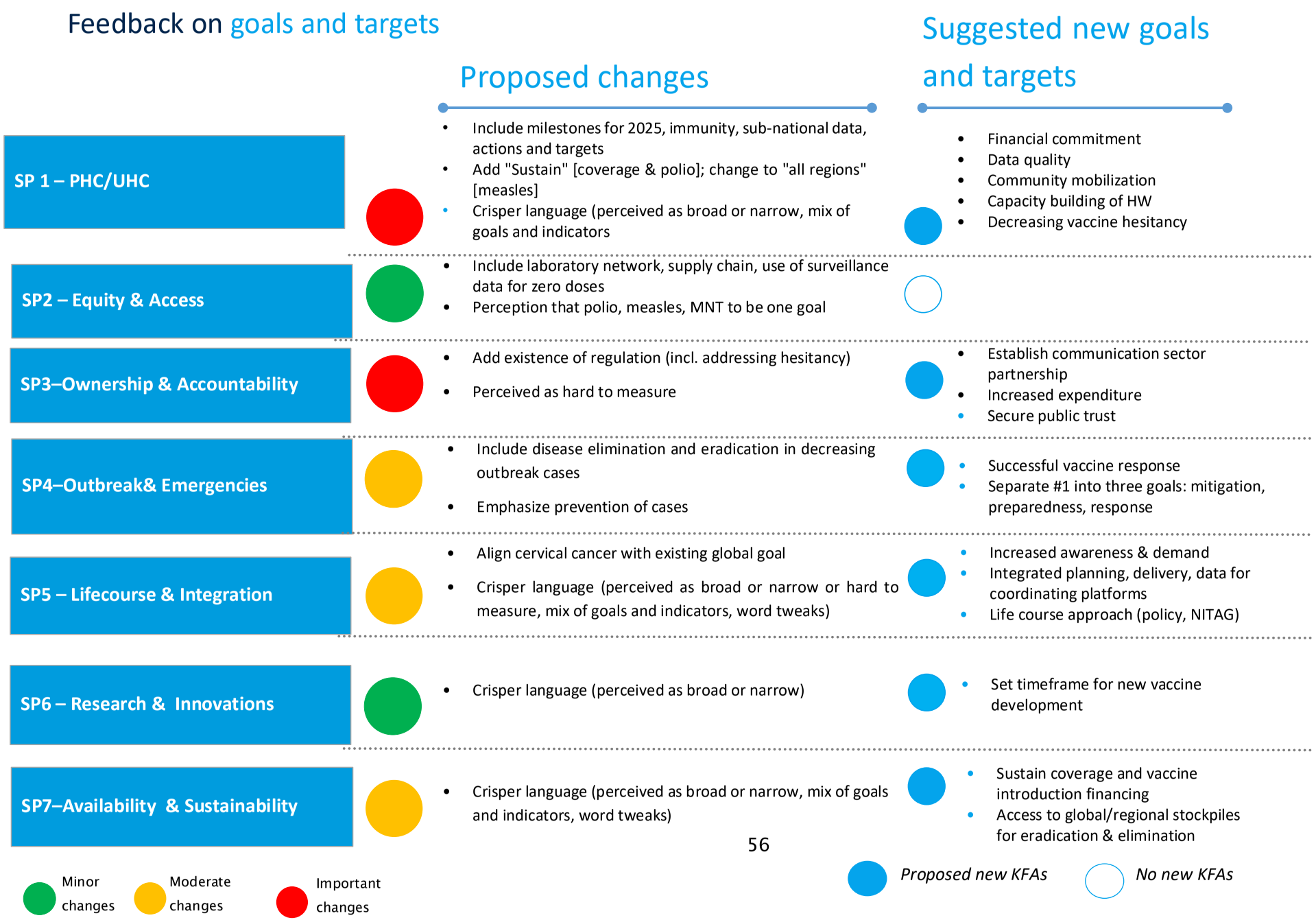
Any significant gaps, issues of regional and country relevance or irrelevance, key priorities, and suggestions for modifications and/or improvement to the above three parameters forming the key elements of the IA 2030 were highlighted. Charts below summarize the key outcomes of this regional consultation, and the feedback was sent to the secretariat of IA 2030 to be incorporated into the final version of the document.

The main themes for feedback to the IA 2030 co-creation process from the SEARO TAG are summarized below:

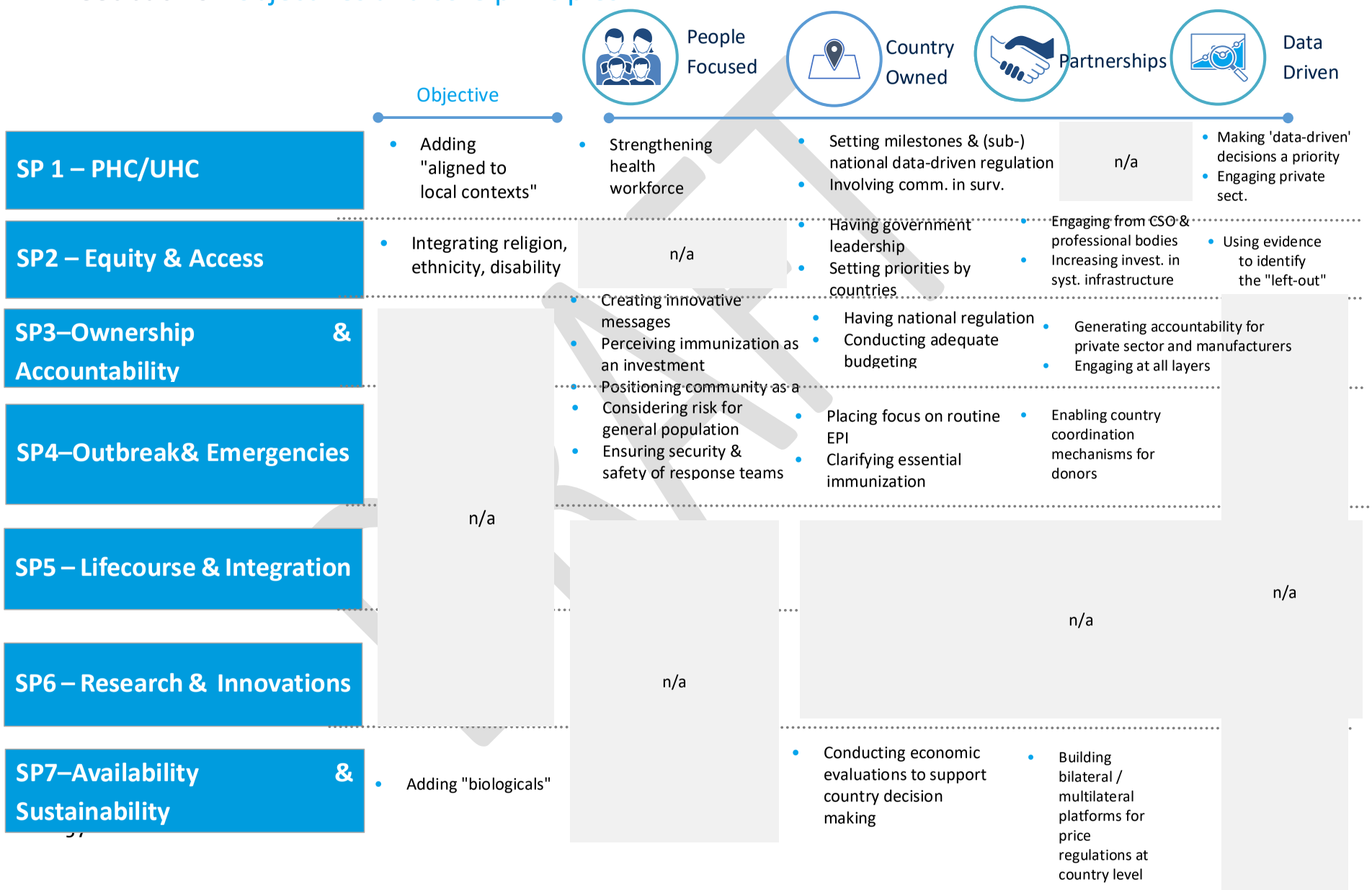
Feedback on key focus areas (KFAs) in the strategic priorities



Feedback on goals and targets



Feedback on objectives and core principles



Reports of other WHO Immunization Advisory Committee Meetings

1. Immunization and vaccines related implementation research advisory committee (IVIR-AC), recommendations-March 2019. WER No. 19, 2019.

www.who.int/wer/2019/wer9419/en/

2. Immunization Practices Advisory Committee (IPAC) 13th meeting 11-13 June 2019. Final meeting report and recommendations.

www.who.int/immunization/programmes_systems/policies_strategies/IPAC2019_Meeting_Report.pdf?ua=1

3. Report of the Global Advisory Committee on Vaccine Safety (GACVS), 5-6 June 2019. WER No. 28, 2019.

www.who.int/vaccine_safety/committee/reports/Jun_2019/en/

4. The 6th Annual meeting of the WHO Product Development for Vaccines Advisory Committee (PDVAC). WHO Headquarters, Geneva, 26-28 June 2019. Executive Summary.

www.who.int/immunization/research/meetings_workshops/PDVAC_2019_exec_summary.pdf?ua=1

Measles and Rubella- Session 4

Executive Summary

Objectives of this session:

1. Review findings of the rubella systematic review and proposed updates to WHO's current rubella vaccine policy recommendations.
2. Review the Feasibility Assessment of Measles and Rubella Eradication, including modelling of the epidemiological impact and cost-effectiveness of different programme performance scenarios.

The session is divided into 3 separate areas as follows:

1. **Global and regional update**:

This short presentation is intended to update the SAGE on the progress towards measles and rubella regional and global goals and highlights the key challenges. This presentation is for information only.

2. Rubella vaccine:

In order to update the current rubella position paper (2011), a systematic review was undertaken to assess any new evidence on immunogenicity, efficacy and effectiveness, duration of protection, serious adverse events, administration to children <9 months of age, and risk of adverse events when rubella containing vaccine (RCV) is administered in pregnancy.

The document in the yellow book summarizes the findings from the systematic review. In addition the following document is provided on the SAGE web:

- Full systematic literature review and meta-analyses of the immunogenicity, duration of immunity, effectiveness/efficacy and safety of rubella vaccination.

Three policy updates are proposed for inclusion in the revised rubella position paper, two of which have already been discussed and endorsed by SAGE:

1. **Co-administration of yellow fever and rubella vaccines.** (SAGE October 2018) The position paper will be updated to continue recommending YF/rubella be co-administered or given at least 4 weeks apart, with removal of all cautionary statements about co-administration.
2. **Health worker vaccination.** (SAGE November 2013) The language in the position paper will be updated to recommend all health workers have evidence of immunity to rubella, with verification of vaccination and/or immunity to be part of standard infection control guidelines or health worker standards.

3. **Removal of the vaccination strategy to reduce congenital rubella syndrome through vaccinating only women of reproductive age.** A review of issues with this strategy will be provided to SAGE for discussion.

3. Feasibility of measles and rubella eradication:

At 2017 World Health Assembly (WHA), the Director General was requested to report through the WHO Executive Board to the 2020 WHA "on the epidemiological aspects and feasibility of, and potential resource requirements for, measles and rubella eradication, taking into account the assessment of the SAGE."

In order to better understand the investment, consequences and value-for-money of efforts to eliminate measles and rubella transmission globally, the relative impact, cost and cost-effectiveness of different strategies for measles-rubella elimination (and potential eradication) have been modelled by a consortium of mathematical modelers. These transmission models projected long-term cases, deaths, and DALYs, along with the number and type of vaccinations given, under four vaccination coverage scenarios. To evaluate the cost-effectiveness of different scenarios, these outputs were used in an economic model which estimated the direct costs of vaccination and treatment associated with each scenario.

SAGE will be presented with the findings of the modeling exercise and economic evaluation.

SAGE will then be provided an overview presentation of the Feasibility Assessment of Measles and Rubella Eradication and a summary of the conclusions and recommendations of that report.

The Feasibility Assessment of Measles and Rubella Eradication as well as a description of the programme scenarios modelled is included in the yellow book. In addition the following documents are provided on the SAGE web:

- A full description of the modelling and economic analysis conducted to inform the feasibility assessment.

Summary of the systematic literature review and meta-analyses of the immunogenicity, duration of protection, effectiveness/efficacy and safety of rubella vaccination

13th September 2019

Jossy van den Boogaard, Brechje de Gier, Priscila de Oliveira Bressane Lima, Hester de Melker, Susan Hahné, Irene Veldhuijzen

The full report can be found on the SAGE website (background documents for SAGE October 2019)

Summary

Background

This report summarises the results of a systematic review of the literature and meta-analyses of the immunogenicity, duration of protection, effectiveness/efficacy and safety of rubella-containing vaccine (RCV) in order to update the WHO rubella vaccine position paper.

Methods

We performed a systematic literature review for studies published since 2010 in which one or more doses of RCV were given at any age. We extracted data on the following outcomes: immunogenicity, duration of protection, vaccine efficacy or effectiveness and safety. Where appropriate, meta-analyses were performed. Quality of all included studies was assessed using the GRADE methodology.

Results of the search and selection

We included 36 papers (32 randomized controlled trials (RCTs) and 4 observational studies) for analysis of the immunogenicity of one or two doses of RCV (RA27/3 strain) in children and adolescent girls, and 14 papers (5 RCTs and 9 observational studies) to assess the duration of protection of RCV. One paper on vaccine effectiveness (VE) (BRDII strain) was included, and 74 studies on safety, including three on safety in pregnancy.

Results of the review of included studies

Seroconversion after a single dose of RCV (RA 27/3 strain) was 99% (95% CI: 98%-99%) in children (GRADE evidence rating, high) and 100% (100%-100%) in adolescent girls (GRADE evidence rating, moderate), independent of co-administration with other vaccines. Seropositivity after a second dose of RCV (RA 27/3 strain) was 100% (99%-100%) (GRADE evidence rating, high). For duration of protection, the studies showed a seropositivity of 88%-100% measured 1-20 years after one or two RCV doses (GRADE evidence rating, moderate). We did not find any additional studies on vaccine efficacy of RCV published since 2010. The single new study on VE of RCV reported 100% VE after one and two doses (BRDII strain) (GRADE evidence rating, low). Among 34,332 individuals participating in the RCTs, after exclusion of severe adverse events (SAE) not associated with RCV according to the authors, 140 SAE were reported as possibly related to RCV. Among the case reports on SAEs, the association with RCV was confirmed in one report, where a previously healthy man died of encephalitis. At post-mortem examination, rubella virus (vaccine strain) was detected in brain tissue. For outcomes on safety in general the GRADE evidence rating was moderate. No cases of CRS or other SAEs were reported in studies following almost 3,000 women who were inadvertently vaccinated against rubella during pregnancy (GRADE evidence rating, low).

Conclusions

Our literature review confirms the evidence that is presented in the current WHO rubella vaccine position paper, dating from 2011. Single and two doses of RCV are highly immunogenic for a long period of time, they are effective in preventing rubella and CRS, and they are safe to be administered to immunocompetent individuals.

Feasibility Assessment of Measles and Rubella Eradication

Introduction

1. At the Seventieth World Health Assembly (WHA) held on May 31, 2017, the Director-General was requested to report through the Executive Board to the Seventy-third WHA in 2020 "on the epidemiological aspects and feasibility of, and potential resource requirements for, measles and rubella eradication, taking into account the assessment of the Strategic Advisory Group of Experts on immunization."[1] This request arose from a proposal from Colombia on behalf of 18 Pan American Health Organization (PAHO) Member States to request a resolution on global eradication at the WHA. A compromise was reached to instead request an update on the feasibility and cost of eradication in 2020 as part of the GVAP resolution. Historically, an Ad Hoc Global Measles Advisory Group was convened by the World Health Organization (WHO) in 2009, leading to a Global Technical Consultation to Assess the Feasibility of Measles Eradication held in July 2010.[2] On the basis of this review, the Strategic Advisory Group of Experts on immunization (SAGE) concluded in November 2010 that measles can and should be eradicated, and that a goal for measles eradication should be established with a proposed target date based on measurable progress made towards existing goals and targets.[3] The *Measles and Rubella Global Strategic Plan: 2012-2020 Midterm Review* also recommended that a decision should be made by 2020 as to whether or not a target be set for measles eradication: "A determination should be made, not later than 2020, whether a formal global goal for measles eradication should be set with timeframes for achievement. In the meantime, all regions should work toward achieving the regional elimination goals."[4]

2. Eradication is defined as reduction of the global incidence of a disease to zero as a result of deliberate efforts, with no more risk of reintroduction obviating the necessity for further control measures. The benefits of disease eradication are permanent, whereas the costs of control programmes continue indefinitely. According to the 1993 International Task Force for Disease Eradication, "Eradication is the ultimate "sustainable" improvement in public health."[5] For measles and rubella, elimination refers to the absence of endemic virus transmission in a defined geographical area, such as a country or region, for more than 12 months in the presence of a well performing surveillance system. While measles elimination is a worthwhile goal in itself because of the health and economic benefits, measles elimination is a fragile state that must be continuously maintained due to the likelihood of importations. Regional elimination is thus a stage on the path toward global eradication. There is, however, urgency for all Regions to accelerate elimination efforts, as it is challenging for countries and regions that achieved elimination to sustain this indefinitely if other countries export measles virus.

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[1] World Health Organization. Resolution WHA 70.14: Strengthening immunization to achieve the goals of the global vaccine action plan. Geneva, World Health Assembly 70, 2017 (http://apps.who.int/gb/ebwha/pdf_files/WHA70/A70_R14-en.pdf).

[2] World Health Organization. Proceedings of the Global Technical Consultation to assess the feasibility of measles eradication, 28-30 July 2010. *Journal of Infectious Diseases* 2011;204:S4-S13.

[3] World Health Organization. Meeting of the Strategic Advisory Group of Experts on Immunization, November 2010. Summary, conclusions and recommendations. *Weekly Epidemiological Record* 2011,86:1–16.

[4] Orenstein WA, Hinman A, Nkowane B, Olive JM, Reingold A. Measles and Rubella Global Strategic Plan 2012-2020 midterm review. *Vaccine* 2018;36 Suppl 1:A1-A34.

[5] Recommendations of the International Task Force for Disease Eradication. *Morbidity and Mortality Weekly Report* 1993;42(RR-16):1-38. (available at https://www.cdc.gov/mmwr/preview/mmwrhtml/00025967.htm).

Definitions

Control: The reduction of disease incidence, prevalence, morbidity or mortality to a locally acceptable level as a result of deliberate efforts; continued intervention measures are required to maintain the reduction. Example: diarrheal diseases.

Elimination of disease: Reduction to zero of the incidence of a specified disease in a defined geographical area as a result of deliberate efforts; continued intervention measures are required. Example: neonatal tetanus.

Elimination of infections: Reduction to zero of the incidence of infection caused by a specific agent in a defined geographical area as a result of deliberate efforts; continued measures to prevent re-establishment of transmission are required. Example: measles, poliomyelitis.

Eradication: Permanent reduction to zero of the worldwide incidence of infection caused by a specific agent as a result of deliberate efforts; intervention measures are no longer needed. Example: smallpox.

Extinction: The specific infectious agent no longer exists in nature or in the laboratory. Example: none.

Dowdle WR. The principles of disease elimination and eradication. *Morbidity and Mortality Weekly Report* 1999;48 (Suppl):23-27.

3. This report addresses the epidemiological aspects and feasibility of measles and rubella eradication and the potential resource requirements in response to the request of the Director-General. A guiding principle is that the path toward measles and rubella eradication should serve to strengthen primary health care, promote universal health coverage, and be a pathfinder for new vision and strategy for immunization over the next decade as laid out in the Immunization Agenda 2030 (IA2030). Specifically, this report: 1) highlights the importance of measles and rubella as global health priorities; 2) reviews the current global measles and rubella situation; 3) summarizes prior assessments of the feasibility of measles and rubella eradication; 4) assesses the progress and challenges in achieving regional measles and rubella elimination; 5) assesses additional considerations for measles and rubella eradication, including the results of modelling and economic analyses; 6) assesses the implications of establishing a measles and rubella eradication goal and the process for setting an eradication target date; 7) proposes a framework for determining preconditions for setting a target date for measles and rubella eradication and how these preconditions should be understood and used; and 8) proposes recommendations to SAGE.

Measles and Rubella as Global Health Priorities

4. Measles was a leading global cause of child morbidity and mortality prior to the introduction of measles vaccines in the 1960's and was responsible for more than an estimated two million deaths annually before the increase in global measles vaccine coverage in the

1980's as a consequence of the Expanded Programme on Immunization (EPI). Measles incidence and mortality declined substantially due to the increasingly widespread use of attenuated measles-containing vaccines administered through immunization programmes and, subsequently, through supplementary mass preventive vaccination campaigns. Measles vaccination is estimated to have prevented 21.1 million deaths globally, and 19.3 million deaths among Gavi-eligible countries, from 2000 to 2017.[6] Despite this enormous progress, measles remains an important vaccine-preventable cause of morbidity and mortality, responsible for more than 100,000 deaths each year, and is a key indicator of the quality of immunization programmes. Due to its high infectiousness, measles serves as the "canary in the coal mine": Outbreaks show where people have not been vaccinated and the age distribution of cases identifies age-specific immunity gaps reflecting past programme performance. Importantly, measles anywhere is a risk for measles everywhere, as witnessed by the frequency of measles outbreaks around the world, often a result of importation of cases from other countries. The current measles burden would rapidly increase if current efforts are not maintained or increased.

Rubella too remains a global health priority and vaccine-preventable cause of morbidity and mortality. As a result of maternal infection with rubella during pregnancy, approximately 105,000 children are born each year with congenital rubella syndrome (CRS), a fully preventable, yet potentially fatal condition that can result in heart disease, hearing impairment and deafness, cataracts, and developmental delay.[7] An estimated 131,000 deaths and 12.5 million disability adjusted life years (DALYs) due to CRS may be prevented from 2001 to 2030 with increased rubella vaccine coverage.[8]

5. **The Sustainable Development Goals, Global Health Security Agenda, Global Vaccine Action Plan, Universal Health Coverage, and the Immunization Agenda 2030.** Measles and rubella vaccination already play an integral and leading role in achieving the architecture that currently guides global health activities, including the Sustainable Development Goals (SDGs),[9] the Global Health Security Agenda,[10] and the Global Vaccine Action Plan (GVAP).[11] In addition, measles and rubella vaccination is central to the IA2030 as a core indicator of the effectiveness of the overall childhood immunization programme and key to strengthening PHC. Immunization in general, and measles and rubella vaccination specifically, plays a central role in the SDG3 to "ensure healthy lives and promote well-being for all at all ages" by contributing to the achievement of two SDG targets: 1) ending preventable deaths in children younger than five years by 2030; and 2) achieving universal access to vaccines. Coverage with the second dose of measles-containing vaccine is a specific SDG3 indicator, selected in part because it encompasses the two doses of MCV and reflects the strength of the second year of life platform. In fact, immunization, and measles and rubella vaccination in particular, contributes in some way to

[6] Dabbagh A, Laws RL, Steulet C, Dumolard L, Mulders MN, Kretsinger K, Alexander JP, Rota PA, Goodson JL. Progress Toward Regional Measles Elimination - Worldwide, 2000-2017. *Morbidity and Mortality Weekly Report* 2018;67:1323-29.

[7] Vynnycky E, Adams EJ, Cutts FT, Reef SE, Navar AM, Simons E, Yoshida L-M, Brown DWJ, Jackson C, Strebel PM, et al. Using seroprevalence and immunisation coverage data to estimate the global burden of congenital rubella syndrome, 1996-2010: a systematic review. *PLoS One* 2016;11:e0149160.

[8] Vynnycky E, Papadopoulos T, Angelis K. The impact of measles-rubella vaccination on the morbidity and mortality from congenital rubella syndrome in 92 countries. *Hum Vaccin Immunother* 2019;15:309-16.

[9] https://sustainabledevelopment.un.org

[10] https://www.ghsagenda.org

[11] https://www.who.int/immunization/global_vaccine_action_plan/GVAP_doc_2011_2020/en/

most SDGs. By reducing the economic burden of infectious diseases, vaccination helps eliminate poverty (SDG1) and promotes sustainable economic growth and productive employment (SDG8). Measles vaccination was shown to have the greatest return on investment, with US$ 58 dollars saved in future costs for every US$ 1 dollar spent, among 10 diseases in 73 Gavi-supported low- and middle-income countries from 2001-2020.[12] By protecting urban public health, measles and rubella vaccination also contribute to sustainable cities (SDG11). In addition, vaccination acts synergistically with other development objectives, enhancing the benefits achieved by other SDGs. For example, the impact of enhanced food security and reduced hunger (SDG2) on child development and maternal health will be greater if vaccine-preventable diseases are controlled or eliminated as these diseases impair physical and cognitive development. Similarly, quality education (SDG4) will deliver greater benefits if children are protected against these illnesses. One example is a recent study that found measles vaccination was associated with improved cognitive functioning and school-grade attainment.[13]

Measles vaccination coverage is an important indicator of the immunization action package for the prevention arm of the Global Health Security Agenda, which emphasizes protection against epidemic-prone vaccine-preventable diseases (VPDs). The goal is at least 90% coverage of the country's fifteen-month-old population with at least one dose of measles-containing vaccine (MCV). Measles vaccination coverage is emphasized because it is recognized as a proxy indicator for overall immunization against VPDs.

GVAP was endorsed in 2012 by the WHA to create a framework for immunization activities through 2020 and set target dates for regional measles and rubella elimination. By 2015, four WHO Regions were to have eliminated measles and two to have eliminated rubella. By 2020, five WHO Regions were to have eliminated measles and rubella. Given the high priority to deliver measles and rubella vaccines through essential immunization services, achieving measles and rubella elimination goals will require higher coverage with measles-containing vaccine first (MCV1) and second (MCV2) doses than currently achieved (86% and 69% in 2018). A focus on measles and rubella elimination can promote both universal health care and primary health care by strengthening essential immunization services, addressing inequities in vaccine coverage, and reducing the number of unvaccinated children (including children and young infants for whom vaccination is not indicated or contraindicated such as immunocompromised children) who are not exposed to the virus when there are high levels of immunity in the population. In addition, a focus on measles and rubella elimination can help in enhancing subnational disease surveillance systems, identifying new approaches to reduce critical immunization gaps, and building national ownership of immunization programmes.

The IA2030 lays out core principles and strategic priorities that are aligned with the need to accelerate progress toward the measles and rubella elimination goals. In fact, progress toward achieving these elimination goals could be a pathfinder for the success of the IA2030. The core principles of the IA2030 are that immunization be people-focused, country-owned, based on partnerships, and data driven, all necessary to achieve the

[12] Ozawa S, Clark S, Portnoy A, Grewal S, Stack ML, Sinha A, Mirelman A, Franklin H, Friberg IK, Tam Y, Walker N, Clark A, Ferrari M, Suraratdecha C, Sweet S, Goldie SJ, Garske T, Li M, Hansen PM, Johnson HL, Walker D. Estimated economic impact of vaccinations in 73 low- and middle-income countries, 2001-2020. *Bulletin of the World Health Organization* 2017;95:629-638.

[13] Nandi A, Shet A, Behrman JR, Black MM, Bloom DE, Laxminarayan R. Anthropometric, cognitive, and schooling benefits of measles vaccination: Longitudinal cohort analysis in Ethiopia, India, and Vietnam. *Vaccine* 2019.

measles and rubella elimination goals. The seven strategic priorities are also key components of effective and successful measles and rubella elimination efforts: 1) immunization programmes for primary health care and universal health care; 2) coverage and equity; 3) commitment and demand; 4) outbreaks and emergencies; 5) lifecourse & integration; 6) research and innovations; and 7) supply and financing. The path towards measles and rubella elimination, and eventually eradication, could not be achieved without achieving these IA2030 strategic priorities and thus put measles and rubella elimination as a key indicator of IA2030 progress and success.

Current Global Measles and Rubella Situation

6. **Progress toward achieving regional and global measles and rubella milestones**. The WHA in 2010 established three milestones for measles control by 2015 that reflect the immunization strategies: 1) increase routine vaccination coverage with MCV1 to at least 90% nationally and at least 80% in every district; 2) reduce global annual measles incidence to less than 5 cases per million population; and 3) reduce global measles mortality by 95% from the 2000 estimate. Although these targets were not achieved, progress is still assessed against these milestones as well as the GVAP regional elimination targets. Substantial gains were made from 2000 to 2010 but progress has slowed, and these milestones and goals remain unmet with variable progress among and within regions.

   Measles and rubella vaccination coverage: Global coverage with MCV1 was estimated at 86% in 2018 according to WHO and UNICEF (WUENIC) estimates.[14] Regional MCV1 coverage was 74% for AFR, 90% for AMR, 82% for EMR, 95% for EUR, 89% for SEAR, and 95% for WPR. In 2018, 118 (61%) Member States achieved 90% MCV1 coverage and 55 (28%) Member States achieved at least 80% MCV1 coverage in all districts. In addition, as of July 2019, 173 (89%) Member States had introduced MCV2, with 69% coverage globally, and 168 (87%) Member States had introduced rubella vaccine into their national programmes. Global coverage for rubella vaccine was 69%, with 32% coverage in AFR, 90% in AMR, 45% in EMR, 95% in EUR, 83% in SEAR, and 94% WPR.

   Measles incidence: Annual measles incidence for reported cases was 49 cases/million population in 2018, with 353,236 cases reported through annual reporting. However, fewer than 5% of measles cases are reported globally, making a measles incidence milestone difficult to accurately measure. In 2017, 6.7 million cases of measles were estimated to have occurred globally; 2018 estimates will be released in November 2019. Of 179 countries, 96 had a measles incidence less than 5 cases per million population in 2018, and 66 countries had fewer than 1 case per million population. Every region had an increase in reported cases in 2018 relative to 2017, and major outbreaks have occurred in all regions, garnering global attention. While the proximate causes of the ongoing outbreaks are multifactorial and include conflict, repeated importations, historical gaps in immunization coverage, weak immunization systems with equity gaps, and insufficient vaccination demand, all outbreaks are characterized by the predominance of cases among unvaccinated persons, reflecting programme failure to systematically administer MCV over multiple birth cohorts. Thus, the current measles epidemiological situation in many settings reflects a predictable consequence of inadequate implementation of current strategies, with the build-up of susceptible individuals, endemic transmission, and imported measles cases sparking outbreaks.

[14] http://www.who.int/entity/immunization/monitoring_surveillance/data/coverage_estimates_series.xls

Measles mortality: The 2017 estimate of measles-related mortality was approximately 110,000 deaths globally, with wide confidence intervals.[15] This reflects an 80% decline in estimated measles mortality since 2000 and over 21 million lives saved due to measles vaccination during that time. While impressive, this number falls short of the 95% mortality reduction goal. 2018 global mortality estimates will be released in November 2019.

Molecular surveillance: Monitoring progress toward measles and rubella elimination requires high-quality case-based surveillance with laboratory confirmation, supported by genetic characterization of measles and rubella viruses to identify sources of transmission and monitor progress toward elimination through changes in genetic diversity. In 2000, WHO established the Global Measles and Rubella Laboratory Network (GMRLN) to provide high-quality laboratory support for surveillance for measles, rubella, and congenital rubella syndrome. GMRLN is the largest globally coordinated laboratory network, with 704 laboratories supporting surveillance in 191 countries. These laboratories support the confirmation of measles and rubella cases, and molecular surveillance provides a means of tracking progress toward elimination and potential sources of imported cases. However, sequence data and geographic representativeness of reported measles and rubella sequences is not complete, with the African Region particularly underrepresented.[16]

During 2016–2018, only six of the 24 recognized measles virus genotypes were detected, and only four in 2018. Two genotypes (B3 and D8) accounted for 95% of reported sequences. During 2016–2018, the diversity index of each measles virus genotype reported to the Measles Nucleotide Surveillance (MeaNS) system, defined as the number of distinct measles sequences divided by the total number of records in the database, decreased overall. Of the 13 known rubella virus genotypes, reported genotypes declined from five to two. Overall, the genetic diversity of detected measles and rubella strains has decreased globally, consistent with progress toward elimination.

7. **Regional measles and rubella elimination goals.** Member States in all WHO Regions adopted measles elimination goals to be reached by or before 2020. The original regional elimination dates were AMRO (2000), WPRO (2012), EURO (2015), EMRO (2015), AFRO (2020) and SEARO (2020, which has recently been updated to 2023). In addition, four of the Regions (AMRO, EURO, SEARO and WPRO) have rubella elimination goals. Regional goals were incorporated into the targets of the Regional Vaccine Action Plans (RVAPs) and GVAP.

   While progress has been made in several metrics, including the number of Member States achieving verified elimination status and the number of Regional Verification Commissions (RVCs) and National Verification Committees (NVCs) established, the Regional elimination goals have not been achieved. All Regions have established RVCs, and 148 of 194 (76%) countries have established NVCs. RVCs review all NVC reports and determine measles and rubella elimination status, following the WHO framework for verifying elimination.[17] As of

[15] Dabbagh A, Laws RL, Steulet C, Dumolard L, Mulders MN, Kretsinger K, Alexander JP, Rota PA, Goodson JL. Progress Toward Regional Measles Elimination - Worldwide, 2000-2017. *Morbidity and Mortality Weekly Report* 2018;67:1323-29.

[16] Brown KE, Rota PA, Goodson JL, Williams D, Abernathy E, Takeda M, Mulders MN. Genetic characterization of measles and rubella viruses detected through global measles and rubella elimination surveillance, 2016-2018. *Morbidity and Mortality Weekly Report* 2019;68:587-591.

[17] World Health Organization. Guidance for evaluating progress towards elimination of measles and rubella. *Weekly Epidemiological Record* 2018; 93:544–552.

September 2019, 82 of 194 (42%) Member States were verified as having eliminated measles and 81 as having eliminated rubella. The overall status of elimination verification progress by Region is summarized in Table 1.

The Region of the Americas was verified as having eliminated measles in 2016,[18] although most countries were verified by their NVCs many years earlier. Unfortunately, this regional elimination status was lost in 2018 due to circulation of measles virus in Venezuela following a decrease in vaccination coverage. Neighboring countries re-established transmission of measles virus (Brazil) or have experienced multiple prolonged outbreaks (Columbia).[19] The Region of the Americas is the only region to have eliminated measles, and thus demonstrates the feasibility of measles elimination. Many Member States have eliminated measles for decades and the last endemic case of measles in the Americas was in 2002. However, the reversal of this situation in 2018 also demonstrates the fragility of elimination status. Elimination status in a country or region should not be viewed as a fixed, stable state but a status that can be lost, requiring intensive efforts to regain. Rubella elimination was verified in the Region of the Americas in 2015 and has been sustained. No other region has yet achieved measles or rubella elimination.

Seven countries have re-established measles virus transmission after having been declared eliminated, and similar loss of elimination status threatens other countries. In the Americas, Venezuela and Brazil lost their measles elimination status as did Mongolia in the Western Pacific Region. In the European Region, Albania, the United Kingdom, the Czech Republic, and Greece lost their elimination status. No country has lost rubella elimination status. The recent reversals in measles elimination status are fundamentally linked to the challenges of achieving and sustaining the high level of population immunity (approximately 92% to 94%) required to interrupt transmission, associated in many countries with insufficient political will, conflict, migration, humanitarian emergencies, national financial investment and vaccine hesitancy. The precariousness of elimination status is also due to the extreme infectiousness of measles virus, more importations in an increasingly interconnected world, and ability to adequately respond to each importation.

[18] Pan American Health Organization. Plan of Action for Maintaining Measles, Rubella, and Congenital Rubella Syndrome Elimination in the Region of the Americas: Final Report. 55th Direction Council; 66th session of the WHO Regional Committee for the Americas; 26-30 September 2016; Washington, DC. Washington, DC: PAHO; 2012 (Resolution CD55/INF/10).

[19] Paniz-Mondolfi AE, Tami A, Grillet ME, Márquez M, Hernández-Villena J, Escalona-Rodríguez MA, Blohm GM, Mejías I, Urbina-Medina H, Rísquez A, Castro J, Carvajal A, Walter C, López MG, Schwabl P, Hernández-Castro L, Miles MA, Hotez PJ, Lednicky J, Morris JG Jr, Crainey J, Luz S, Ramírez JD, Sordillo E, Llewellyn M, Canache M, Araque M, Oletta J. Resurgence of Vaccine-Preventable Diseases in Venezuela as a Regional Public Health Threat in the Americas. *Emerging Infectious Diseases* 2019;25:625-632.

Table 1. Measles and Rubella Elimination Verification by Region (as of September 2019)

WHO Region (number of countries)	Regional Verification Commission Established	Elimination Achieved, Number (%) of Member States (n=194)	
		Measles	Rubella
Americas (35)	**Yes**	33 (94)	35 (100)
Europe (53)*	**Yes**	35 (66)	39 (74)
Western Pacific (27)	**Yes**	7+2 non-Member States (26)	4+1 non-Member States (15)
Eastern Mediterranean (21)**	**Yes**	2 (10)	3 (14)
South-East Asia (11)	**Yes**	5 (45)	0
Africa (47)	**Yes**	0	0
TOTAL		**82 (42%)**	**81 (42%)**

* In addition, a number of countries in EUR have been verified as having interrupted transmission of measles for 12 (n=1) or 24 (n=1) months and rubella for 24 (n=3) months; these are not reflected in the totals as 36 months is required for the RVC to declare elimination achieved.

**The EMR RVC verified three countries as having eliminated rubella, despite the absence of a regional rubella elimination goal.

8. **Strategies to achieve measles and rubella elimination**. Measles virus is one of the most highly contagious directly transmitted human pathogens. In a completely susceptible population, a single case of measles can result in 12 to 18 secondary cases, on average,[20] although this number varies across a wide range in different demographic settings.[21] Based on these estimates of the reproductive number, and the simplifying assumption of random mixing in a population, current strategies for measles elimination aim to achieve population immunity of 92% to 94%. This level of population immunity is the theoretical threshold needed to prevent sustained transmission of measles virus (i.e., reproductive number is less than one). However, measles cases and short chains of transmission can occur in settings that have achieved this level of population immunity, particularly if there are spatial clusters of susceptible persons. This level of population immunity requires at least 95% coverage with two doses of measles-containing vaccine (MCV), one in the first year of life and the second dose preferably in the second year of life,[22] at national and district levels. This high

[20] Gay NJ. The theory of measles elimination: implications for the design of elimination strategies. *Journal of Infectious Diseases* 2004;189:Suppl 1:S27-S35.
[21] Guerra FM, Bolotin S, Lim G, Heffernan J, Deeks SL, Li Y, Crowcroft NS. The basic reproduction number (R0) of measles: a systematic review. *Lancet Infectious Diseases* 2017;17:e420-e428.
[22] World Health Organization. Measles vaccines: WHO position paper – April 2017. *Weekly Epidemiological Record* 2017;92:205-28.

coverage should be achieved in every birth cohort, every community, and every district to ensure sufficiently high and homogeneous population immunity to interrupt virus transmission.[23] High coverage with the first dose of MCV is critical, with the goal of MCV2 to immunize those children who fail to respond to the first dose (approximately 15% vaccinated at nine months of age). Administration of measles vaccine in the second year of life also offers an additional opportunity for those children who did not receive a dose in the first year of life. For rubella, the herd immunity threshold is considerably lower, at approximately 83-85% because of the lower reproductive number (R_0 = 5-8) than measles.[24]

Supplementary immunization activities (SIAs) targeted to specific age groups regardless of prior vaccination status are widely used to fill immunity gaps and address deficits in prior programme performance. Low MCV coverage through essential services results in a substantial fraction of susceptible older cohorts because they have neither been vaccinated, nor exposed to wild-type virus due to reductions in virus circulation. SIAs are implemented to prevent the accumulation of susceptible persons to a size that can sustain transmission and, thereby, prevent measles outbreaks. SIAs must be well planned to ensure very high coverage and to reach children who did not receive a dose of MCV ("zero-dose children") and immunize those who failed to respond to MCV1 but who did not receive MCV2 (under-immunized), rather than simply revaccinating already immunized populations. Subnational vaccination campaigns, targeting spatial immunity gaps, may be more efficient in some settings and additional strategies are needed to identify and target those who are unvaccinated and non-immune.

Periodic intensification of routine immunization (PIRI) is an intermediate strategy marked by periodic or intermittent and intensified improvements to routine immunization services that often include information, education, communication (IEC) and social mobilization activities. Achieving high vaccination coverage, through these approaches, is a tactic to achieve the goal of high population immunity. The objectives of SIAs and PIRISs are to vaccinate susceptible (zero-dose and under-immunized) children and better methods of identifying these children would make these activities more efficient.

9. **Linking measles and rubella elimination**. Rubella elimination should be achieved in concert with measles elimination. Because rubella virus is less contagious than measles virus, rubella elimination will be easier than measles elimination where the vaccines are co-administered. To date, rubella virus transmission has not been re-established in any country following verification of elimination. The WHO recommends that countries take the opportunity offered by measles elimination activities to introduce rubella vaccine.[25] Measles vaccine delivery strategies provide an opportunity for synergy and a platform for advancing elimination of rubella, particularly congenital rubella syndrome. Sustained high coverage of rubella vaccine is needed to prevent the potential risk of increased incidence of rubella in women of child-bearing age and thus of CRS. Without sustained high coverage, girls may

[23] Field studies of the effectiveness of the measles vaccine have found high effectiveness after one dose administered at the age of 12 months or later (median effectiveness, 93%; range, 39 to 100) and even higher effectiveness after two doses (median, 97%; range, 67 to 100). McLean HQ, Fiebelkorn AP, Temte JL, Wallace GS. Prevention of measles, rubella, congenital rubella syndrome, and mumps, 2013: summary recommendations of the Advisory Committee on Immunization Practices (ACIP). *Morbidity and Mortality Weekly Report* 2013;62(RR-4):1-34.
[24] Fine PEM, Mulholland K, Scott JA, Edmunds WJ. Community Protection in Ploktin's Vaccines 7th edition. Plotkin SA, Orenstein WA, Offit PA, Edwards KM eds. Elsevier 2018:1512-153.
[25] World Health Organization. Rubella vaccines: WHO position paper. *Weekly Epidemiological Record* 2011;86:301-16.

reach puberty neither vaccinated nor immune from infection with wild-type virus, potentially leading to susceptibility of pregnant women, rubella outbreaks, and increased cases of CRS. Thus, introduction of rubella vaccine into the childhood immunization programme requires long-term commitment to achieving and maintaining sufficient vaccine coverage to ensure a sustained reduction in the incidence of CRS and ultimately the interruption of rubella virus transmission. Strong political commitment to the elimination of rubella and CRS, and sustainable financing for vaccination and surveillance activities, should be in place before introducing rubella vaccination into the childhood immunization programme.

Measles and Rubella Eradication

10. Feasibility of measles and rubella eradication

The feasibility of measles eradication encompasses a combination of biological, technical and operational factors, as well as political, social and financial factors. Biologic feasibility refers to characteristics of the measles virus, including the fact that humans are the only natural reservoir of measles virus (although non-human primates can be infected) and the absence of persistently-infected humans who remain contagious, sustained subclinical virus transmission, or viral evolution away from vaccine-induced immunity.[26] Technical feasibility refers to the availability of tools needed to achieve measles eradication, including a low-cost, safe, and effective vaccine and accurate diagnostic tests. Operational feasibility refers to the ways these tools are deployed, including delivery of two doses of MCV through a strong routine immunization system supplemented by mass vaccination campaigns as needed to fill immunity gaps that accumulate over time, a sensitive surveillance system with timely and accurate reporting at the subnational level, and efficient and effective outbreak response. The elimination of measles and rubella in the Americas provides demonstration in a large geographical area that elimination can be achieved under rigid programmatic, political, financial and social conditions.

While biologic, technical and operational feasibility are necessary to achieve measles and rubella eradication, they are not sufficient. The feasibility of measles and rubella eradication requires broad public support and political will as well as sufficient financial resources to stop virus transmission everywhere. Eradication requires access to children in humanitarian and conflict settings and in areas controlled by anti-government elements. In addition, an eradication programme requires strong governance, oversight and accountability as well as long-term commitment from all stakeholders. The International Task Force for Disease Eradication (ITFDE), established at The Carter Center in 1988 and currently supported by The Bill & Melinda Gates Foundation (BMGF), listed the following criteria for assessing whether a disease can be eradicated, highlighting the importance of both scientific feasibility and the need for political will and public support:[27]

Scientific Feasibility

- Epidemiologic characteristics, including the potential existence of nonhuman reservoirs; ease of spread; induction of natural immunity; and ease of diagnosis
- Availability of an intervention, such as a vaccine, that ideally should be effective, safe, inexpensive, long-lasting, and easily deployed

[26] Moss WJ, Strebel P. Biological feasibility of measles eradication. *Journal of Infectious Diseases* 2011; 204 Suppl 1:S47-53.

[27] Recommendations of the International Task Force for Disease Eradication. *MMWR* 1993;42(RR-16):1-38. (available at https://www.cdc.gov/mmwr/preview/mmwrhtml/00025967.htm).

- Demonstrated feasibility of elimination, such as documented elimination from a defined country or region

Political Will/Popular Support

- Perceived burden of disease
- Expected cost of eradication
- Synergy of eradication efforts with other interventions
- Necessity for eradication rather than control

Measles and rubella meet the criteria for scientific feasibility of eradication. However, the ITFDE report did not fully address the programmatic feasibility of eradication. Significant challenges concern garnering the political will, public support, financial resources, and commitment to an eradication goal, and the programmatic feasibility of achieving and sustaining sensitive surveillance systems, vaccine delivery mechanisms to achieve the necessary coverage, and strategies to define and identify susceptible individuals and groups who require innovative tactics to vaccinate.

11. **Global Technical Consultation to Assess the Feasibility of Measles Eradication**. Since the introduction of measles vaccine in the early 1960's, there have been several rigorous assessments of the feasibility of measles eradication.[28] More recently, the Executive Board of the WHO requested in May 2008 that an ad hoc group of experts assess the feasibility of measles eradication. The Global Technical Consultation to Assess the Feasibility of Measles Eradication concluded in 2010 that "measles can and should be eradicated" and "recommended that the World Health Assembly consider establishing a target date for measles eradication once the South East Asian Region established an elimination target", which was then set in September 2013.[29] The assessment considered the feasibility of measles elimination in each WHO Region as well as the biological, technical, programmatic, and economic feasibility of measles eradication. Also considered were the impact of measles eradication on health systems and the implications for vaccine supply. The Advisory Group recognized that building the required political, social, and economic platforms for measles eradication would be both a disease control opportunity and an important developmental opportunity, requiring a broad multidisciplinary partnership, and stressed that the success of measles eradication would depend on strong management, accountability, communication, advocacy, and resource mobilization at all levels. Thus, the Advisory Group acknowledged the biological and technical feasibility of measles eradication but recognized the challenges in garnering the public support, political will, and financial resources that will be required to eradicate measles. A similar global technical consultation to assess the feasibility of rubella eradication has not been conducted.

12. **International Task Force for Disease Eradication**. A decade ago, in 2009, the ITFDE concluded that "measles eradication is biologically possible, using tools that are currently available . [but that] the delay in eradication of polio is a special obstacle to global measles eradication."[30] The ITFDE reassessed measles eradication in 2015. The ITFDE restated the

[28] Sencer DJ, Dull HB, Langmuir AD. Epidemiologic basis for eradication of measles in 1967. *Public Health Rep* 1967;82:253-6.

[29] World Health Organization. Proceedings of the Global Technical Consultation to assess the feasibility of measles eradication, 28-30 July 2010. *Journal of Infectious Diseases* 2011;204:S4-S13.

[30] Summary of the 14th Meeting of the International Task Force for Disease Eradication, 2009 (available at http://www.cartercenter.org/resources/pdfs/news/health_publications/itfde/ITFDEsum0609.pdf).

belief that measles and rubella eradication are technically feasible and recognized that efforts to control and eliminate measles and rubella accelerated since 2000. However, measles eradication "will require a much more demanding enterprise than the current effort, which has suffered from insufficient resources and wavering political commitment."[31] The ITFDE will again discuss measles and rubella eradication in October 2019 and the findings should be available prior to the Seventy-third WHA in 2020.

13. **The Measles and Rubella Midterm Review**. A comprehensive review of the *Global Measles and Rubella Strategic Plan, 2012-2020*[32] was conducted in 2016, assessing the global strategy for measles and rubella elimination. The *Measles and Rubella Midterm Review*[33] acknowledged that tremendous progress had been made towards measles and rubella elimination since 2001 and identified ten key points regarding the global strategy for measles and rubella elimination: 1) measles eradication is the ultimate goal but regional elimination goals should be pursued to enable a decision by 2020 as to whether or not a target be set for measles eradication; 2) the basic strategic approaches articulated in the *Global Measles and Rubella Strategic Plan 2012–2020* are valid to achieve the goals but have not been fully implemented; 3) reliance on SIAs should be changed to primary reliance on well-performing essential immunization services to assure administration of two doses of MCV; 4) reliance on vaccine coverage to measure progress should be changed to measurement of measles and rubella incidence as the metric to track progress toward elimination; 5) measles and rubella vaccination programmes should be considered an indicator of the quality of the overall immunization programme, and incidence and vaccination coverage should be considered primary indicators of immunization programme performance; 6) polio transition presents risks and opportunities for measles and rubella eradication, and the opportunities should be maximized; 7) school entry immunization checks could contribute to strengthening overall immunization services; 8) programme decisions should increasingly be based on high quality data and appropriate analysis; 9) incorporation of rubella vaccination into the immunization programme should be accelerated; and 10) outbreak investigation and response are critical but most important is the prevention of measles and rubella outbreaks. The *Measles and Rubella Midterm Review* emphasized the need to achieve and sustain elimination by strengthening health systems. Specifically, the report recommended "focusing on improving ongoing immunization systems – although this may delay reaching measles and rubella elimination goals – in order to ensure that gains in measles and rubella control can be sustained. Reorienting the measles and rubella elimination program to increase emphasis on surveillance so that programmatic and strategic decisions can be guided by data is critical."

Progress and Challenges in Achieving Measles and Rubella Elimination Goals

14. **Operational challenges to measles and rubella eradication**. Several operational challenges will need to be addressed to achieve measles and rubella eradication, including the: 1) high vaccine coverage required to achieve and sustain 92-94% homogeneous population immunity to measles virus and delivered through strong essential immunization programmes; 2) need for high quality data on vaccine coverage and measles and rubella

[31] World Health Organization. Meeting of the International Task Force for Disease Eradication, November 2015. *Weekly Epidemiological Record* 2016;91:61-72.
[32] World Health Organization. Global Measles and Rubella Strategic Plan: 2012-2020 (http://apps.who.int/iris/bitstream/10665/44855/1/9789241503396_eng.pdf).
[33] Orenstein WA, Hinman A, Nkowane B, Olive JM, Reingold A. Measles and Rubella Global Strategic Plan 2012-2020 midterm review. *Vaccine* 2018;36 Suppl 1:A1-A34.

incidence at the subnational level (e.g. district or health center catchment area); 3) need for logistically and financially feasible methods to identify immunity gaps, including zero-dose and under-immunized children; 4) risk of rapid, global spread of measles virus through unimmunized travelers; 5) potential for increased susceptibility among young infants from decreased levels of maternal antibody as a result of maternal vaccination and limited boosting; 6) possibility of significant waning immunity in vaccinated persons no longer boosted by exposure to wild-type virus; 7) and risk of measles and rubella virus re-introduction from laboratories after eradication.

Most importantly, region and country-specific challenges will continue to hinder progress: 1) weak health infrastructure and immunization programmes, including an inadequately trained workforce; 2) restricted access to children in regions of conflict, insecurity, and humanitarian emergency; and 3) vaccine hesitancy based on mistrust and misinformation about vaccines. These issues are likely to be major challenges to measles and rubella eradication and were identified among the ten threats to global health in 2019 (i.e., weak primary health care, fragile and vulnerable settings, and vaccine hesitancy).[34]

15. **Progress and challenges in implementing the recommendations of the *Measles and Rubella Midterm Review*.** The *Measles and Rubella Midterm Review* provided detailed recommendations on programme performance that have been used to guide immunization and surveillance programmes. The five strategic areas described in the *Measles and Rubella Midterm Review* are summarized and progress and challenges assessed.

    Measles and Rubella Midterm Review Strategy 1. Monitor disease using effective surveillance and evaluate programmatic efforts to ensure progress.

    - *All countries must implement case-based, laboratory-supported surveillance for measles and rubella, and report case information to the WHO Regional Office on a weekly basis.*
    - *A working group on surveillance and outbreak investigation and response should be developed at the global level.*
    - *Protocols should be updated or, when necessary, developed, to guide surveillance and outbreak investigation and response.*
    - *Countries must dedicate resources for surveillance and partners need to supplement resources, including resources for staffing, laboratory support, training, and other operational costs.*
    - *Sentinel surveillance for congenital rubella syndrome (CRS) should be implemented.*
    - *Cases should be classified to determine the proportion of cases attributable to program failure, i.e. cases who should have been vaccinated according to the national schedule but were not, to allow for the underlying reasons to be identified and addressed. For cases that are not program failures, analysis should be undertaken to determine whether changes in strategy are needed such as changing the age for recommended vaccination.*

    Progress and challenges: Most of the *Measles and Rubella Midterm Review* surveillance recommendations have been adopted or are in the process of being adopted. Global

[34] https://www.who.int/emergencies/ten-threats-to-global-health-in-2019

surveillance standards were updated for measles,[35] rubella,[36] and CRS,[37] and a roadmap to elimination quality surveillance was published.[38] All 194 Member States except one (Mauritius) report having measles case-based surveillance, although implementation and quality are variable. Member states report data weekly or monthly to the WHO Regional office. India is replacing previous outbreak-based surveillance with national case-based surveillance as it rolls out measles-rubella catch-up campaigns by state. In 2016, 126 countries reported conducting CRS surveillance, of which 95 (49%) have either population-based or sentinel surveillance. Monthly global surveillance bulletins are published and disseminated broadly and a working group on comprehensive disease surveillance was formed. Updated global guidance on outbreak investigation and response is under development but has not yet been completed. A global analysis of the proportion of cases that are attributable to programme failure was published,[39] with 63% of the 434,956 cases with available vaccination data categorised as programmatically preventable, but this approach has yet to be systematically implemented at the programme level in many countries.

While country investment in surveillance is generally considered inadequate, the extent of the gap is unknown. Substantial investment in surveillance will be needed for countries and regions to achieve and sustain regional elimination goals. A surveillance costing tool is under development and the completed version should help countries budget appropriately for surveillance needs. Several challenges remain in optimizing laboratory confirmation of measles and rubella cases. Elimination quality surveillance requires an investment to test and discard suspected cases. In outbreak settings, use of epidemiologic confirmation can prove problematic in countries without a clear protocol to select cases for laboratory confirmation, which requires close collaboration at the national level between the laboratory and surveillance epidemiologists. Specific threats to optimal implementation of elimination quality surveillance include reliance on polio staff and funding to conduct field surveillance, and dependence of the GMRLN on a single funding agency, the U.S. Centers for Disease Control and Prevention.

Measles and Rubella Midterm Review Strategy 2. Achieve and maintain high levels of population immunity by providing high vaccination coverage with two doses of measles and rubella-containing vaccines

- *Two doses of measles and rubella-containing vaccine delivered through routine immunization services should be the standard for all national immunization programs, with the goal of 95% coverage with both doses.*

[35] World Health Organization. Measles - Vaccine Preventable Diseases Surveillance Standards, 2018. (available at https://www.who.int/immunization/monitoring_surveillance/burden/vpd/WHO_SurveillanceVaccinePreventable_11_Measles_R2.pdf?ua=1)

[36] World Health Organization. Rubella - Vaccine Preventable Diseases Surveillance Standards, 2018. (available at https://www.who.int/immunization/monitoring_surveillance/burden/vpd/WHO_SurveillanceVaccinePreventable_20_Rubella_R2.pdf?ua=1)

[37] https://www.who.int/immunization/monitoring_surveillance/burden/vpd/WHO_SurveillanceVaccinePreventable_03_CRS_R2.pdf?ua=1

[38] Sniadack DH, Crowcroft NS, Durrheim DN, Rota PA, Roadmap to elimination standard measles and rubella surveillance. *Weekly Epidemiological Record* 2017;92:97-105.

[39] Patel MK, Orenstein WA. Classification of global measles cases in 2013-17 as due to policy or vaccination failure: a retrospective review of global surveillance data. *Lancet Glob Health* 2019;7:e313-e320.

- *Preventive supplementary immunization activities (SIAs) should be conducted as a rescue effort when countries have not yet implemented a routine second dose or when two dose coverage is insufficient to achieve and maintain high population immunity, with a focus on immunizing unvaccinated children.*
- *Immunization strategies and surveillance strategies should be tailored to the country categorization and immunity gaps should be addressed by a set of interventions based on whether disease incidence is low, medium or high.* [40]
- *All countries should institute a school entry check for immunization to provide missed doses of vaccines, particularly vaccination against measles and rubella as well as against other vaccine-preventable diseases.*
- *Immunity gaps among adolescents and adults need to be addressed by promoting effective strategies for vaccinating susceptible older children, adolescents, and adults.*

Progress and challenges: Implementation of the *Measles and Rubella Midterm Review* population immunity recommendations has proven challenging. Globally, MCV1 is part of the national immunization schedule in all countries and MCV2 has been introduced into 173 Member States, with another 3 countries planning to introduce MCV2 in 2019. WUENIC estimates of global coverage for MCV1 and MCV2 in 2018 was 86% and 69%, respectively, far below the 95% coverage with both doses that is generally required to achieve measles elimination. In fact, MCV1 coverage has remained at approximately 85% for a decade despite substantial investments. Thus, the continued need for preventive SIAs are forecast for many years based on projections of the accumulation of susceptible children. However, delays in conducting SIAs are common and are often linked to postponing the funding request submission or delays in approval for countries needing support. School entry vaccination checks are not universally implemented. WHO is currently documenting country case studies on the implementation of school entry vaccination checks to develop guidance on best practices. Although the benefits of catching-up children on missed doses is obvious, implementation of the strategy is complex, requiring legislative and policy frameworks, reliable monitoring systems, and collaboration with Ministries of Education. In addition, policies for school entry vaccination checks often focus on first entry (at 5-6 years of age), and not on older children. Where measles and rubella surveillance show disease occurring in older school-aged children, school vaccination checks for all age groups should be implemented to close susceptibility gaps for children already in school when a school entry check policy is introduced, or for those who entered the system later on. Unless effective campaigns are conducted and catch-up opportunities used, birth cohorts with immunity gaps will continue to age, resulting in older cohorts with residual immunity gaps. Closing immunity gaps in susceptible, older individuals out of school is much more challenging to implement and obtain high coverage. Although guidance on supplementary doses exists, there continues to be a gap in effective guidance on how to administer, record and report these doses.

Measles and Rubella Midterm Review Strategy 3. Develop and maintain outbreak preparedness, respond rapidly to outbreaks and manage cases.

[40] Susan Reef, Jennifer Harris, Alan Ou, Ty Kraniak. Guidance to Increasing Population Immunity against Measles and Rubella. https://www.who.int/immunization/sage/meetings/2018/october/3_Country_classification_Guidance_measles_session_yellow_book_doc.pdf?ua=1

- *The primary goal must be to prevent outbreaks through monitoring risk status and increased attention to vaccination of underserved communities and in high risk settings.*
- *All measles outbreaks should be promptly investigated, and a susceptibility profile developed to inform measles control and elimination strategies.*
- *Training materials should be developed for use at global, regional and country levels on performing outbreak investigations as well as to understanding the underlying reasons for the outbreaks.*
- *Adequate financial, human and laboratory resources to conduct rigorous outbreak investigations should be ensured.*
- *Countries should take steps to mitigate measles and rubella outbreaks through vaccination, with the magnitude of the response based on the characteristics of the outbreak, the stage of measles control, and the country categorization.*

Progress and challenges: Global outbreak preparedness and response is quite variable. Although many initiatives to tailor preventive immunization approaches have been promoted, subnational risk stratification has not been conducted systematically across all countries. In some countries, outbreak response is rapid and rigorous, particularly those with sufficient domestic technical and financial resources. However, in many countries with weaker surveillance and competing priorities, outbreaks can go undetected for long periods, followed by inadequate response. The Measles & Rubella Initiative (M&RI) has administered Gavi-supported outbreak response funding (up to US$ 10 million per year) to enable rapid outbreak response in Gavi-eligible countries and is in the process of revising the standard operating procedures to enhance speed and effectiveness. Likewise, WHO is updating the measles and rubella outbreak response guidance documents and developing training materials in parallel.

Despite these efforts, measles outbreaks continue to occur with increasing frequency and magnitude, in low-, middle- and high-income countries, illustrating the challenges of controlling a virus with high contagiousness. Repeated importations in an increasingly interconnected world present an ongoing challenge to countries that have already eliminated endemic measles virus transmission, even those with very high levels of population immunity. In countries with endemic transmission, immunity gaps from substandard programme implementation result in repeated outbreaks and the potential to export virus to other countries.

Measles and Rubella Midterm Review Strategy 4. Communicate and engage to build public confidence and demand for immunization.

- *Resources for effective communication must be available to raise the visibility of vaccine-preventable diseases, with a focus on measles and rubella.*
- *Demand for immunization should be created and promoted through long term investment and as an integral part of the routine immunization strategy.*
- *Communication strategies should be planned and specific messages for different audiences developed (e.g., politicians, public health leaders and workers, health care providers, and caregivers).*
- *A range of audiences should be educated on measles incidence, complications, and deaths, as well as on the costs associated with outbreaks, supplemented with stories of actual cases to illustrate the statistical data.*
- *Case studies should be identified and promoted of how measles and rubella elimination efforts enhanced the overall immunization and health systems.*

Progress and challenges: Implementation of the *Measles and Rubella Midterm Review* recommendations are in progress; however, in most places these efforts have not achieved their potential impact due to a lack of locally-targeted interventions and measurement. Increasingly, there is awareness of the need to move away from one-size-fits-all and traditional communications-based approaches to generate community vaccination demand. There is also growing recognition of the full range of determinants of acceptance and demand, considering both attitudinal and supply-side factors, e.g. access, and related practical and logistical factors. However, programmes are yet to systematically gather and use local data to inform planning that covers the full range of social and behavioral drivers of uptake. Further, a range of new approaches and interventions are yet to be fully exploited by programmes to drive sustained uptake. Three main areas may be considered: 1) effective integration across services and communities and within PHC, leveraging new thinking and tools within systems science;[41] 2) innovation, such as the use of digital technologies for prompts and reminders, and engagement of non-traditional stakeholders to build local ownership and support; and, 3) specific strategies for high risk populations, including efforts to anticipate, assess, and address the emergence of pockets of vaccine hesitancy and refusal. The application of these more advanced strategies may be limited by capacity, resources, or limited user-centered planning to meet the needs of all caregivers. However, the opportunities should be seized to enable programmes to increase and sustain equitable coverage of both MCV1 and MCV2, and to benefit essential immunization services more broadly.

Measles and Rubella Midterm Review Strategy 5. Perform the research and development needed to support cost-effective operations and improve vaccination and diagnostic tools.

- *Programmatically-oriented operations research, in addition to technologically-oriented research, should be used to determine how to best interrupt measles virus transmission and should include achieving optimal uptake of vaccination in populations, which populations should be targeted for special immunization efforts, how to optimize surveillance systems, and the economic impact of disease.*
- *Sustained commitment to adequately funding measles and rubella research is required and an advocacy plan to secure funding for research should be developed.*
- *A measles and rubella research committee should be formed and supported, focusing on advocating for, promoting, and prioritizing measles and rubella research, similar to the Polio Research Committee.*

Progress and challenges: Priority research questions were identified by the M&RI Research Prioritization Process in 2016 across four strategic areas: 1) epidemiology and economics; 2) surveillance and laboratory; 3) immunization strategies; and 4) demand creation and communications.[42] The most transformative technologies would augment the technical feasibility of measles and rubella eradication, such as microarray patches for vaccine administration, rapid diagnostic tests, field-deployable molecular tests for measles and rubella virus detection and genotyping, and novel methods for rapid assessment of

[41] Dowell AC, Menning L, MacDonald N, Turner N. An evolution in thinking to support the post 2020 global vaccine strategy: The application of complexity and implementation science. *Vaccine* 2019;37:4236-4240.

[42] Grant GB, Masresha BG, Moss WJ, Mulders MN, Rota PA, Omer SB, Shefer A, Kriss JL, Hanson MP, Durrheim DN, Linkins R, Goodson JL. Accelerating Measles and Rubella Elimination through Research and Innovation --- Findings from the Measles & Rubella Initiative Research Prioritization Process, 2016. *Vaccine* 2019.

population immunity. See Section 23 below on the potential impact of innovations on the feasibility of measles and rubella eradication.

Additional Considerations for Measles and Rubella Eradication

16. **Vaccine access.** Ensuring access to vaccines will be critical to measles and rubella elimination, eradication and achieving equity. Limited or poor access to measles and rubella vaccines could also be a major impediment to measles and rubella eradication, particularly in regions affected by prolonged conflict, mass population movement, and humanitarian emergencies. Marginalized populations, who lack recognition and government support, and those people in regions of internal conflict, face particular challenges in accessing vaccines. Efforts to achieve measles and rubella eradication would require strategies to maintain vaccine access in the most challenging countries and settings, with lessons learned from the GPEI.[43]

17. **Vaccine hesitancy and demand**. Critical to achieving progress toward measles and rubella elimination and eradication is ensuring demand for and access to measles and rubella vaccines. Vaccine hesitancy, particularly for measles vaccines, is an increasingly prevalent and complex challenge to measles and rubella elimination, in part enhanced because of misinformation spread through social media platforms and in distinct communities, and could be a major impediment to measles and rubella eradication. WHO identified vaccine hesitancy as one of the ten threats to global health in 2019.[44] Much has been written about vaccine hesitancy and demand, and the reasons underlying these views are complex. A vaccines advisory group to the WHO identified complacency, inconvenience in accessing vaccines, and lack of confidence as some of the key reasons underlying hesitancy.[45] Efforts to achieve measles and rubella elimination and eventually eradication would need on-going, multi-disciplinary approaches to address vaccine hesitancy and increase vaccine demand, within a broader framework of building trust and confidence in effective and engaged health services, to be successful.

18. **Vaccine and diagnostic test supply for measles and rubella eradication**. Measles and rubella eradication efforts require careful planning to ensure the necessary vaccine supply. The shortage of inactivated poliovirus vaccine at the time of widespread vaccine introduction provides a cautious reminder of the potential risks to an eradication initiative. Vaccine manufacturers should be fully engaged in the planning processes and the possible use of measles and rubella vaccines after eradication should be considered. An assessment of the feasibility of measles eradication by WHO in 2008 concluded that the number of MCV doses estimated at that time to be needed for eradication were within existing and planned MCV-manufacturing capacity, but supply-chain disruptions could reduce supply or increase prices.[46] Proposed mitigation strategies included stockpiling, long-term contracts, and further coordination with manufacturers. The WHO (MI4A) initiative is currently updating a global forecast for measles-containing vaccines supply and demand through 2030 and the analysis

[43] Nnadi C, Etsano A, Uba B, Ohuabunwo C, Melton M, Wa Nganda G, Esapa L, Bolu O, Mahoney F, Vertefeuille J, Wiesen E, Durry E. Approaches to Vaccination Among Populations in Areas of Conflict. Journal of Infectious Diseases 2017;216(suppl_1):S368-S372.

[44] https://www.who.int/emergencies/ten-threats-to-global-health-in-2019

[45] https://www.who.int/immunization/programmes_systems/vaccine_hesitancy/en/

[46] Smith G, Michelson J, Singh R, Dabbagh A, Hoekstra E, van den Ent M, Mallya A. Is there enough vaccine to eradicate measles? An integrated analysis of measles-containing vaccine supply and demand. *Journal of Infectious Diseases*. 2011;204 Suppl 1:S62-70.

is expected by the end of 2019. A risk with the current vaccine supply is the heavy reliance on a single supplier. According to data reported through the WHO MI4A/V3P vaccine purchase database for 2017,[47] the Serum Institute of India supplies as much as 87% and 97% of the global measles and measles-rubella vaccine market, respectively. Having additional manufacturers supplying pre-qualified measles and measles-rubella vaccines would reduce the supply risks associated with a dominant manufacturer in these markets and help to secure adequate supplies. There are currently three manufacturers that internationally supply measles-mumps-rubella and measles-mumps-rubella-varicella vaccines, which are principally used in non-Gavi eligible, middle- and upper-income countries. However, they are not expected to significantly change their supply strategy and should not be relied upon for additional supplies of measles or measles-rubella vaccine even if there is significantly more demand.

Also critical to achieving measles and rubella eradication is having an adequate supply of diagnostic test kits to support case-based surveillance with laboratory confirmation. Elimination standard surveillance, in which all suspected cases are laboratory confirmed or discarded, requires a robust and diverse supply of pre-qualified and quality-assured test kits.

19. **Data needs for measles and rubella eradication.** Measles and rubella eradication will require high quality and highly sensitive data on measles incidence and vaccination coverage (MCV1, MCV2 and supplementary doses). Importantly, an integrated and open data platform, rather than disparate data streams currently in use, will be needed for programme management.

    The *Measles and Rubella Midterm Review* highlighted that measles incidence and case trends could serve as an important indicator for progress toward elimination and eradication, and recommended case-based surveillance with weekly reporting and laboratory confirmation. The *Measles and Rubella Mid-Term Review* also identified the need to classify cases to determine the proportion attributable to programme failure, i.e., cases in persons who should have been vaccinated according to the national schedule but were not, to allow for the underlying reasons to be identified and addressed. For cases that are not programme failures, analysis should be undertaken to determine whether changes in strategy are needed such as changing the age for recommended vaccination. Surveillance systems for measles and rubella eradication will differ from those used for the GPEI, as the diseases and viruses are different (e.g., no environmental surveillance will be needed for measles and rubella; few or no asymptomatic infections). Surveillance for CRS will be particularly challenging as the condition is likely to be rare after the introduction of rubella vaccine, and identification and confirmation can be challenging in countries without access to specialized medical care.

    Surveillance systems for measles, rubella, and congenital rubella syndrome in many countries are inadequately sensitive. The 2017 *Roadmap to Elimination Standard Measles and Rubella Surveillance*[48] report identified eight key attributes of a measles and rubella surveillance system: 1) detection of cases and outbreaks; 2) notification; 3) investigation and confirmation; 4) data collection on cases, potential risk factors for infection, spread, complications and death; 5) data analysis; 6) feed-forward to higher levels; 7) feedback to peripheral levels; and 8) interpretation and use of data. Effective use and interpretation of

[47] https://www.who.int/immunization/programmes_systems/procurement/v3p/platform/module1/en/

[48] World Health Organization. Roadmap to elimination standard measles and rubella surveillance. *Weekly Epidemiological Record* 2017;92:97-105.

data applies to case classification, risk factors, spread, complications and death, vaccine effectiveness, outbreak source, extent and characteristics of the outbreak, monitoring surveillance performance, monitoring immunization programme performance, calculation of the effective reproduction number, actions to prevent further transmission, and evaluation of interventions. At a minimum, these eight elements need to be in place throughout every country for surveillance to be adequate to verify elimination. For elimination standard surveillance, all suspected cases, defined as fever with rash, need to be reported following rapid investigation within 24 hours, with laboratory testing of all suspected cases and comprehensive contact tracing to target chains of transmission for interruption. Cases should also be classified according to the source of infection as imported, importation-related, endemic or unknown, and reporting should be weekly rather than monthly.

The global measles and rubella surveillance system necessary to achieve, sustain and verify eradication will need to improve upon current practices. Currently, fewer than 5% of global measles cases, and many fewer rubella or CRS cases, are reported to the WHO. However, a strengthened measles and rubella surveillance should not constitute a vertical disease surveillance programme but could be a key component of a broader comprehensive effort to strengthen surveillance for all VPDs. Notwithstanding, for measles and rubella eradication, countries would need to better implement current recommendations everywhere and work to achieve surveillance targets. Epidemiologic and laboratory data need to be better linked so that all cases are accounted for. More granular data, such as data on risk factors, might be requested at regional and global levels, and those levels will need to be staffed properly to handle the increased data demands. Innovation in laboratory methods will be needed to help refine virus tracking, and rapid diagnostic tests that are under development will need to be integrated into disease surveillance. CRS surveillance will need to be expanded. WHO is currently undertaking an exercise to estimate the cost of comprehensive surveillance, which includes measles, rubella, and CRS surveillance, and preliminary data will be available in the second quarter of 2020.

20. **Impact of measles and rubella eradication on health systems**. Measles and rubella eradication efforts could be leveraged to strengthen health systems, specifically the essential immunization and primary health care systems.[49,50] For example, delivery of MCV2 in the second year of life could be further deployed as a platform to deliver other child health interventions, and enumeration of high-risk communities in planning SIAs could be used to design strategies to deliver essential immunization and other health services to these communities. Measles and rubella SIAs have been used to deliver several child health interventions, including administration of vitamin A supplementation, deworming medications, and insecticide treated bed nets. As measles and rubella elimination efforts are accelerated, the potential positive and negative effects on immunization and health systems should be measured, and the positive impact maximized. Three approaches to achieve this goal are: 1) focus on strengthening immunization services to generate positive effects on other primary health care services; 2) increase integration with multifunctional health services; and 3) change partner and donor behavior that prioritizes vaccination campaigns and use uncoordinated staff incentives.[51] A survey of 23 countries working toward measles

[49] Andrus JK, Cochi SL, Cooper LZ, Klein JD. Combining global elimination of measles and rubella with strengthening of health systems in developing countries. *Health Affairs* (Millwood) 2016;35:327-33.
[50] Orenstein WA, Seib K. Beyond vertical and horizontal programs: a diagonal approach to building national immunization programs through measles elimination. *Expert Review of Vaccines* 2016;15:791-3.
[51] Griffiths UK, Mounier-Jack S, Oliveira-Cruz V, Balabanova D, Hanvoravongchai P, Ongolo P. How can measles eradication strengthen health care systems? *Journal of Infectious Diseases* 2011;204 Suppl 1:S78-81.

and rubella elimination identified ways to strengthen essential immunization services through measles and rubella SIAs and other elimination activities,[52] including: 1) advocacy for immunization and educational activities; 2) skills training for health professionals; 3) expansion of cold chain capacity to reach more communities, introduce new vaccines, and reduce the risk of vaccine stock-outs; 4) identification of zero-dose and under-vaccinated children; 5) generation of data through SIA microplanning exercises that permit revision of catchment populations for fixed site and outreach immunization services; 6) strengthen overall vaccine-preventable disease surveillance and outbreak preparedness; and 7) introduce school-entry vaccination checks covering other vaccines in addition to measles and rubella. The vision and strategy of the vaccine and immunization global enterprise for the decade spanning 2021 to 2030 is grounded in the concept that immunization is a foundation for and driver of primary health care.

21. **The polio transition and lessons from the GPEI**: The *Measles and Rubella Midterm Review* recognized the importance of learning from the GPEI and leveraging the know-how, tools, and human resources developed through the polio programme for measles and rubella regional elimination through the polio transition process. Importantly, the *Polio Endgame Strategy 2019-2023* specifically states integration as one of three goals, along with eradication and certification and containment.[53] Integration, as described in the strategy, consists of: 1) contributing to the strengthening of immunization and health systems; 2) ensuring sensitive poliovirus surveillance through integration with comprehensive vaccine-preventable disease surveillance systems; and 3) preparing for and responding to outbreaks and emergencies. However, there are great risks in relying on polio transition funding to support specific measles and rubella elimination activities, including surveillance. Country plans for the polio transition have prioritized mainstreaming polio functions and using polio assets to strengthen essential immunization services and strengthening surveillance for vaccine-preventable diseases, with little specific mention of measles.

    Several attempts have been made to derive lessons for consideration of measles and rubella eradication from the experiences of the GPEI, including the need to mobilize political and social support, policy development and strategic planning, programme operations and tactics, and partnership management and donor coordination.[54] Several key lessons were derived from polio eradication for measles and rubella eradication, including the need for: 1) high quality data and surveillance; 2) data-driven outbreak response; 3) building acceptance and demand for vaccines; 4) continued research and innovation; 5) strong programme management, governance, oversight, and accountability; 6) leveraging International Health Regulations and Global Health Security to establish and enforce travel requirements for vaccination; and 7) strengthening global partnerships and garnering political will.[55] An additional lesson from the GPEI is that the most challenging places for eradication (such as the Pakistan-Afghanistan border or north-eastern Nigeria) should be engaged early rather than left to the final efforts of the programme.

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[52] Biellik RJ, Orenstein WA. Strengthening routine immunization through measles-rubella elimination. *Vaccine* 2018;36:5645-5650.

[53] *Polio Endgame Strategy 2019-2023: Eradication, integration, certification and containment*. Geneva: World Health Organization; 2019 (WHO/Polio/19.04).

[54] Cochi SL, Freeman A, Guirguis S, Jafari H, Aylward B. Global polio eradication initiative: lessons learned and legacy. *Journal of Infectious Diseases* 2014;210 Suppl 1:S540-6.

[55] Goodson JL, Alexander JP, Linkins RW, Orenstein WA. Measles and rubella elimination: learning from polio eradication and moving forward with a diagonal approach. *Expert Review of Vaccines* 2017;16:1203-1216.

The GPEI has been a 30-year effort with many missed target dates, costs of almost US$ 1 billion per year, a large global workforce and complex partnership management structures to ensure financial oversight and accountability, reliance on frequent SIAs leading to community fatigue and resistance, and in some cases creation of incentives that draw resources from other health priorities. A measles and rubella eradication initiative will have to be based on a different model and avoid a prolonged, expensive eradication effort.

22. **Management and accountability framework**. A strong management and accountability framework will be critical to measles and rubella eradication, building on lessons learned from the GPEI,[56] and linked to the IA2030 management and accountability structure. The accountability framework for the GPEI is much more extensive than that described for measles and rubella in the *Global Vaccine Action Plan* and *Measles and Rubella Strategic Plan 2012-2020*. The *Measles and Rubella Midterm Review* emphasized that governments have primary responsibility for measles and rubella elimination and the need for local accountability. Given the central role of measles and rubella within the IA2030, the management and accountability framework for measles and rubella eradication should be consistent with this broader context.

23. **Potential impact of innovations on the feasibility of measles and rubella eradication**. Although measles and rubella were eliminated in the Americas with current vaccines and diagnostic tests, it is likely that novel tools will be needed to achieve similar impact in other settings. Innovative tools and strategies could facilitate progress toward measles and rubella eradication, particularly in the most challenging settings. Lessons from the GPEI highlight the importance of continuing to pursue a research agenda and the need to modify strategies and tools to meet unexpected programme needs. Examples include the adoption of monovalent and bivalent oral polio vaccines and recognition of the importance of environmental surveillance for polioviruses. The *Measles and Rubella Midterm Review* emphasized that sustained commitment to adequately funded measles and rubella research is required and that an advocacy plan to secure funding should be developed. The *Review* identified several priority research areas, including how best to: 1) achieve optimal uptake of vaccination in populations with low coverage; 2) accurately identify populations that should be targeted for focused immunization efforts; 3) optimize surveillance systems at the subnational level; and 4) measure the economic impact of measles and rubella. An eradication research agenda would need to be dynamic and responsive to and anticipatory of program needs.

    Microarray patches consist of coated microneedles that deliver vaccine antigens into the dermis (i.e., skin patch), where many antigen-processing cells reside.[57] Delivery of measles and measles-rubella vaccines through microarray patches offers several potential advantages over the use of needles and syringes, including: 1) increased acceptability; 2) administration by persons who are not trained health care workers, or even self-administration, facilitating house-to-house vaccination and immunization in disordered settings; 3) reduced medical waste; and 4) increased thermostability, decreasing cold chain requirements.[58] The availability of microneedle patches for the delivery of measles and

[56] http://polioeradication.org/who-we-are/governance-and-structure/

[57] Peyraud N, Zehrung D, Jarrahian C, Frivold C, Orubu T, Giersing B. Potential use of microarray patches for vaccine delivery in low- and middle- income countries. *Vaccine* 2019.

[58] Arya, J, Prausnitz MR. Microneedle patches for vaccination in developing countries. *Journal of Controlled Release* 2016;240:135-41.

rubella vaccines is probably 7-9 years away given the time it will take to conduct clinical trials, gain regulatory approval, and build manufacturing capacity at commercial scale. However, experience with the Ebola vaccine showed that aspects of this process can be expedited and the timelines shortened. Rapid diagnostic tests for measles IgM antibodies (to assess acute infection) and IgG antibodies (to assess measles immunity) have been developed and pilot tested but are not yet widely available or pre-qualified.[59] A rapid diagnostic test for measles IgM antibodies could facilitate outbreak detection, obviating the need to send samples to a central laboratory, and a rapid diagnostic test for measles IgG antibodies could facilitate identification of susceptible individuals or subpopulations for targeted vaccination efforts. Work on rubella diagnostic tests is ongoing. More efficient strategies to identify and target susceptible individuals could be developed using a combination of serosurveillance and modeling,[60] and eradication strategies that do not rely on achieving 95% coverage could be explored based on synchronized campaigns and targeted vaccination of exporters and importers of measles virus. However, a major challenge has been the availability of funding to support the measles and rubella applied research agenda.

24. **Modeling measles and rubella eradication strategies**. The investment case for measles and rubella eradication is a critical component to inform setting an eradication goal and timeline with a target date, including the expected cost and return on investment. To better understand the investment, consequences and value-for-money of efforts required to eliminate measles and rubella transmission globally, the relative impact, cost, and cost-effectiveness of different strategies for measles-rubella elimination (and potential eradication) have been modelled by a consortium of mathematical modelers. The consortium consists of a single-country measles model in Nigeria (the IDM model[61]), two multi-country measles models (the DynaMice[62] and PSU[63] models) and two multi-country rubella models (the PHE[64] and JHU[65,66] models). The IDM model tracks subnational measles epidemiology, potentially offering greater realism for the situations modeled. These transmission models projected long-term cases, deaths, and DALYs, along with the number and type of vaccinations administered, under four vaccination coverage scenarios (one

[59] Shonhai A, Warrener L, Mangwanya D, Slibinskas R, Brown K, Brown D, Featherstone D, Samuel D. Investigation of a measles outbreak in Zimbabwe, 2010: potential of a point of care test to replace laboratory confirmation of suspected cases. *Epidemiology and Infection* 2015;143:3442-50.

[60] Winter AK, Martinez ME, Cutts FT, Moss WJ, Ferrari M, McKee A, Lessler J, Hayford K, Wallinga J, Metcalf CJE. Serological surveys for measles and rubella elimination: benefits and challenges. *Journal of Infectious Diseases* 2018;218:355-364.

[61] Zimmermann M, Frey K, Hagedorn B, Oteri AJ, Yahya A, Hamisu M, Mogekwu F, Shuaib F, McCarthy KA, Chabot-Couture G. Optimization of frequency and targeting of measles supplemental immunization activities in Nigeria: A cost-effectiveness analysis. *Vaccine* 2019;37:6039-6047

[62] Verguet S, Johri M, Morris SK, Gauvreau CL, Jha P, Jit M. Controlling measles using supplemental immunization activities: a mathematical model to inform optimal policy. *Vaccine* 2019;33:1291-6.

[63] Eilertson KE, Fricks J, Ferrari MJ. Estimation and prediction for a mechanistic model of measles transmission using particle filtering and maximum likelihood estimation. *Statistics in Medicine* 2019;38:4146-58.

[64] Vynnycky E, Papadopoulos T, Angelis K. The impact of measles-rubella vaccination on the morbidity and mortality from Congenital Rubella Syndrome in 92 countries. *Human Vaccines & Immunotherapeutics* 2019;15:309-16.

[65]Metcalf CJ, Lessler J, Klepac P, Cutts F, Grenfell BT. Impact of birth rate, seasonality and transmission rate on minimum levels of coverage needed for rubella vaccination. *Epidemiology & Infection* 2012;140:2290-301.

[66] Metcalf CJ, Lessler J, Klepac P, Morice A, Grenfell BT, Bjørnstad ON. Structured models of infectious disease: inference with discrete data. *Theoretical Population Biology* 2012;82:275-82.

based on assuming that routine coverage stays at 2017 levels, and three that project improved levels of coverage; see Annex). To evaluate the cost-effectiveness of different scenarios, outputs were used in an economic model which estimated the direct costs of vaccination and treatment associated with each scenario.

The inherent limitations of the models qualify the interpretation and inferences that can be drawn from this exercise. An “elimination threshold” of 5 cases per million was used, representing the point at which incidence is likely low enough to produce transmission interruption at national levels. It is important to note that the models were not designed to actually represent elimination itself, because they do not explicitly model many factors that influence measles and rubella transmission, particularly when close to elimination (such as, localized outbreaks and the resulting outbreak response activities, decreases in coverage due to political and other crises, and enhanced surveillance). While case importation was accounted for in varying manners by the different models (thus allowing for the possibility for re-introduction), explicit cross-border transmission was not accounted for, although this is likely less of an issue for the rubella results. Countries were modeled independently, which fails to capture the impact of regional interactions (which both complicates elimination but also offers potential benefits of coordinated efforts). In addition, the scenarios themselves were coarsely specified and provided information on a national scale only, neglecting subnational heterogeneity (the single-country Nigeria analysis provides some sensitivity to this).

Results from the models indicated that it is *possible* for all countries to achieve the elimination threshold for rubella and measles under most scenarios, including some in the base case scenario. However, the *probability* of reaching and sustaining the elimination threshold, and the time required to do so, varied by pathogen and across countries. The measles models suggest that a few countries may not reach the elimination threshold because the cessation of SIAs after high coverage with two doses of MCV would lead to measles resurgences. As expected, achieving and maintaining the elimination threshold for rubella is more probable and happens more quickly than for measles. Reaching the rubella elimination threshold is likely for most countries by 2060 under the three improved vaccination coverage scenarios. However, there remains a small risk of transient rubella outbreaks in a handful of countries that demonstrate variability in elimination probability and stability, producing a residual risk for elevated CRS cases.

All three improved coverage scenarios lead to dramatic (orders of magnitude) reductions in measles incidence and achieve the elimination threshold in most countries. Reaching conditions needed for elimination in <u>all</u> countries is unlikely under the modeled coverage scenarios as some countries have a low probability of reaching the conditions for elimination under any scenario. Targeted strategies, including enhanced surveillance, outbreak response, and prioritized subnational interventions, may increase the feasibility of elimination in these countries. The subnational model for Nigeria demonstrated that equity of coverage (i.e. ensuring that coverage improvements benefit the worst-performing districts and zero-dose children first) would greatly improve the probability of reaching low measles incidence.

The three improved coverage scenarios were more cost-effective for both measles and rubella (discounting costs but not DALYs) than the base case during the period from 2018 to 2047. The intensified investment scenario was the most cost-effective of these three for both diseases, and the continuing trends was more cost-effective than the constant improvement scenario for rubella only. However, the economic analyses had to make several

assumptions on costs of surveillance, vaccination and treatment due to limited availability of these data. In addition, limited data were available on the cost of increasing immunization coverage in low- and middle-income countries. Outbreak response activities were also omitted due to lack of information on costs and frequency, and because the benefits of these activities were also not captured by the transmission models.

Overall, this analysis shows that each of the three improved coverage scenarios are predicted to realize substantial and cost-effective reductions in measles, rubella and CRS morbidity and mortality over the next three decades. Many countries would be likely to achieve the conditions for elimination under these three scenarios. While successful global rubella eradication is highly probable, global measles eradication would remain unlikely, leaving a risk of reimportation into post-elimination countries (as the Region of the Americas is currently experiencing) and highlighting the need for improvements in both routine and SIA coverage to be coupled with new tools, efforts, and strategies to tip the balance in the most challenging contexts. The large variance in the time to achieve eradication indicates that countries that achieve elimination early will need to maintain vigilance (with investments in surveillance and outbreak response) to prevent outbreaks or re-establishment due to imported cases. This will require accelerated efforts as even maintaining the already achieved reductions in measles and rubella morbidity and mortality over the past two decades will need continued effort and investment.

Global eradication necessarily requires the interruption of virus transmission even in the most poorly performing contexts, and its success thus relies critically on strategies to address and relieve persistent inequities (spatial, accessibility, etc.) in vaccination coverage. These analyses highlight that achieving levels of low incidence at which elimination is feasible, perhaps through coordinated “end game” strategies, is indeed possible. A full assessment of the feasibility of measles and rubella eradication requires consideration of political, financial, supply, and distribution challenges as well as other contextual factors.

To generate a more complete picture of the path to eradication, further research is required. Additional modeling to evaluate strategies for implementing outbreak response, enhanced surveillance, and the appropriate conditions for ending SIAs would provide heightened detail around the degree of effort needed to make the final push to eradication as low incidence levels make stochastic extinction a possibility. Such work may benefit from modeling conditions seen in settings that have achieved elimination in the past, such as the Region of the Americas. Further sub-national modeling that allows for differential ramp-up of routine coverage in lower- and higher-performing districts would shed light on the importance of access and equity within countries. And finally, additional economic analyses are needed to determine variability in costs within and between countries, and to clarify the investment required in the end game to maintain rapid outbreak response and high-quality surveillance efforts until measles and rubella virus transmission is interrupted.

25. **Public, political and donor support and responsibility**. The global landscape has changed significantly since polio eradication was first declared in 1988, and bold global health goals consisting of top-down, vertical, disease-specific eradication programmes no longer have the public, political and donor support they once had. Early discussions of polio eradication took place in the context of the successful smallpox eradication programme (eradication was declared in 1980), whereas discussions of measles and rubella eradication have the prolonged polio eradication efforts and stagnant global vaccine coverage, despite large investments over the past decade, as their backdrop. Public, political and donor support will be essential to measles and rubella eradication, particularly country

commitment. Engagement with key stakeholders, including governments, political leaders, donors, and policy makers, is needed. Heads of state, Ministries of Health and Ministries of Finance must support measles and rubella eradication, in addition to major donors. Planning should begin with an analysis of current political and donor support for measles and rubella eradication and development of a plan to engage such support.

Measles and rubella eradication cannot be achieved without public support, community ownership, and committed accountability. Comprehensive communication and stakeholder engagement strategies should be implemented, with monitoring and review of successes and learning. The *Measles and Rubella Midterm Review* identified multiple strategies to garner and sustain public support for measles and rubella eradication, including: 1) increase resources for communication to raise the visibility and perceived risks of vaccine-preventable diseases, with a focus on measles and rubella; 2) create and promote sustained demand for immunization through tailored and targeted strategies that are informed by local evidence; 3) develop targeted communication and engagement plans for different audiences, including politicians, public health leaders and workers, healthcare providers, caregivers, and non-traditional stakeholders; 4) use data on measles incidence, including complications and deaths, as well as information on the costs associated with outbreaks, to communicate the importance of eradicating measles and rubella and the related investment case; 5) supplement these data with stories of actual cases and deaths, including cases of congenital rubella syndrome; 6) identify the most effective means of communication, including methods to counter misinformation; 7) use the opportunity of measles and rubella outbreaks to promote the importance of vaccination; 8) collect stories on how a focus on measles and rubella elimination enhanced overall immunization and health systems; and 9) ensure community engagement in planning, implementation and oversight of immunization. Carefully crafted communication and advocacy strategies are particularly important as the disease burden decreases, when there is less public memory of the disease burden and an increased concern for potential risks associated with vaccines.

26. **Can measles vaccination be stopped after eradication?** Measles and rubella eradication will face many of the same challenges faced by the GPEI to contain infectious laboratory materials after eradication.[67] A risk analysis concluded that measles will become a credible agent for bioterrorism through intentional release should population immunity decrease.[68] Genetic engineering of a measles virus strain that was not neutralized by antibodies induced by the current measles vaccines would likely have reduced infectivity, although virulence could potentially be augmented. Whether the threat from bioterrorism precludes stopping measles vaccination after eradication is unclear but a single-dose rather than a 2-dose measles vaccination strategy could be adopted, and the high levels of population immunity required for eradication would not need to be sustained.[69] Countries that decide to add mumps and varicella vaccines to their immunization schedule could include measles and rubella as part of a combined vaccine at relatively low cost.

Costs of Delaying Measles and Rubella Elimination and Eradication

[67] Bandyopadhyay AS, Singh H, Fournier-Caruana J, Modlin JF, Wenger J, Partridge J, Sutter RW, Zaffran MJ. Facility-associated release of polioviruses into communities - Risks for the posteradication era. *Emerging Infectious Diseases* 2019;25:1363-1369.

[68] Sanders R, Dabbagh A, Featherstone D. Risk analysis for measles reintroduction after global certification of eradication. *Journal of Infectious Diseases* 2011;204 Suppl 1:S71-7.

[69] Meissner HC, Strebel PM, Orenstein WA. Measles vaccines and the potential for worldwide eradication of measles. *Pediatrics* 2004; 114:1065–9.

27. **Costs to countries and regions that have eliminated measles.** The costs of delaying measles and rubella elimination and eradication are considerable and include both human and financial costs.[70] Human costs are counted in preventable deaths (currently estimated to be more than 100,000 per year), morbidity (e.g. hospitalizations, clinic visits, neurologic impairment, blindness), poverty, and poor school performance, among the numerous effects of measles and rubella, which have negative impact on long-term productivity and economic growth. These benefits are seen by countries and regions that have achieved elimination. However, elimination status is fragile, expensive to maintain and may not be sustainable in the long-term while the risk of virus importation persists. Several studies reported the cost of containing measles outbreaks in high-income settings where elimination was achieved. For example, the estimated cost of containing an outbreak of 34 measles cases in Indiana, United States in 2005 was US$ 167,686 following exposure to an unvaccinated 17-year-old adolescent who contracted measles in Romania.[71] A measles outbreak in 2008 in California, United States was sparked by an intentionally unvaccinated child who acquired measles in Switzerland and led to an additional eleven cases, with the outbreak response costing US$ 10,376 per case.[72] Another outbreak in 2008 in Arizona, United States, resulting from an infected traveler from Switzerland who visited a hospital, led to 14 cases and a cost to two hospitals of US$ 799,136 to respond to and contain seven cases.[73] An outbreak of 58 measles cases in New York City in 2013, following importation from London, England, was estimated to cost the local health department US$ 394,448.[74] A total of 10,054 hours were spent responding to and controlling the outbreak. Although these examples are from the United States, they highlight the enormous financial costs of sustaining elimination when measles virus is circulating in other countries and the potential to lose the political and public will to maintain elimination. Costing of current measles outbreak responses in several countries is underway.

28. **Equity and ethical considerations for measles and rubella elimination and eradication.** Measles and rubella elimination and eradication raise issues related to equity and ethics. The 1989 Convention on the Rights of the Child states that children have the right to the best health care possible and that rich countries should help poorer countries achieve this right.[75] Governments should ensure that children enjoy the protection offered by measles and rubella vaccines, which are both affordable and effective in preventing severe disease and death. Because children who are at high-risk for missing out on vaccination, including migrants, nomadic communities, those residing in urban slums, and the rural poor, are often at greatest risk of severe disease because of poor nutrition, co-infections, and limited access to health care, reaching them with vaccines can have a substantial impact on health

[70] Durrheim DN, Crowcroft NS. The price of delaying measles eradication. *Lancet Public Health* 2017; 2: e130–e131.

[71] Parker AA, Staggs W, Dayan GH, Ortega-Sánchez IR, Rota PA, Lowe L, Boardman P, Teclaw R, Graves C, LeBaron CW. Implications of a 2005 measles outbreak in Indiana for sustained elimination of measles in the United States. *New England Journal of Medicine* 2006;355:447-55.

[72] Sugerman DE, Barskey AE, Delea MG, Ortega-Sanchez IR, Bi D, Ralston KJ, Rota PA, Waters-Montijo K, Lebaron CW. Measles outbreak in a highly vaccinated population, San Diego, 2008: role of the intentionally undervaccinated. *Pediatrics* 2010;125:747-55.

[73] Chen SY, Anderson S, Kutty PK, Lugo F, McDonald M, Rota PA, Ortega-Sanchez IR, Komatsu K, Armstrong GL, Sunenshine R, Seward JF. Health care-associated measles outbreak in the United States after an importation: challenges and economic impact. *Journal of Infectious Diseases* 2011;203:1517-25.

[74] Rosen JB, Arciuolo RJ, Khawja AM, Fu J, Giancotti FR, Zucker JR. Public health consequences of a 2013 measles outbreak in New York City. *JAMA Pediatrics* 2018;172:811-817.

[75] https://www.ohchr.org/en/professionalinterest/pages/crc.aspx

inequities. Furthermore, because of the herd immunity conferred in communities with high levels of measles vaccine coverage, measles vaccination can protect those too young to be vaccinated or those with immunodeficiencies who cannot be immunized. Measles and rubella viruses could be called the equity viruses: without vaccination, everyone gets them, and without equitable health-care systems to deliver vaccination, measles and rubella will continue to present a threat to the most vulnerable.

29. **Risks in delaying measles and rubella elimination and eradication.** The changing epidemiology of measles could make elimination and eradication even more challenging in the future, thus creating urgency in accelerating progress toward regional elimination goals. First, as more women of child bearing age have vaccine-induced immunity and are not exposed to wild-type measles virus, lower levels of maternal antibodies are transferred to their infants, who then become susceptible to measles at a younger age.[76] This has led to discussions as to whether the age of administration of MCV should be reduced from nine to six months of age and a change to the EPI schedule. The WHO currently recommends an early dose of measles-containing vaccine at six months of age, in addition to the routine doses at nine months and in the second year of life, in some circumstances, including during outbreaks, for refugees or internally displaced persons, and to HIV infected or exposed infants.[77] However, measles vaccination at six months of age results in reduced immunogenicity and effectiveness compared to nine months of age.[78] Second, there remains the possibility that vaccine-derived measles immunity may wane in older individuals, particularly those receiving their first vaccination below 12 months of age who were not subsequently exposed to wild-type virus, expanding the age range of susceptibility and need for vaccination.[79] The experience thus far in the United States suggest this has not contributed to sustained measles virus transmission but more data from other settings are needed, particularly from countries where MCV1 was administered at nine months of age. Third, increasing urbanization,[80] resulting in increased contact rates and thus measles virus transmission, could lead to higher levels of population immunity needed to interrupt measles virus transmission, hindering eradication efforts. Finally, increasing globalization, travel, and population movement greatly amplify the risk of re-importations into countries that have eliminated measles. The constant threat of measles outbreaks creates an unsustainable burden even on the countries with strong programmes and sustainability for an indefinite time period may not be feasible.

Measles and Rubella Elimination Goals and Benchmarks toward an Eradication Goal

30. **Reaffirming country and Regional elimination goals and the vision of a world without measles and rubella**. Enormous progress has been made in reducing global measles and

[76] Guerra FM, Crowcroft NS, Friedman L, Deeks SL, Halperin SA, Severini A, Hatchette TF, Bolotin S, and the Immunity of Canadians and Risk of Epidemics (iCARE) Network. Waning of measles maternal antibody in infants in measles elimination settings - A systematic literature review. *Vaccine* 2018;36:1248-1255.
[77] World Health Organization. Measles vaccines: WHO position paper – April 2017. *Weekly Epidemiological Record* 2017;92:205-27.
[78] Lochlainn LN, de Gier B, van der Maas N, Strebel PM, Goodman T, van Binnendijk RS, de Melker HE, Hahné SJM. Immunogenicity, effectiveness, and safety of measles vaccination in children younger than 9 months: a systematic review and meta-analysis. *Lancet Infectious Diseases* 2019 (in press).
[79] Hughes SL, Bolotin S, Khan S, Li Y, Johnson C, Friedman L, Tricco AC, Hahné S, Heffernan JM, Dabbagh A, Durrheim DN, Orenstein WA, Moss WJ, Jit M, Crowcroft NS. Is there evidence for waning measles vaccine effectiveness? A systematic review. 2019 (in press).
[80] https://ourworldindata.org/urbanization

rubella incidence, morbidity, and mortality through vaccination. However, global MCV1 coverage has stalled at about 85% for the past decade and global milestones for vaccine coverage and reductions in measles incidence and mortality have not been met. Countries and regions are at different stages along the path to measles and rubella elimination.[81] Global, regional, country, and donor support for pathogen-specific eradication initiatives has shifted and become more diverse, influenced by the challenges faced by the GPEI and changing global health and development priorities. Although there is general agreement that measles and rubella eradication is biologically and technically feasible, there are conflicting views on the need for and value of a global measles and rubella eradication goal and how such a goal would require changes to programme strategies, political will, public support, and available resources.

A measles and rubella eradication goal should be set only when accelerated progress has been made, benchmarks that establish the conditions for a successful endgame to achieve eradication have been achieved, and there is evidence of a clear trajectory toward the goal. Setting an eradication goal when the endgame is in sight could catalyze a surge in commitment, effort, and resources to complete the task, thus heeding the call to go "big and fast" with measles and rubella eradication, and avoid a premature and drawn-out eradication effort with the potential for unmet goals, delayed milestones, and prolonged input of financial and human resources.[82] Setting a target date for measles and rubella eradication prematurely could create the expectation of an initiative modeled after the GPEI: a large vertical programme with a substantial management structure, and billions of dollars in funding. Such an initiative is unlikely to receive the needed support in light of the ongoing challenges to polio eradication and the changing strategic approaches to global health and development in the coming decade.

Nevertheless, reaffirming the importance of achieving and sustaining the country and Regional measles and rubella elimination goals, and restating the vision of a world without measles and rubella, would convey an aspirational vision and provide further support and motivation for accelerating the rate of progress. Such a reaffirmation would highlight the fact that the global public health community remains firmly committed to the country and Regional measles and rubella elimination goals. A goal and target date for measles and rubella eradication would then be set when the endgame is in sight and benchmarks for setting such a goal have been achieved. A reaffirmation of the measles and rubella elimination goals and a vision for a world without measles and rubella could be based on the following principles:

- The status quo is unacceptable and progress toward achieving and sustaining country and Regional measles and rubella elimination goals must be accelerated. Measles and rubella remain global public health priorities and require increased global, regional and national commitment.
- Current, uncoordinated approaches toward measles and rubella elimination in individual countries is inadequate to achieve our existing goals. Measles and rubella transmission in any country is a threat to elimination in all countries. Stronger support and more coordinated strategies within Regions and across transmission blocks must be developed to complement individual country efforts to achieve elimination.

[81] Graham M, Winter AK, Ferrari M, Grenfell B, Moss WJ, Azman AS, C. Jessica E. Metcalf CJE, Lessler J. Measles and the canonical path to elimination. *Science* 2019;364:584-587.
[82] Omer SB, Orenstein WA, Koplan JP. Go big and go fast--vaccine refusal and disease eradication. *N Engl J Med* 2013;368:1374-6.

- Accelerated progress should be based on strengthening immunization, primary healthcare, and surveillance systems, supplemented by targeted vaccination campaigns and other programme innovations to reach unvaccinated and under-vaccinated populations, rather than reliance on repeated emergency responses or non-selective and wide-age range supplementary immunization activities to make up for weak immunization services.
- Reaffirmation of country and Regional elimination goals, and the aspirational vision of a world without measles and rubella, could foster increased political and public will to facilitate country efforts to achieve their elimination goals, would be aligned with the strategic priorities of the IA2030, and could foster strategic programme development and innovation for the endgame, including contingency planning for expected and unexpected obstacles and promotion of new strategies and technologies to support eradication such as rapid diagnostic tests and microarray patches.
- A measles and rubella eradication goal should only be set when substantial and measurable progress has been made, and the strategies, resources and commitment are likely to be in place to interrupt the final transmission pathways. The endgame would comprise a time-limited (e.g. five years) intensification of efforts with a realistic chance of achieving eradication by the target date. Updated analyses and models would be needed to inform the decision to set an eradication goal and target date.

31. **Benchmarks toward measles and rubella eradication.** The path toward measles and rubella eradication should strengthen routine immunization, primary health care and universal health coverage to achieve equity and the strategic priorities of the IA2030. Benchmarks for setting a measles and rubella eradication goal should be developed through a consultative process with key stakeholders, including representatives from countries, regions, donors, industry, Civil Society Organizations, the M&RI partners, and the public, informed by rigorous analyses and modeling. The benchmarks should be used to gauge when it is appropriate to commit to an eradication goal and target date through a well-developed and sufficiently resourced endgame strategy. The benchmarks should not be absolute and final but should be modified and updated based on changing epidemiological conditions, innovations, updated analyses and models, the public, political and financial landscape, and other contextual factors, such as conflict, political instability and large-scale population movements that impact the feasibility of eradication. Judgement will continually be needed to assess the prospects of measles and rubella eradication and the progress necessary to accomplish the goal. A measles and rubella eradication advisory group should be established to lead development of the benchmarks and metrics, monitor progress and trajectories toward achieving these benchmarks, and to ensure accountability. The benchmarks should include a range of categories essential to achieving measles and rubella eradication, based on evidence and analyses with measurable metrics and trajectories, and could include:

    - Introduction of MCV2 and RCV into national immunization programs
    - MCV1 and MCV2 coverage
    - Vaccine coverage data quality
    - SIA quality and efficiency
    - School entry checks
    - Surveillance quality
    - Measles incidence

- Equity measures
- Verification of elimination
- Vaccine and diagnostic test supplies
- Communications and advocacy
- Technology and innovations

Thus, the path toward measles and rubella eradication should be through accelerated progress toward country and Regional measles and rubella elimination goals and integral to the strategic priorities of the IA2030, including strengthening primary health care, fostering universal health coverage, and achieving equity. Benchmarks on the path toward measles and rubella eradication should be specified and progress and trajectories toward achieving these benchmarks should be assessed.

32. Recommendations

1. Reaffirm the importance of country and Regional measles and rubella elimination goals and stress the need for all countries to accelerate progress toward achieving and sustaining measles and rubella elimination. Measles and rubella virus transmission in any country is a threat to elimination in all countries. Efforts to achieve and maintain measles and rubella elimination should strengthen immunization and primary health care systems, advance the IA2030 strategic priorities, and serve as an important marker for progress towards achieving equity in access to vaccination.

2. SAGE concluded in November 2010 that measles can and should be eradicated, and that a goal for measles eradication should be established with a proposed target date based on measurable progress made towards existing goals and targets. Reaffirm the vision of a world without measles and rubella but that an eradication goal should only be established when substantial and measurable progress has been made toward achieving country and Regional elimination goals.

3. Establish a measles and rubella eradication advisory group, working within the future governance structures of IA 2030, to convene a consultative process to identify new benchmarks that should be achieved before setting an eradication goal. The purpose of the benchmarks would be to gauge when it is appropriate to set a measles and rubella eradication goal by providing metrics toward achieving the necessary conditions for a successful eradication endgame within a defined time period (e.g. five years).

4. The advisory group should monitor progress towards achieving these benchmarks and recommend adjustments to the benchmarks in light of changing epidemiological conditions, innovations, updated analyses and models, the public, political and financial landscape, and other contextual factors that impact the feasibility of eradication. The advisory group should provide a report every three years on progress toward achieving the benchmarks.

5. A measles and rubella eradication goal should be considered when recommended by the advisory group based on progress toward achieving the benchmarks. A strategic plan for the measles and rubella eradication endgame should be in place at the time of setting a goal, including estimates of the cost of implementing the plan.

Annex 1: Vaccination scenarios
Base year: 2017

Three vaccination scenarios were developed by US Centers for Disease Control and Prevention, and one was based upon assumptions provided by the Vaccine Impact Modeling Consortium (VIMC)[83]: (i) base case (routine coverage remains at 2017 levels), (ii) continuing trends (coverage increases based on current trends and existing introduction commitments), (iii) constant improvement (coverage improves at 1%/year with all countries introducing MCV2 and RCV by 2020, up to 95% for Gavi-eligible countries and up to 90% for all others), and (iv) intensified investments (coverage increases at 4.4%/year compounded, with all countries introducing MCV2 and RCV by 2024). All scenarios aside from base case include termination of SIAs when two-dose MCV coverage is sufficiently high. An "elimination threshold" of 5 cases per million was used as a proxy for elimination, providing a conservative threshold at which incidence is likely low enough to produce transmission interruption at national levels. These models do not explicitly account for enhanced surveillance or outbreak response; thus, this elimination threshold is a conservative indicator of the feasibility of elimination.

Scenario	**1** **CDC Scenario A – Base case**	**2** **CDC Scenario B – Continuing trends**	**3** **Constant improvement**	**4** **CDC Scenario C – Intensified investments**
Assumptions	- Constant, inflation-adjusted investments in national programmes - Policies, practices implemented by 2017 held constant throughout analytic period - Counterfactual, but establishes a baseline for programmatic inputs, health costs, and outcomes	- Current investments and conservative projection of future investments - Includes limited set of improvements that national programmes and global partners are expected to support even in the absence of a formal, unified commitment to eradication - Incorporation of RCV and MCV2 into routine immunization programs is expected to continue	- Current investments and conservative projection of future investments - Includes a limited set of improvements that national programmes and global partners are expected to support even in the absence of a formal, unified commitment to eradication	- Intensified investments and inputs in national programs - Models the minimum reasonable, if optimistic, time to achieve eradication - Serves as a lower bound for costs, upper bound for benefits - Increased coverage, more frequent preventive SIAs
MCV1 coverage	All countries remain at base year coverage.	Historical coverage used to fit natural log function up to 99%. Countries with high, constant or inconsistent recent coverage,	All Gavi supported countries with coverage <95% improve coverage from base year by 1%/year up to 95%.	Global median compound rate (**CGR**) (4.4%) used to estimate coverage up to 99% for countries that have not yet eliminated measles /

[83] https://www.vaccineimpact.org/

		prospective coverage held constant at average of recent coverage.	All other countries with coverage <90% improve coverage from base year by 1%/year up to 90%.	rubella, or reached 95%, by 2016.
MCV2 introductions	No new MCV2 introductions beyond 2017.	MCV2 introductions continue as projected by current country commitments and SME assessment. MCV2 age in countries introducing MCV2 in 2017 or later based on MCV1 age and coverage, and regional schedules	All countries introduce MCV2 in 2020 if they have not already done so. MCV2 coverage starts at 10% below MCV1 coverage at introduction.	MCV2 introduced in 2018-2024 if not already done so, timing as projected by SMEs. MCV2 age based on MCV1 age and coverage, and regional schedules
MCV2 coverage	All countries remain at base year coverage.	For countries w/ ≥ 4 yrs of MCV2 data, historical coverage used to fit natural log function up to 99%; countries with high, constant or inconsistent recent coverage, prospective coverage held constant at average of recent coverage. For countries w/ < 4 yrs of MCV2 data, coverage projections based on region- and income level-derived natural log functions: - Countries w/ 1-3 yrs of MCV2 data: 2017 MCV2 = I.V. for prospective coverage (2018-2055) - Countries w/o MCV2 intro by end of 2017: MCV2 coverage = % of MCV1 coverage based on WB income level-specific MCV1-MCV2 differences	All Gavi supported countries with MCV2 coverage <95% improve coverage from base year by 1%/year up to 95%. All other countries with coverage <90% improve coverage from base year by 1%/year up to 90%.	For countries that have not yet eliminated measles / rubella, or reached 95% MCV1 coverage by 2016: - Countries w/ MCV2 by end of 2017: 2017 MCV2 = I.V. for prospective coverage - Countries w/o MCV2 by 2018: MCV2 coverage = % of MCV1 coverage based on WB income level-specified MCV1-MCV2 differences - Forecasted MCV2 coverage subject to dynamic capping such that MCV2 ≤ MCV1 and relative values are realistic

RCV introductions	No new RCV introductions beyond 2017.	RCV introductions continue as projected by current country commitments and SME assessment. RCV1 coverage = MCV1 coverage; RCV2 coverage = MCV2 coverage.	All countries introduce MR in 2020 if they have not already. MR coverage assumption is the same as MCV1 coverage.	RCV2 introduced in 2018-2024 if not already done so, timing as projected by SMEs. RCV1 coverage = MCV1 coverage; RCV2 coverage = MCV2 coverage.
SIAs	SIAs up to 2017 based on historical events. SIAs beyond 2017 based on the current WHO rule of thumb.	SIAs up to 2017 based on historical events. Age categories and frequency for prospective SIAs based on historical SIAs. SIA coverage based on historical averages and increased by 10% of the incremental difference between the previous coverage estimate and 100% for 3 subsequent SIAs and then held constant through 2055. Cessation of SIAs in countries w/ both MCV1 and MCV2 ≥ 90.5% for 5 years; RCV introduction; accumulation of susceptibles < 1 birth cohort w/in 8 years after previous SIA	SIAs up to 2017 based on historical events. Any SIA scheduled up to 2020 continues. After 2020, countries with MCV2 coverage below 90% have SIAs every 3 years.	SIAs up to 2017 based on historical events. Age category <5 years old following MR introduction. Frequency based on accrual of susceptibles (as driven by MCV1 & MCV2 activities) = 75% of size of birth cohort. Cessation of SIAs in countries w/ MCV2 ≥ 5 yrs; RCV introduction; MCV1 & MCV2 coverage high enough to prevent 75% threshold accumulation w/in 8 years after previous SIA.
Within country variation	No change in variation between admin level 1 division within each country. No variation assumed below admin level 1 divisions.	No change in variation between admin level 1 division within each country. No variation assumed below admin level 1 divisions.	No change in variation between admin level 1 division within each country. No variation assumed below admin level 1 divisions.	Variation between admin level 1 division within each country halves every year. No variation assumed below admin level 1 divisions.

Executive Summary: Human papilloma virus

Background

In the meeting of SAGE in October 2018[1], SAGE affirmed that HPV vaccination is the most critical intervention for eliminating cervical cancer. Introduction of HPV vaccine should be prioritized in all countries but especially in countries with the highest cervical cancer rates. The SAGE Working Group on HPV immunization held a meeting in Menthon-Saint-Bernard, France on 6-7 June 2019. The Terms of Reference for the Working Group, list of participants with Working Group membership and meeting agenda are provided in Appendices.

All three licensed HPV vaccines – bivalent (HPV genotypes 16/18), quadrivalent (HPV 6/11/16/18) and nonavalent (HPV 6/11/16/18/31/33/45/52/58) – have excellent safety, efficacy, immunogenicity and effectiveness profiles. The risk attribution of HPV 16/18 in women with cervical cancer is approximately 70%

The (draft) Global Strategy Towards the Elimination of Cervical Cancer as a Public Health Problem[2] calls for a comprehensive, population-based approach to put all countries on the path to the elimination of cervical cancer as a public health problem within the century. The strategy proposes an approach that will enable countries to reach 2030 global targets for key interventions that, in turn, will lead to elimination of cervical cancer as a public health problem. The proposed targets for 2030 are: (i) 90% of girls being fully vaccinated with HPV vaccine by 15 years of age; (ii) 70% of women being screened with a high-precision test[3] at 35 and 45 years of age; and; (iii) 90% of women identified with precancer lesions or invasive cervical cancer receive treatment.

As of June 2019, 96 countries (49%) have introduced HPV vaccines in the national immunization programmes or in part of the countries. Currently, an estimated 30% of girls aged 9-14 years globally live in countries that have introduced the HPV vaccine. However, preliminary data on WHO estimates of the HPV vaccine coverage show that the average HPV coverage in countries with available data is 64% for the first dose and 52% for the second dose[4]. Since 2018, limited number of doses in supply has affected HPV introductions and introduction plans across the global. In 2019, all planned Gavi-supported HPV introductions are going ahead for the routine recommended cohorts. However, the multiple age-cohorts vaccination (MACs) have been postponed to later dates in the majority of these countries. Introductions in non-Gavi Middle Income Countries are constrained including by limited vaccine supply. Concerned by constrained HPV vaccine supply, in October 2018 SAGE called for a

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[1] World Health Organization. Meeting of the Strategic Advisory Group of Experts on Immunization, October 2018 – Conclusions and recommendations, Dec 2018. Weekly epidemiological record 2018;49(93):661-680. https://apps.who.int/iris/bitstream/handle/10665/276544/WER9349.pdf

[2] https://www.who.int/cancer/cervical-cancer/cervical-cancer-elimination-strategy

[3] A WHO recommended high-precision test which would have performance characteristics similar to or better than a clinically approved HPV DNA test. In the future, however, new technologies may be available.

[4] WHO IVB database, preliminary results, as of May 2019

comprehensive evaluation of options for the best use and allocation of the limited vaccine supply[5]. In response to this recommendation, the SAGE Working Group on HPV Immunization reviewed the data on vaccination barriers and immunization schedules, reviewed modelling results on vaccination strategies and assessed options to achieve more equitable allocation of HPV vaccines in the context of supply constraint.

Purpose of the session and summary

This session will consist of seven presentations: (1) introduction and key questions, (2) update on access to HPV vaccines, (3) systematic review of the evidence on different HPV immunization strategies, (4) summary of ongoing-trials on single-dose HPV vaccine schedule, (5) global analysis of HPV vaccine supply and demand, (6) impact of different HPV immunization strategies in the context of supply constraint, and (7) conclusions and proposed recommendations.

For this SAGE meeting, members are requested to provide recommendations in the context of HPV vaccine supply constraint, on the barriers and strategies to overcome obstacles to achieving introduction of HPV vaccines, on the HPV supply allocation and how HPV vaccine introduction be prioritized. In addition, the SAGE members will be invited to consider the evidence on the immunogenicity and efficacy of a single-dose of HPV vaccine, the different intervals between doses and the number of doses in the older age group (i.e. 15 to 18 years old).

Background documents in the yellow book

- None

Background documents on the web

- Report from meeting of SAGE WG on HPV vaccines (held on June 6-7, 2019)
    - This report provides summary of the deliberations and recommendations of the SAGE Working Group
- Presentation on HPV vaccines uptake and barriers
- Off-label HPV vaccine recommendations: a survey of NITAGs and EPI program managers
- Final one dose HPV vaccine report v4.
- Final longer interval versus shorter interval of HPV vaccines v3.1
- Final Two doses of HPV vaccine in 15-18 year old v2.0
- Global HPV Vaccine Market Study
- Global HPV Vaccine Market Study - Demand Methodology
- HPV vaccination LMIC.ppt - Optimal HPV vaccination strategies to prevent cervical cancer in LMIC
- HPV vaccination impact supply constraints.ppt - Impact on burden of disease by demand scenario under supply constraints.

[5] World Health Organization. Meeting of the Strategic Advisory Group of Experts on Immunization, October 2018 – Conclusions and recommendations, Dec 2018. Weekly epidemiological record 2018;49(93):661-680. https://apps.who.int/iris/bitstream/handle/10665/276544/WER9349.pdf

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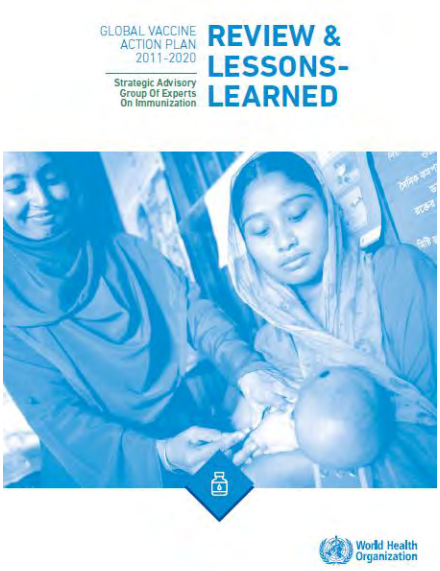


The Global Vaccine Action Plan and the Decade of Vaccines

Review and Lessons Learned

Draft

13 September 2019 for Yellow book

Preface

The Global Vaccine Action Plan 2011–2020 (GVAP) was developed to help realize the vision of the Decade of Vaccines, that all individuals and communities enjoy lives free from vaccine-preventable diseases. As the decade draws to a close, it is time to take stock of the progress made under GVAP and to apply the lessons learned to the global immunization strategy for the next decade.

This report has been prepared for the Strategic Advisory Group of Experts on Immunization (SAGE) by the SAGE Decade of Vaccines Working Group (Annex 1).

This report expands on the annual assessment reports prepared by the SAGE Decade of Vaccines Working Group. It considers the entire decade, drawing on a review of progress toward GVAP's goals and objectives as well as the perceptions of stakeholders captured through three surveys, which elicited 310 responses from immunization stakeholders, and two sets of semi-structured interviews with 80 stakeholders undertaken in 2017–2019. It also incorporates valuable insights from Working Group members and the representatives of partner organizations and WHO regional offices who have made important contributions to annual assessments. Annex 2 provides links to the full body of evidence used to generate this report.

This document reflects on the lessons learned from GVAP, and makes recommendations for the development, content and implementation of the next global immunization strategy.

I. Executive Summary

Much progress, but unmet objectives

During the past decade, great strides have been made in immunization. More children are being vaccinated than ever before, ever-growing numbers of countries have introduced new vaccines, and the global research and development (R&D) community is generating a steady stream of new and improved vaccines.

Nevertheless, many Global Vaccine Action Plan (GVAP) targets have not been met. Globally, coverage of essential vaccines has stagnated. Despite intensive efforts, polio has not been eradicated and measles is undergoing an alarming resurgence. The benefits of immunization are still unequally shared, both within and between countries.

However, GVAP included ambitious targets to catalyse action. Focusing only on the binary distinction between 'met/not met' does not do justice to the significant progress made during the decade in a wide range of countries, often under highly challenging circumstances. Lack of progress in a relatively small number of countries, generally affected by chronic conflict or political instability, masks major advances achieved elsewhere.

A comprehensive global strategy

GVAP was developed through an extensive **global consultation** with an unprecedentedly wide range of stakeholders, including countries. It created a comprehensive **global framework** for addressing key issues in immunization. It established a common vision and a forum in which immunization stakeholders could collectively discuss matters of concern, as well as a mechanism to connect the activities of global partners. And it acted as a key focal point, maintaining the high global profile of immunization.

GVAP was a **comprehensive global strategy** spanning both disease elimination/eradication initiatives and national immunization programme activities. For the first time, it also included a focus on R&D of new vaccines and vaccine technologies.

Limited scope to drive change

Despite these strengths, in practice GVAP had limited capacity to influence the actions of countries and partners in order to achieve its goals.

Global–country disconnects

GVAP is widely seen as a **top-down strategy**, focused on global goals and targets. Furthermore, as GVAP adhered to the principle of equity, it aspired to achieve similar goals for all countries, irrespective of their current status. In addition, contrary to many expectations, GVAP did not come with additional resources. This led to targets and timelines that were perceived by some countries to be unrealistic, limiting buy in to GVAP's aims.

In addition, countries and partners often adopted a 'pick and choose' approach to GVAP goals, according to their own priorities, rather than fully committing to all aspects of GVAP.

Partial implementation

Implementation of GVAP was envisaged to occur at a country level through updating of national immunization plans, supported by development partners. This happened to only a limited extent, and resourcing was often not sufficient to achieve national aspirations or GVAP goals.

Later in the decade, **Regional Vaccine Action Plans** played a key role in bridging the strategy and planning gap between global and country levels. However, they took time to develop, creating a lag in translation of GVAP into action in regions and countries.

Integration of immunization and other health services and relationship-building outside the health sector were limited. While many productive partnerships were established, activities were not always fully coordinated at either global or national levels. Groups such as civil society organizations (CSOs) and the private sector have the potential to play a wider range of roles. In the absence of a specific organizational structure for GVAP, opportunities to establish closer ties with emerging health priorities, such as global health security, were not fully grasped.

Extensive communications and advocacy activities were undertaken at the launch of GVAP. However, they were not sustained throughout the decade, and GVAP's **low visibility,** particularly among country stakeholders, may also have lessened its impact.

Extensive monitoring but limited accountability

GVAP developed an innovative and comprehensive **monitoring, evaluation and accountability framework.** It established a common set of metrics to assess progress and to enable countries to benchmark their achievements. Similarly, it focused attention on the value of high-quality data, and raised awareness of inequities in coverage within countries.

However, extensive annual reporting was not sufficient to achieve **accountability**, or to influence the activities of countries and partners to the extent needed to achieve GVAP goals. In countries, data collected in GVAP reporting often had insufficient impact on programme planning and operations.

A focus on global averages masked considerable national variation, obscuring exceptional progress in many countries and regions. Global averages also provided limited insight into underlying causes and appropriate corrective action. In addition, attention to national-level indicators masked significant disparities at sub-national levels. Some indicators were complicated and hard to interpret, or did not capture the full complexity of issues.

Continuing relevance amid changing contexts

Most of the goals and objectives identified by GVAP remain relevant today, and its targets are globally agreed upon commitments that will advance progress towards the Sustainable Development Goals (SDGs).

The past decade has been characterized by considerable volatility. Accelerating urbanization, migration and displacement, conflict and political instability, vaccine unaffordability in middle-income countries, unexpected vaccine supply shortages both locally and globally, and rising

vaccine hesitancy all presented major challenges through the decade. While these challenges were recognized, GVAP had limited 'levers' to influence global and national responses to them.

The world is continuing to experience infectious disease **outbreaks**, and disease elimination goals have not yet been achieved. GVAP covered both disease-specific initiatives and strengthening of national immunization programmes; both approaches have their merits, but the experience of the past decade suggests that elimination is ultimately dependent on the platform provided by strong national immunization programmes.

These insights argue in favour of a renewed global immunization strategy, building on GVAP's strengths and the lessons learned during the past decade.

High-level recommendations

A post-2020 global immunization strategy should:

1. Build on GVAP's lessons learned, ensuring more timely and comprehensive implementation at global, regional and national levels

2. Have a key focus on countries:

- 2a. Place countries at the centre of strategy development and implementation to ensure context specificity and relevance
- 2b. Strengthen country-led evidence-based decision-making
- 2c. Encourage the sourcing and sharing of innovations to improve programme performance
- 2d. Promote use of research by countries to accelerate uptake of vaccines and vaccine technologies and to improve programme performance

3. Maintain the momentum towards GVAP's goals:

- 3a. Incorporate key elements of GVAP, recognizing its comprehensiveness and the need to sustain immunization's successes each and every year.
- 3b. Add a specific focus on humanitarian emergencies, displacement and migration, and chronic fragility
- 3c. Encourage stronger integration between disease-elimination initiatives and national immunization programmes
- 3d. Encourage greater collaboration and integration within and outside the health sector

4. Establish a governance model better able to turn strategy into action:

- 4a. Create a robust and flexible governance structure and operational model based on closer collaboration between partners
- 4b. Incorporate the flexibility to detect and respond to emerging issues
- 4c. Develop and maintain a strong communications and advocacy strategy

5. Promote long-term planning for the development and implementation of novel vaccine and other preventive innovations, to ensure populations benefit as rapidly as possible

6. Promote use of data to stimulate and guide action and to inform decision-making

7. Strengthen monitoring and evaluation at the national and sub-national level to promote greater accountability

More detailed technical recommendations can be found on page 35.

II. History of GVAP

The catalyst for GVAP was the call by Bill and Melinda Gates at the 2010 World Economic Forum for the next decade to be the 'Decade of Vaccines'. Following the launch of the Expanded Programme on Immunization in 1974 and the commitment to Universal Childhood Immunization in 1984, global immunization coverage with the three-dose series of DTP (diphtheria–tetanus–pertussis) vaccine quadrupled, climbing to 84% by 2010. Smallpox had been eradicated and use of vaccines was making significant inroads into other infectious diseases. Gavi, the Vaccine Alliance, established in 2000, was making newer vaccines accessible to the poorest countries, while the Global Immunization Vision and Strategy, launched in 2006, provided a common vision and specific strategies for protecting more people against more diseases. New vaccines were being developed that held even greater promise.

Even so, not all people were benefiting equally from immunization's advances. Major inequities in access and coverage existed both between and within countries. These inequities led to the vision of the Decade of Vaccines – '*A world in which all individuals and communities enjoy lives free from vaccine-preventable diseases'*.

Development of GVAP

The Decade of Vaccines Collaboration was launched in 2010 to develop a shared plan to realize this vision. The Collaboration was led by WHO, UNICEF, Gavi, the US National Institute of Allergy and Infectious Diseases, and the Bill & Melinda Gates Foundation, coordinated by the Instituto de Salud Global Barcelona, Spain, and funded by the Bill & Melinda Gates Foundation. A Leadership Council, comprising executives of the lead organizations and a representative of the African Leaders Malaria Alliance, provided sponsorship and strategic guidance.

The Collaboration established a steering committee and assembled several working groups to draft GVAP and conducted a series of consultations with a diverse array of experts to refine its content – including elected officials, health professionals, academics, manufacturers, global agencies, development partners, CSOs and media from more than 140 countries and 290

organizations. An additional working group subsequently developed a monitoring, evaluation and accountability framework.

Ministers of health unanimously endorsed GVAP at the 2012 World Health Assembly; the monitoring and evaluation framework was endorsed a year later. In the following years, Regional Vaccine Action Plans and national multi-year plans were developed or updated to align with GVAP. African stakeholders went further to build political will for immunization, convening the Ministerial Conference on Immunization in Africa in 2016. This meeting launched the Addis Declaration on Immunization, through which heads of state and ministers of health, finance, education and social affairs as well as local leaders made ten specific commitments to promote health on the African continent through continued investment in immunization.

Design of GVAP

GVAP drew together immunization goals already endorsed by the World Health Assembly and set ambitious new targets in other areas. Pre-existing goals included eradicating polio, eliminating measles and rubella region by region, eliminating maternal and neonatal tetanus from priority countries, and achieving high and equitable vaccination coverage. GVAP also called for action to reduce inequities in coverage due to geographic location, age, gender, disability, educational level, socioeconomic level, ethnic group or work condition and to reduce dropout rates. In addition, a range of input and process indicators were developed to assess country ownership, financing, service integration, data quality and vaccine availability. Similarly, indicators were also developed to track progress in the development and deployment of new vaccines and innovative technologies.

To guide countries and partners, GVAP defined a comprehensive set of activities to achieve these ambitions and described how each immunization stakeholder, from families to global agencies, could contribute to its success. GVAP looked to stakeholders, including national governments, to take responsibility for implementing these activities, including translating the strategy into detailed operational plans and mobilizing the human and financial resources needed to carry them out.

GVAP at a Glance

Vision A world in which all individuals and communities enjoy lives free from vaccine-preventable diseases.

Guiding principles

1. **Country ownership** - Countries have primary ownership and responsibility for establishing good governance and for providing effective and quality immunization services for all
2. **Shared responsibility and partnership** – Immunization against vaccine-preventable diseases is an individual, community and governmental responsibility that transcends borders and sectors
3. **Equity** – Equitable access to immunization is a core component of the right to health
4. **Integration** –Strong immunization systems, as part of broader health systems and closely coordinated with other primary health care delivery programmes, are essential for achieving immunization goals
5. **Sustainability** – Informed decisions and implementation strategies, appropriate levels of financial investment, and improved financial management and oversight are critical to ensuring the sustainability of immunization programmes
6. **Innovation** – The full potential of immunization can only be realized through learning, continuous improvement and innovation in research and development, as well as innovation and quality improvement across all aspects of immunization

Goals

1. Achieve a world free of poliomyelitis
2. Meet vaccination coverage targets in every region, country and community
3. Exceed the Millennium Development Goal 4 target for reducing child mortality
4. Meet global and regional elimination targets
5. Develop and introduce new and improved vaccines and technologies

Strategic objectives

1. All countries commit to immunization as a priority
2. Individuals and communities understand the value of vaccines and demand immunization as both their right and responsibility
3. The benefits of immunization are equitably extended to all people
4. Strong immunization systems are an integral part of a well-functioning health system
5. Immunization programmes have sustainable access to predictable funding, quality supply, and innovative technologies
6. Country, regional, and global research and development innovation maximize the benefits of immunization

Implementation

GVAP implementation took two forms. First, GVAP encompassed the ongoing work of national immunization programmes and existing global partnerships and alliances. The global partnerships and alliances included well-resourced programmes such as Gavi and the Global Polio Eradication Initiative, as well as less well-resourced initiatives such as the Measles and Rubella Initiative and the Maternal and Neonatal Tetanus Elimination Initiative.

Second were the actions that arose directly from GVAP. These included the development or updating of Regional Vaccine Action Plans and the Addis Declaration on Immunization; the global monitoring, evaluation and accountability process; and World Immunization Weeks and other activities undertaken to increase the visibility of immunization.

ADDIS DECLARATION ON IMMUNIZATION

The **global monitoring, evaluation and accountability** process was the only aspect of GVAP with dedicated resources. In this effort, GVAP indicators were added to the WHO/UNICEF Joint Reporting Form and SAGE established the Decade of Vaccines Working Group to assess progress and draft recommendations for course corrections. Through the decade, countries reported annually, WHO and partner agencies compiled progress reports, and the SAGE independent assessment report and its recommendations were reviewed annually as a standing agenda item at the **World Health Assembly**.


World Health Organization

SEVENTY-FIRST WORLD HEALTH ASSEMBLY
Provisional agenda item 20.1

A71/39
15 March 2018

SEVENTIETH WORLD HEALTH ASSEMBLY
Agenda item 14.1

WHA70.14
31 May 2017

Strengthening immunization to achieve the goals of the global vaccine action plan

Additional immunization-related World Health Assembly resolutions calling for price transparency and greater affordability for vaccines, and for accelerated progress

toward GVAP targets, were adopted in 2015 and 2017, respectively.

III. Progress during the Decade of Vaccines

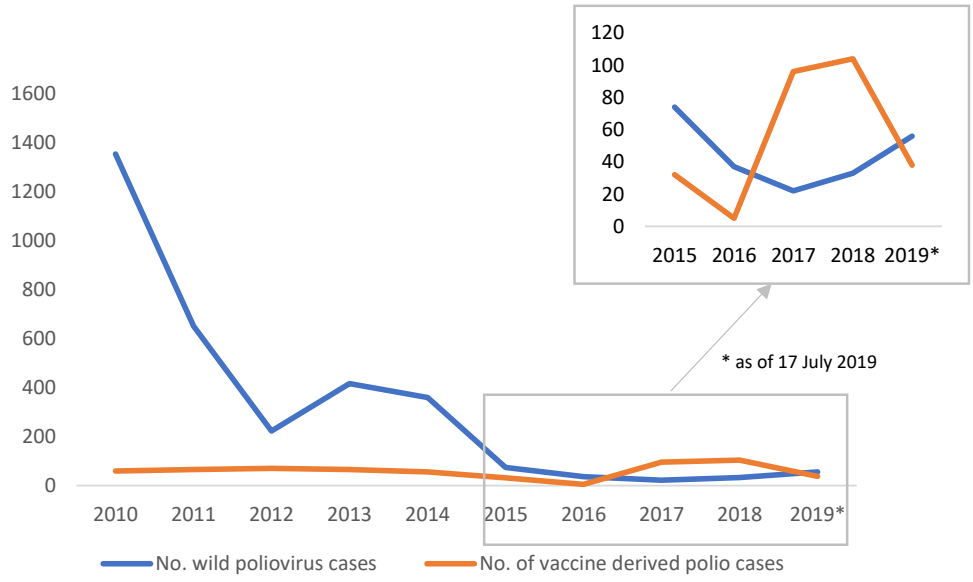
Most GVAP goals are not likely to be achieved by 2020 (see Annex 2 for links to full data). Even so, the 'off track' label masks steady progress in many areas.

Goal 1: Polio eradication

In spite of tremendous progress (Figure 1), polio eradication efforts face major security and community acceptance challenges in the last remaining sites of wild poliovirus transmission. Wild poliovirus type 2 was certified as eradicated in 2015 and wild poliovirus type 3 has not been detected since 2012. Wild poliovirus type 1 currently appears to be circulating only in Afghanistan and Pakistan.

Vaccine-derived poliovirus remains in circulation in a number of countries. These cases highlight the importance of maintaining high vaccine coverage within national immunization programmes.

Figure 1. Global wild poliovirus cases and circulating vaccine-derived poliovirus cases 2010-2019 (as of 17 July 2019)

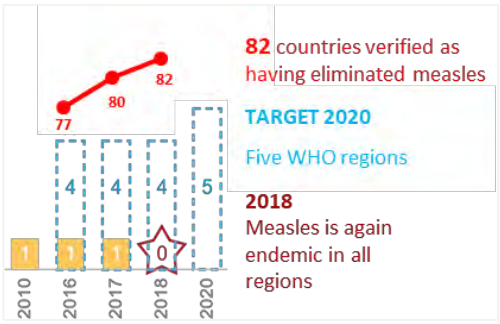


Goal 2: Meet global and regional elimination targets

Measles elimination. Vaccination has reduced the reported incidence of measles by 83% since 2000, preventing 21.1 million deaths. However, measles cases have recently rebounded in all regions, and global incidence has doubled from 2017 to 2018; this trend is continuing in 2019. All six WHO regions committed to measles elimination by 2020. The Americas was certified as having eliminated measles in 2016, only to suffer outbreaks in multiple countries starting in 2017 and a loss of certification in 2018.

Multiple countries have managed to interrupt transmission of measles and sustain measles-free status. However, measles continues to circulate uninterrupted in all regions of the world (Figure 2).

Figure 2. Number of regions and countries verified for measles elimination



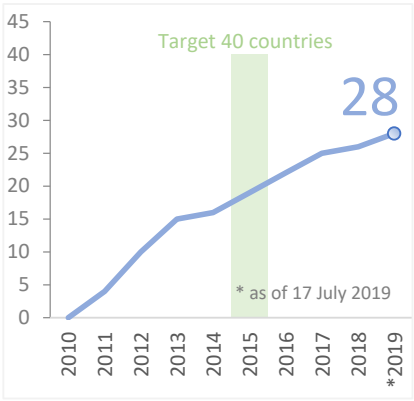
Global coverage with the first dose of measles vaccine has plateaued at around 86%, too low to achieve elimination, with major variations in coverage across and within countries. Global coverage with the second dose of measles vaccine in national immunization programmes has increased steadily, from 42% in 2010 to 69% in 2018. However, nearly one-third of all children still do not receive the two doses needed to maximize protection.

Even in countries with high coverage, clusters of unvaccinated children and adults perpetuate the risk of measles outbreaks. Outbreaks, especially from importations, have affected high-, middle- and low-income countries, reflecting the need for cross-border coordination at regional and global levels. Issues of immunization programme performance and vaccine hesitancy are also challenges.

Rubella and congenital rubella syndrome (CRS) elimination. Rubella is not as infectious as measles and requires only a single dose of vaccine, so should be easier to eliminate. Even so, the GVAP target – rubella and CRS elimination in five WHO regions by 2020 – will not be met. As of 2018, 168 out of 194 countries have implemented rubella vaccination and one WHO region is rubella-free.

***Maternal and neonatal tetanus elimination*.** Progress has been steady but the global target – elimination in 40 priority countries – is unlikely to be met by 2020 (Figure 3). As of July 2019, only 28 of these countries have eliminated the disease. Although more than 30 000 neonates died of tetanus infections in 2017, this represents an 85% reduction since 2000.

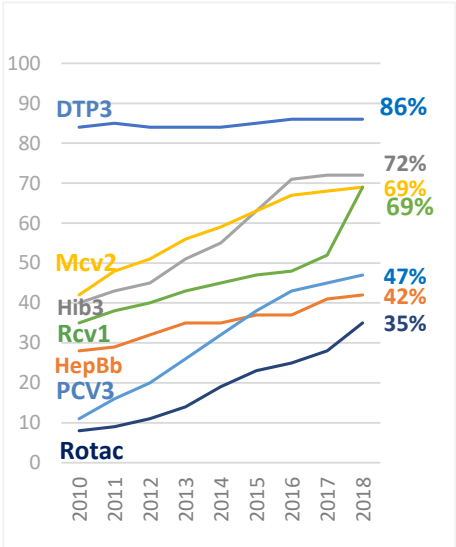
Figure 3. Number of priority countries having validated maternal and neonatal tetanus elimination



Goal 3: Meet vaccination coverage targets in every region, country and community

Coverage with three doses of DTP has plateaued at about 86% globally between 2010 and 2018. However, because of population growth, more children than ever are receiving the recommended three doses of DTP before their first birthday: in 2018, 116 million infants received three doses of DTP, about 4.9 million more than in 2010. Nevertheless, every year, nearly 20 million infants do not receive the full set of recommended vaccines.

Figure 4. Global coverage for selected vaccines



DTP3	Third dose of diphtheria, tetanus toxoid and pertussis vaccine
Mcv2	Second dose of measles-containing vaccine
Hib3	Third dose of *Haemophilus influenzae* type B vaccine
Rcv1	First dose of rubella-containing vaccine
HepBb	Hepatitis B virus vaccine birth dose
PCV3	Third dose of pneumococcal conjugate vaccine
Rotac	Rotavirus vaccine last dose

Globally, coverage has increased for many vaccines (Figure 4). Vaccine coverage rates vary substantially between countries and regions, and while national wealth is an important factor, it is not the

only driver of success – some low-income countries have achieved high and equitable coverage while several high-income countries are lagging. Low coverage has persisted in several countries over the decade, and coverage has declined in some countries, including several affected by conflict and economic and social crises.

While coverage has improved for numerous vaccines, many inequities remain within as well as between countries. Only about one-third of countries meet the target of 80% or greater DTP3 coverage in every district.

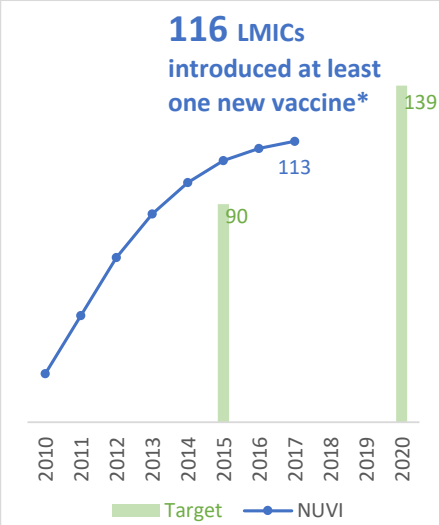
Goal 4. Develop and introduce new and improved vaccines and technologies

A total of 116 low- and middle-income countries have introduced at least one vaccine between 2010 and 2017. The GVAP target to introduce at least one new vaccine by 2020 in all 139 low- and middle-income countries will likely be missed by a small margin (Figure 5).

Nevertheless, countries introduced new vaccines more rapidly in the past decade than ever before. Since 2011, over 470 vaccine introductions have occurred in low- and middle-income countries and several of these countries have introduced as many as six or seven vaccines.

Middle-income countries that are not eligible for Gavi support have introduced fewer vaccines due in part to slow adoption of newer, more costly vaccines.

Figure 5. New vaccine introductions between 2010 and 2017 in low- and middle-income countries



* among the following: Hib-containing vaccine, pneumococcal conjugate vaccine, rotavirus vaccine, human papillomavirus vaccine, rubella-containing vaccine and Japanese encephalitis virus vaccine.

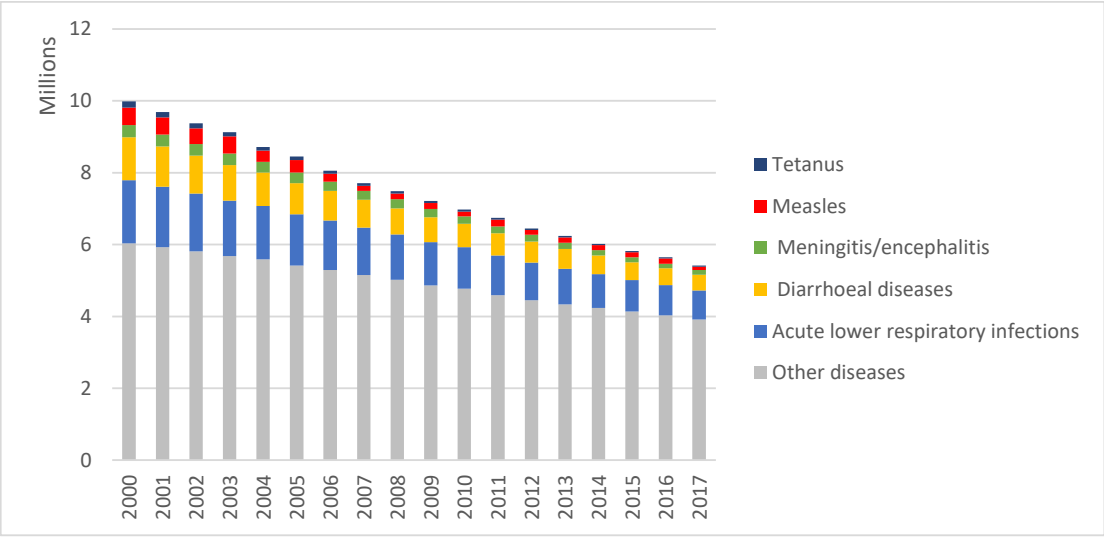
Particularly notable over the decade was the widespread introduction of a meningococcal group A vaccine ('MenAfriVac'), designed specifically for use in Africa. Use of the vaccine has virtually eliminated meningitis A disease in the 26 countries of the African 'meningitis belt', where a 2016 outbreak affected 250 000 people and claimed 25 000 lives.

As of 31 December 2018, *Haemophilus influenzae* type b (Hib) vaccine has been introduced in 190 out of 194 countries, pneumococcal conjugate vaccine (PCV) in 140 countries, and rotavirus vaccine in 97 countries. Human papillomavirus (HPV) vaccine is now being delivered to adolescent girls in 90 countries. The globally coordinated introduction of inactivated poliovirus vaccine (IPV) – now used in 192 countries – was a major achievement during the decade. Reinforcing the trend toward life-course vaccination, the global recommendation for tetanus is for vaccination at multiple ages to ensure lifelong protection.

Goal 5: Exceed the Millennium Development Goal 4 (MDG4) target for reducing child mortality

The mortality rate among children under five years has fallen substantially in recent decades, and much of the decline in child deaths since 1990 has been due to reductions in vaccine-preventable disease (Figure 6). Between 2010 and 2017, the mortality rate declined by 24%, from 52 to 39 deaths per 1000 live births. The MDG4 target was to reduce the rate of under-five deaths by two-thirds between 1990 and 2015; with recent progress, this reduction is very close to being achieved.

Figure 6. Global number of deaths of children under five for selected vaccine-preventable diseases between 1990 and 2017



Source: WHO, Global Health Observatory data, November 2018.

Strategic objectives

Significant progress has been made towards GVAP's six strategic objectives.

Prioritizing immunization

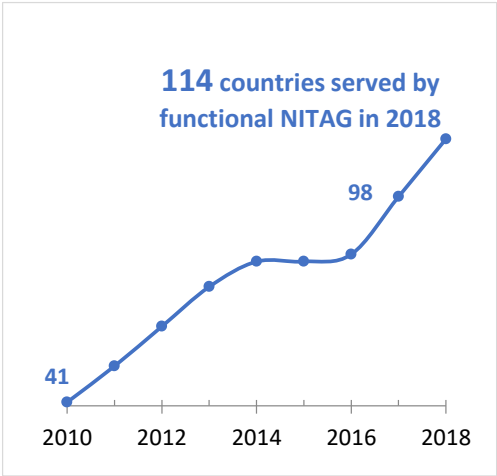
Government expenditure on national immunization programmes has increased by about one-third between 2010/11 and 2017/18 in low- and middle-income countries reporting data. However, newer vaccines are typically more expensive and availability is currently heavily dependent on Gavi funding, raising questions about the long-term sustainability of access. In addition, government expenditure has shown great year-by-year volatility over the decade, and has declined in a dozen countries.

Countries have invested in strengthening their **evidence-based decision-making capacity**. The number of countries with National Immunization Technical Advisory Groups (NITAGs) meeting all GVAP process criteria has nearly tripled, from 41 in 2010 to 114 in 2018 (Figure 7). Now, 85% of the world's population is served by such NITAGs, up from 52% in 2010.

Stimulating demand

More countries are routinely reporting data on vaccine hesitancy (161 countries as of 2017). The causes of hesitancy are varied, with no single factor accounting for more than a third of issues, and are often highly context-specific. WHO has recommended a multi-pronged strategy to address hesitancy, and UNICEF, Gavi and many countries are developing programmes to proactively counter vaccine hesitancy.

Figure 7. Numbers of functional NITAGs globally



Addressing inequities and emergencies

The nature and extent of inequities vary between and within countries. Economic status and social marginalization remain key factors associated with low coverage, while growing poor urban

communities as well as remote rural communities are still often underserved. Existing strategies such as Reach Every Community are being used to address sub-national inequities in coverage.

In addition, new initiatives have been launched to ensure that people affected by disease outbreaks and humanitarian crises receive immunization services. In recognition of the burden of outbreak-prone diseases, Gavi has extended its support to vaccines for emergency use to control cholera, meningococcal meningitis, yellow fever and Ebola.

With conflict and migration creating the largest population of vulnerable people in human history, and climate change likely to compound disruption, a 'humanitarian mechanism' has been developed for procurement of affordable vaccines for populations facing humanitarian emergencies. In addition, Gavi has established a policy for fragility, emergencies and refugees.

Health system strengthening and integration

Immunization system capacity has been strengthened in many countries, for example by redesigning supply chains in countries as diverse as Ethiopia, Benin and Canada. As of 2017, 69 countries have been approved for health system strengthening support from Gavi to enhance immunization programme functions. Stockouts have declined since 2016, but the number of countries reporting national-level stockouts remains well above the 2020 target, and distribution/delivery systems remain weak in many countries.

The decade has seen a trend towards more **integrated disease control strategies** that combine immunization with other interventions such as enhancing surveillance, reducing risks and improving treatment. Unfortunately, limited progress has been achieved in the implementation of some long-standing strategies.

New global control strategies have been developed for cholera and yellow fever, and integrated strategies for meningitis and malaria are being formulated, anticipating the availability of new vaccines for these diseases.

GVAP envisaged greater coordination between immunization and other aspects of **primary health care**. Some integration of service delivery has occurred, such as antenatal care and

maternal immunization (e.g. diphtheria/tetanus/pertussis and influenza vaccination of pregnant women) and school-based HPV vaccination. Immunization continues to have a greater reach than other services, suggesting there is scope to use immunization to improve access to other health services.

Sustainable funding and vaccine supply

Global donor support for immunization has increased, from just under half a billion dollars in 2010 to more than one billion dollars in 2018. With development assistance budgets under pressure in some donor countries, multiple competing interests for donor support, more countries transitioning out of eligibility for Gavi support, and funding for polio eradication beginning to decline, immunization is likely to face increasingly significant challenges securing external financial support. Effective polio transition planning will be vital to maintain essential functions within national immunization programmes.

To improve **vaccine markets**, Gavi has created incentives for new manufacturers to enter the market, improving access to PCV, HPV and Ebola vaccines. Innovative procurement and funding mechanisms developed by UNICEF and Gavi have reduced the weighted average price of pentavalent vaccine for Gavi countries from US$2.98 in 2010 to US$0.79 in 2019, saving hundreds of millions of dollars. Notably, greater clarity on likely future needs has encouraged more companies to begin manufacturing pentavalent and rotavirus vaccines. However, shortages of several vaccines have been experienced, including BCG, IPV and yellow fever vaccine. Growing diversity in vaccine formulations and combinations is also raising issues about countries' increasing reliance on a relatively small number of manufacturers for some products.

Middle-income countries still report that the cost of vaccines is a major obstacle to their introduction. Such countries pay higher prices for vaccines, in part because of a lack of procurement capacity and suboptimal regulatory processes within countries. To help address their needs, the **Market Information for Access to Vaccines** initiative aims to enhance vaccine-pricing transparency, better link global supply and national needs, and improve countries' vaccine procurement capacities.

Research and development

During the decade, **improved vaccines** for typhoid and rotavirus and **novel vaccines** for dengue, meningitis B and cholera have been licensed and begun to be used. In addition, exciting progress has been made in vaccine development for other diseases. The most advanced malaria vaccine is undergoing pilot implementation studies in three African countries, alongside continuing promotion of vector control and bed net use. A novel tuberculosis vaccine was recently shown to reduce progression from latent infection to active disease. Pivotal efficacy trials are underway for two HIV vaccine candidates. Progress towards a universal influenza vaccine has been slower, although several candidates are in early clinical evaluation, and key priorities for future research have been identified.

The West Africa Ebola outbreak and Zika virus infections in the Americas refocused the world on the threat of **emerging and re-emerging infections**. Mechanisms have been established to coordinate and support global responses, including the WHO Research and Development Blueprint for Action to Prevent Epidemics, and the Coalition for Epidemic Preparedness Innovations (CEPI). Highly promising efficacy date were obtained on Ebola vaccine candidates during the West Africa Ebola outbreak, and an Ebola vaccine was deployed under compassionate use provisions in the Democratic Republic of the Congo in 2019.

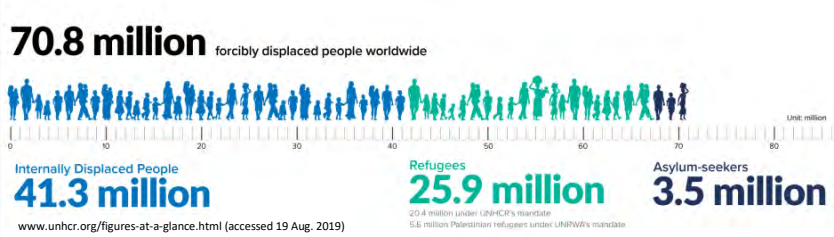
Multiple new **delivery technologies,** such as needle-free administration, blow-fill-seal primary containers, and improved vaccine vial monitors have been licensed and WHO-prequalified. However, field implementation has been slow, in part because of the costs associated with transitioning to new technologies. Similarly, while three vaccines have been licensed for use under controlled-temperature chain conditions, their implementation at scale has been limited.

Awareness of the importance of implementation and operations research has increased. Notable **implementation research** programmes have been organized for HPV and malaria vaccination. Even so, the potential of implementation and operations research to accelerate the introduction of new products and processes, and to improve programme performance, has yet to be fully exploited.

Major shifts in the global context of immunization 2010-2019

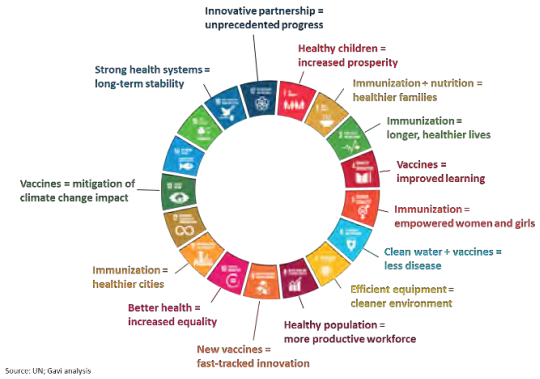
- **Demographic changes**. Global population has increased from 6.96 billion in 2010 to 7.71 billion in 2019, with the fastest growth in the African and Eastern Mediterranean regions. The proportion of people living in urban areas has increased from 50.7% of the global population in 2010 to 55% in 2018.

- **Humanitarian crises and population migration**. In 2010 the population of forcibly displaced people, according to the United Nations High Commissioner for Refugees, was 33.9 million. In 2018 it was 70.8 million, an all-time high. This included 25.9 million refugees, 41.3 million internally displaced persons, and 3.5 million asylum seekers. One of every 108 people worldwide is displaced.



- **Increased focus on emerging infectious diseases, epidemic preparedness, and global health security.** Recent years have seen major outbreaks of infectious diseases such as Zika virus in the Americas, Ebola in Africa, cholera in Yemen and Syria, and diphtheria in Rohingya refugees in Bangladesh. In addition, antimicrobial resistance is increasingly a threat.

- **Sustainable Development Goals succeeding Millennium Development Goals in 2016.** Immunization contributes to 14 of the 17 SDGs and plays an especially important role in SDG3, good health and wellbeing. Immunization is less prominent in the SDG measurement framework as it is monitored through a composite measure of access to medicines.



- **Political and economic volatility**. Support for immunization is vulnerable to changing economic and socio-political climates at national and global levels.

- **Rapid spread of anti-vaccination messaging**
New tools such as social media enable misleading vaccination information to be disseminated rapidly and widely, affecting confidence in vaccination.

IV. Reflections and lessons learned

Collectively, much can be learned from GVAP indicator data, feedback from immunization stakeholders, and the collective insights of GVAP working group members, staff from WHO regional office and representatives of partner organizations.

Although many GVAP targets were not met, much progress was made during the Decade of Vaccines

A focus solely on the achievement of targets could give the impression that GVAP had limited impact. However, this overlooks the important progress that has been made. More children are being vaccinated each year than ever before, regions such as South-East Asia and many low- and middle-income countries have taken huge strides in increasing immunization coverage, and most low- and middle-income countries have introduced at least one new vaccine. Deaths from infectious disease have declined markedly, particularly among infants. These are achievements to be celebrated.

GVAP targets were bold and aspirational, designed to catalyse action. However, for some regions and in some areas, the timelines for their achievement may have been unrealistic. Furthermore, many of the 'failures' to achieve targets reflect highly challenging circumstances – particularly the impact of conflict and political instability. A true picture of progress therefore requires a more nuanced reading than that provided by a binary distinction between success and failure in achieving GVAP targets.

Incomplete implementation: GVAP provided a comprehensive strategy that described in broad terms what needed to be done to achieve its goals. It was designed to be implemented mainly through updating of national immunization plans. This happened to only a limited extent, and depended on the priorities of countries, partners and existing disease control initiatives. Partners, in light of their own strategic priorities, drove progress in some areas without prioritizing others.

Implementation was given impetus by the development of **Regional Vaccine Action Plans**, which were more responsive to country situation and calibrated to regional capacities and issues. In some cases, they set more pragmatic targets and added new, regionally relevant goals. However, most of the regional plans were endorsed midway through the decade, contributing to a lag in GVAP implementation, and had less input from global partners.

Learning through the decade: Importantly, much has been learned over the past decade – in terms of the nature of the key challenges facing immunization, how they can best be addressed, and how a global immunization strategy could more effectively drive forward change.

GVAP did not take sufficient consideration of differences in individual countries' circumstances

The development of GVAP involved extensive **consultation** with a huge range of stakeholder organizations, with particular efforts made to integrate the country perspective. It was therefore one of the most collaboratively focused global health initiatives ever undertaken.

However, being focused on the achievement of global goals and targets, GVAP is widely perceived to be a **top-down strategy** (even though the goals were endorsed by member states). Furthermore, as GVAP adhered to the principle of equity, it aspired to achieve similar goals for all countries, irrespective of their current status. This led to targets and timelines that were unrealistic for some countries, limiting their buy in.

Despite a sophisticated monitoring and evaluation framework, these factors contributed to **weak accountability** for achieving GVAP targets**,** particularly at national and sub-national levels.

Middle-income countries ineligible for Gavi funding were assumed to be able to self-support their immunization programmes and had little access to financial or technical support, contributing to the slower introduction of new vaccines in such countries.

Nevertheless, many countries with limited resources have achieved high coverage or significantly improved coverage levels. Although external financial resourcing clearly is

important, it is not the only factor affecting national immunization programme performance. In many countries, stronger political commitment and additional technical assistance have had major impacts.

Unique challenges: In each region, a small number of 'outlier' countries with low coverage rates have typically lowered regional and global averages, partially obscuring global progress. Many of these countries are affected by conflict and political volatility, sometimes exacerbated by extreme poverty, and large communities of vulnerable populations. It has become clear that each faces its own unique set of challenges, and solutions will need to be similarly tailored to national context.

From global to country (and beyond): To a degree, and after a delay, the development of Regional Vaccine Action Plans mitigated the top-down nature of GVAP, leading to the development of more tailored support for countries based on assessments of national immunization programme capacities. In addition, later in the decade, more attention was paid to **sub-national political structures** – key contributors to immunization programmes in many large countries.

NITAGs: A success story

The decade saw spectacular progress in the number of NITAGs globally, with 85% of the world's population now living in a country with a NITAG meeting GVAP process criteria. Furthermore, the role of NITAGs has expanded from advising on new vaccine introductions to more general support for national evidence-based policymaking. Good evidence has emerged of how NITAGs can influence national decision-making and improve immunization programme function. NITAGs are integral to country ownership of immunization programmes, and have a key role to play as the number and diversity of vaccine products increase and decision-making becomes more complex.

Notably, NITAGs and their regional equivalents, RITAGs, have evolved context-specific roles. In some regions, NITAGs have become an integral part of the immunization landscape, developing

a national immunization programme monitoring function and contributing to accountability, coordinated through regional structures.

However, NITAGs are not yet perceived as essential components of immunization systems in all countries. The technical and financial sustainability and capacity of NITAGs remain issues in many countries. Smaller countries may lack the breadth of expertise to establish fully functioning NITAGs, which is being addressed through sub-regional collaborations.

If these challenges are addressed, there is significant potential to build upon the NITAG and RITAG infrastructure, and its links to global decision-making processes, building on the dynamic changes seen over the past decade.

Local innovation

The evolution of NITAGs and RITAGs to serve national and regional functions is an illustration of tailored innovation to solve local challenges. Throughout the decade, imaginative and innovative solutions have been developed at country and regional levels, with regions often playing important facilitating or coordinating roles. Examples include the electronic immunization registry developed in the Region of the Americas, as well as resources on building community support and countering anti-vaccination messaging developed by the European Region.

However, stakeholders may not be aware of relevant resources, or may find them hard to locate. A major challenge for the future is to ensure that potential users of these tools and resources are made aware of their existence and that they are more easily accessible for others to adapt and use.

Local research

For the first time, GVAP included a focus on R&D, including vaccine technologies and new vaccine development – where significant progress has been made. Although local research capacity and vaccine production capabilities in some middle-income countries have significantly

increased, there is still much progress to be made to encourage local involvement in vaccine R&D and production, especially in low-income countries of disease-endemic regions.

Although part of GVAP, less attention has been given to the use of implementation science (including continuous quality improvement), operational research, and behavioural and social research to improve the performance of immunization programmes and to scale up innovations that fit local contexts.

Looking forward, many new vaccines licensed in the next decade will have complex immunization schedules or target people who are not routinely vaccinated today. Implementation research will therefore play an increasing role in generating the evidence to inform policy decisions and guide the most effective and efficient use of vaccines.

GVAP goals remain relevant – but the remaining challenges are tough

Immunization coverage has increased substantially since the 1990s. Millions of lives have been saved as a result. Now, however, progress is inevitably slower – those most easily reached are generally well served but reaching less-accessible populations continues to pose significant challenges.

Achieving immunization goals requires constant commitment and vigilance. As recent measles, diphtheria and other outbreaks have illustrated, there is a significant risk of backsliding. Measles outbreaks are an important early warning sign of gaps in coverage and shortcomings in immunization programme performance.

Achieving immunization and disease control targets will therefore be challenging. Success will require an **unwavering commitment to the 'basics'** – ensuring that national immunization programmes are effective, efficient and sustainable, well-resourced and well-led, year after year. There are no magic bullets that will transform programmes overnight.

Extending coverage to currently under-served populations will undoubtedly be challenging. So too will be understanding and addressing the reasons behind people's reluctance to take up immunization services when they are available.

GVAP's goals and strategic objectives, endorsed in 2012, are equally relevant today and should form the core of a future immunization strategy, updated to take account of the lessons learned from the past decade and ways in which the world has changed. The aim should be both to secure the gains made to date and to extend the benefits of immunization to all those who are currently missing out.

Integrating disease-specific activities and national immunization programmes

Disease-specific activities focus attention and action on concrete disease-control goals, such as elimination. Such high-profile goals have been strong motivators of action at national, regional and global levels. Often, they have also built capacity that has benefited other programmes. However, disease-specific activities can also draw attention and resources away from other infectious disease priorities, and in some cases, especially with polio eradication, have led to the development of parallel structures and lack of coordination within countries.

Exciting new tools to improve coverage and disease surveillance – such as GIS-based population mapping and community-based surveillance – have been developed within disease-specific initiatives. Sometimes these tools have been assimilated into national immunization programmes, but not always (in part because they can be costly and require significant technical expertise). In addition, without integration, some important functions are at risk of being lost during funding transitions.

Given their interdependency, strong national immunization programmes provide a more solid foundation for disease-control initiatives, making it more likely that global eradication and elimination targets will be met. At the same time, disease-control efforts should be seen as opportunities to enhance national immunization programmes.

Partnerships and integration – the expanding scope of immunization

The past decade has seen a growing awareness that immunization has relevance far beyond its traditional core role – protecting infants against infectious disease. The expanding scope of

immunization has critical implications for the immunization community's relationship with groups both within and outside health.

Notably, the importance of **primary health care** has been reinforced during the decade. Delivery of integrated services within primary health care was an important theme of GVAP, yet only limited progress has been achieved.

Immunization is increasingly seen as fundamental to health and wellbeing at all ages. Again, the **life-course perspective** was incorporated into GVAP, but in reality immunization of infants has remained its key focus. The need to expand immunization at older ages will require more concerted efforts to forge links with other sectors inside and outside the health system.

Integration of services and other key functions such as **surveillance** can be organizationally challenging; however, coordinated development and deployment of services and disease surveillance offers the prospect of greater efficiency and more sustainable impact.

Civil society organizations (CSOs) were identified as a key constituency in GVAP. Their main involvement has been in community mobilization and service delivery, but CSOs are a highly diverse group, and have the potential to play a much wider range of roles. Professional societies, academia and other groups could be more engaged in national immunization activities, and community-focused organizations could be more actively involved in planning, monitoring and long-term community engagement.

GVAP did not say enough about **private sector providers** (for-profit and non-profit), which play important roles in extending access to vaccines in many countries. The role of private sector service delivery is highly context-specific, and likely to evolve as countries progress economically.

In addition, opportunities to establish closer ties with communities involved in emerging global health priorities such as global health security and antimicrobial resistance were not fully grasped, despite common interests in areas such as infectious disease surveillance as well as vaccine development.

Finally, another important lesson has been the importance of fostering dialogue and collaboration across the full spectrum of R&D from basic research through to implementation and deployment. To accelerate development of vaccines that are appropriate for field use, it is important for researchers to understand potential use scenarios and constraints; similarly, in order to plan for timely clinical and field evaluation of promising candidates and their eventual uptake, downstream developers, public health officials, communities, and potentially other stakeholders need to be informed of the progress of potential candidates.

Humanitarian emergencies and chronic fragility

The past decade has been characterized by extensive political upheaval, civil conflict and natural disasters. In many settings, these have severely disrupted health infrastructure and services, led to mass displacement of people, and undermined efforts to deliver immunization and other health services to vulnerable populations.

Although GVAP did not specifically focus on humanitarian emergencies, some important mechanisms have been developed to improve access to immunization in such situations. Given the number of humanitarian emergencies each year, and persistent conflict and fragility in several countries, a dedicated strategy is required to secure the availability and distribution of essential vaccines, recognizing that each emergency setting is likely to have its own unique set of challenges. Experience over the past decade has highlighted the critical need to engage communities in emergency responses, and to improve both preparedness and coordination of responses to ensure access to immunization and other services in emergencies.

Accelerating urbanization and migration have also raised humanitarian immunization issues. In some instances, immunization programmes have been sufficiently flexible to ensure that urban migrants and migrants transiting through a country are immunized but in others this has been problematic. Strategies for transient populations are needed, with clear definitions of roles and responsibilities among countries, partners and CSOs so no groups fall through the immunization net.

Monitoring of national immunization and other indicators could also provide early warning signs of backsliding and more general fragility, triggering actions to prevent major disruption to services.

GVAP created a global framework for immunization, but was unable to drive sufficient change to achieve its goals

GVAP created a comprehensive **global framework** for addressing key issues in immunization. It established a common vision and a forum in which immunization stakeholders could collectively discuss matters of concern across the full spectrum of activities relevant to immunization. As a global strategy and advocacy tool, GVAP helped to maintain immunization's visibility globally.

Through its consultation process, GVAP aligned stakeholders around the need to improve immunization coverage and equity. Its endorsement by all member states reinforced access to immunization as a global priority, building political will and helping to make the case for vaccination among political and business decision-makers.

Implementation of GVAP, and achieving GVAP targets, was the responsibility of countries and a diversity of partners and programmes – whose commitment to GVAP was mixed. Rather than fully embracing all its goals and targets, many stakeholders adopted GVAP priorities selectively, according to their institutional priorities.

Alignment was not optimal at either a global strategic level or, often, within countries, as partners too often undertook activities without full coordination with other stakeholders.

Driving action: With no formal organizational infrastructure, GVAP had limited 'levers' to accelerate progress towards its goals. In particular, contrary to many initial expectations, GVAP did not have its own additional dedicated resourcing (except for monitoring and evaluation at the global and regional levels), which may have deterred country buy in. This misperception may also have diverted attention away from maximizing domestic resourcing and making the

best possible use of existing resources. These factors may have limited GVAP's capacity to effect change and to catalyse action to achieve targets – and GVAP may therefore have overestimated what was achievable.

Without a formal organizational infrastructure to represent immunization, integration and relationship building with sectors outside health have also lagged.

Responding to emerging challenges

Emerging infectious diseases, measles resurgence, accelerating urbanization, migration and displacement, conflict and political instability all presented major challenges. High-profile anti-vaccination campaigns, ambivalence about the value of vaccines, and the politicization of vaccination – all powered by the rise of social media – have become significant concerns. The rise of antimicrobial resistance has heightened interest in expanding the use of vaccines.

Such threats and opportunities were recognized in annual progress reports. However, there was no mechanism to update GVAP. In addition, as with initial implementation, GVAP had limited scope to influence national, regional or global priorities to address emerging challenges.

Spreading the word

Extensive GVAP-related **communications and advocacy** activities were undertaken around its launch. However, less activity was undertaken later during the decade. In addition, global GVAP partners made a strategic decision to focus on promotion of immunization more generally rather than GVAP specifically, through initiatives such as the successful World Immunization Week.

Awareness of GVAP among country stakeholders was often low, particularly among those who became involved with immunization later in the decade. This low visibility may have lessened its impact, and limited GVAP's ability to secure alignment around goals, targets and principles.

Important regional communications and advocacy activities have been undertaken, particularly the development of the Addis Declaration on Immunization in the African Region. A potentially

important mechanism for securing political commitment, the Addis Declaration was signed by heads of states only in 2017, further evidence of the time it can take to convert a global strategy into regional actions.

Inclusion of R&D in GVAP was a major advance

GVAP was the first global immunization strategy to include R&D – widely seen as a highly positive innovation. Inclusion of R&D focused attention on the emerging pipeline of new vaccine products and vaccine technologies, and the need to consider potential bottlenecks across the entire translational pathway, including post-licensing implementation stages.

Although global investment in vaccine development is still sub-optimal, particularly for infectious diseases primarily affecting low- and middle-income countries, product pipelines are better stocked now than a decade ago. Regulatory, implementation and production-capacity issues have emerged as significant challenges to providing populations with timely access to vaccines.

Progress in the R&D field has been highly promising. Despite major technical challenges, encouraging progress has been made in the development of vaccines against the main diseases highlighted by GVAP, malaria, TB, HIV and influenza. Typhoid and Ebola vaccines are beginning to be used in the field, and vaccines are in the pipeline for major killers such as respiratory syncytial virus, which causes an estimated 3 million hospitalizations and 60 000 deaths of children under five every year.

Furthermore, a range of exciting new developments could have significant impact over the next decade. These include innovative vaccine platforms to enable rapid development of new and strain-specific vaccines, novel preventive interventions such as broadly neutralizing antibodies, more vaccines to protect against non-communicable diseases, therapeutic vaccines, and vaccines against sexually transmitted infections. The implications of these advances for regulatory systems, implementation and public acceptance need to be carefully thought through to minimize any delays in their uptake to protect people's health.

GVAP highlighted the critical role of data and stimulated important initiatives to improve data quality and use for action

Data serve multiple purposes, informing programmatic decision-making, national, regional and global policy-making, and supporting advocacy. A wide range of information beyond coverage data, including infectious disease surveillance data, and both country-generated and external data, is needed to meet these different purposes. Depending on their roles, different users will have very different data needs.

GVAP's focus on data raised awareness of inequities in coverage within countries and drew attention to the need for high-quality data. This led to important initiatives to improve the value of data to users, and encouraged greater reflection on the key attributes of 'data quality' (particularly that it be fit for purpose). The quality of national and sub-national administrative data remains a concern in some countries, with the risk of decision-making being based on an inaccurate picture of coverage. Lack of up-to-date data on local population sizes remains a key factor contributing to uncertainties in coverage estimates.

Despite this strong focus on data, data collection for GVAP reporting was not sufficiently tied to action, particularly at national levels. Data collection can be time-consuming for frontline staff, who may see no benefits from their data-collecting activities. Without a strong linkage to action at all levels, there is a growing risk that data reporting becomes an end in itself.

GVAP's monitoring and evaluation framework delivered many benefits, but did not achieve full accountability

GVAP's monitoring and evaluation framework established a common set of metrics to assess progress, identify bottlenecks, and to enable countries to benchmark their achievements.

The annual reporting process provided regular updates on progress and highlighted emerging issues of concern. Annual reporting, to the World Health Assembly and often also WHO Regional Committees, reinforced the political will demonstrated by World Health Assembly

endorsement, ensuring that ministers of health were aware of global progress in immunization and how their countries compared to their peers. Countries used these discussions to raise issues such as affordability of new vaccines for middle-income countries.

At the global level, the recommendations in annual assessment reports were generally perceived as useful, highlighting specific issues of concern. At the regional and country levels, many – including some key stakeholders within national immunization programmes – were unaware of the specific recommendations or saw them as vague or impractical.

Poor data quality hampered the monitoring of several indicators. In some cases, as for vaccine hesitancy, the measures used did not adequately capture the complexity of issues. Some GVAP indicators were cumbersome to monitor. Some of the more detailed indicators were omitted from annual assessment reports meant for wide audiences, and it is unclear how effective the detailed targets were in driving progress.

Importantly, headlines that sounded the alarm on 'off track' results often masked important underlying progress. In addition, global averages and country-level data generally provided little clue to the causes of under-achievement, again limiting the scope for corrective action.

GVAP's monitoring and evaluation framework therefore generated a rich data stream but had limited impact in driving achievement of GVAP targets. Ultimately, monitoring and evaluation failed to ensure accountability among stakeholders, including global partners. While country results were evaluated progressively at country, regional and global levels, global accountability processes did not effectively cascade to the country level and had little impact on the activities of partners. As a result, evaluations of progress did not necessarily catalyse the actions needed to achieve GVAP targets.

Conclusions

The past two decades have seen tremendous advances in immunization coverage, particularly in low- and middle-income countries. Between 2000 and 2018, an estimated 35 million deaths have been averted through use of vaccines in such countries – 96% of them of infants. These efforts have almost halved the number of deaths from vaccine-preventable disease.

Looking forward, 122 million deaths are likely to be averted by immunization over the lifetime of people born between 2000 and 2030.

These statistics speak to the extraordinary impact of vaccines. They are almost uniquely successful interventions – highly effective, extremely safe, mostly affordable and not vulnerable to the development of resistance, as occurs with antimicrobials.

Indeed, vaccines are so successful that it is easy to take them for granted. Recent outbreaks should be warning signs against complacency. In addition, it is still the case that not everyone is benefiting from these proven interventions.

GVAP created a united global coalition to extend the benefits of immunization. The challenge for the next ten years is to maintain the momentum it created, to absorb important learnings, and to shape a new strategy to drive forward even greater achievements.

IV. Technical recommendations

A post-2020 global immunization strategy should:

1. Build on GVAP's lessons learned, ensuring more timely and comprehensive implementation at global, regional and national levels

- Take forward the foundation established by GVAP, maintaining its positive elements and updating and adapting as necessary in light of the valuable experience gained over the past decade.
- Ensure development and implementation of National and Regional Vaccination Action Plans begins as rapidly as possible, to maintain momentum and ensure rapid operationalization.
- Develop Regional Vaccination Action Plans within the framework of existing regional planning/approval cycles.
- Ensure National Vaccination Action Plans are used to update national immunization plans and are integrated into wider health service plans.

2. Have a key focus on countries:

2a. Place countries at the centre of strategy development and implementation to ensure context specificity and relevance

- Incorporate flexibility to accommodate the needs of all types of country, allowing each country to tailor its national plan within the global framework, taking account of its development requirements, the vaccination needs of its population, available resources, competing priorities and other contextually important factors.
- Enable countries to set ambitious but realistic national targets for key indicators with accompanying milestones, with the long-term aim of achieving agreed global goals; all countries should recognize the need for ambition and urgency in target setting.
- Enable countries to develop country-led strategies to achieve targets, in collaboration with external and internal partners and with clearly defined roles and responsibilities.
- Encourage regions and partners to provide tailored and coordinated technical support to countries according to countries' specific needs.
- In countries with devolved political/health systems, ensure similar planning processes are undertaken with sub-national authorities.

2b. Strengthen country-led evidence-based decision-making

- Promote strong national commitment to National Immunization Technical Advisory Groups (NITAGs).
- Enhance and extend the technical capacity and capabilities of NITAGs.
- Regularly assess NITAG functions and impact.
- Develop innovative solutions such as sub-regional NITAGs for countries with small populations or limited technical expertise.
- Encourage sub-regional, regional and global networking of NITAGs, including enhanced sharing of experience through the Global NITAG Network.
- Explore the potential for greater NITAG involvement in monitoring and advising on national programmes and serving as an independent voice for immunization.

2c. Encourage the sourcing and sharing of innovations to improve programme performance

- Encourage greater peer-to-peer exchange of expertise, lessons learned, tools and resources at regional, country and sub-national levels, with tools, technical resources and expertise made more visible and easier to access and adopt or adapt.
- Promote wider uptake of innovative tools developed by elimination/eradication programmes.
- Encourage countries, regions and partners to look to other fields, inside and outside health, for potentially adoptable innovations.

2d. Promote use of research by countries to accelerate uptake of vaccines and vaccine technologies and to improve programme performance

- Promote the use of implementation science, operational research, delivery science, behavioural and social research, and data science to develop, pilot and evaluate improvements to national programmes.
- Prioritize development of national capacity in these areas of research.
- Emphasize collaborative development and evaluation of needs-driven and potentially scalable innovations.

3. Maintain the momentum towards GVAP's goals:

3a. Incorporate key elements of GVAP, recognizing its comprehensiveness and the need to sustain immunization's successes each and every year

- Maintain the drive towards previously agreed global and regional elimination and eradication goals.
- Retain the focus on GVAP's other goals and objectives:
    - Strengthening of all aspects of national immunization programme function, with a systems perspective and a focus on leadership, human capacity building and people-centred service delivery.
    - Promoting integration of immunization with other primary health care services.
    - Generating active public support for immunization.
    - Ensuring timely and reliable access to affordable vaccines.
    - Promoting national financial self-sustainability.
- Retain research and development (R&D) as a core feature of a new strategy.

3b. Add a specific focus on humanitarian emergencies, displacement and migration, and chronic fragility

- Encourage greater collaboration between immunization and health emergency programmes globally and regionally.
- Promote greater attention to preparedness, including surveillance to provide early warnings and risk assessments.
- Encourage greater collaboration among partners (including communities) in emergency responses, with greater clarity on roles and responsibilities.
- Explore innovative approaches for capturing the size and improving tracking of displaced and migrating groups.
- Promote research and evidence generation in emergency situations.
- Develop regional mechanisms to detect and respond to incipient national fragility.

3c. Encourage stronger integration between disease-elimination initiatives and national immunization programmes

- Stress the importance of building stronger national immunization programmes as the foundation for disease-specific initiatives.

- Ensure disease-specific initiatives contribute to capacity building of national immunization programmes.
- Strengthen coordination across different disease-specific initiatives.
- Promote development of integrated infectious disease surveillance, within the wider context of Internal Health Regulations (IHR) monitoring.

3d. Encourage greater collaboration and integration within and outside the health sector

- Promote a wide-ranging view of collaboration and integration, at all levels (globally, regionally, nationally and sub-nationally) and across all functions.
- Ensure that coordination of immunization and other services within the health sector contributes to the development of integrated primary health care systems.
- Strengthen links outside health to build platforms for immunization across the life course.
- Encourage active participation in integrated disease control partnerships in which immunization is just one element of coordinated strategies (e.g. malaria, cholera).
- Explore opportunities for mutually beneficial collaborations in areas such as primary health care, global health security, antimicrobial resistance, climate change, food security and the Sustainable Development Goals.
- Explore the potential for additional partners within and outside health (e.g. the full spectrum of CSOs, the non-profit and for-profit private sector).

4. Establish a governance model better able to turn strategy into action:

4a. Create a robust and flexible governance structure and operational model based on closer collaboration between partners

- Incorporate a stronger emphasis on roles, responsibilities, contributions and accountability for achieving global and national goals.
- Encourage global partners to establish closer collaborations, ensuring greater coordination of partner activities.
- Develop a governance model that promotes the above and incorporates greater global partner accountability.
- Encourage collaboration with a wider range of partners, allowing for more flexible partnership models.
- Include primary responsibility for establishing global monitoring and evaluation and communications and advocacy strategies within the governance mechanism.

4b. Incorporate the flexibility to detect and respond to emerging issues

- Include the flexibility to respond to new challenges and emerging opportunities with a potentially major impact on immunization over the next decade.

4c. Develop and maintain a strong communications and advocacy strategy

- Develop a coordinated communications and advocacy (C&A) strategy, establishing goals, key messages and target audiences.
- Ensure that the C&A strategy clearly focuses on 'corporate communications', complementing communication for other purposes (e.g. to generate support immunization more generally).
- Focus C&A activities on building awareness, encouraging buy in and maintaining momentum for implementation; a specific visual identity/branding may not be needed.
- Ensure that the C&A strategy is mindful of health system context and the perspectives of other actors in the health sector
- Sustain C&A activities over the decade, monitoring and adapting as required.

5. Promote long-term planning for the development and implementation of novel vaccine and other preventive innovations, to ensure populations benefit as rapidly as possible

- Maintain the momentum behind new product/technology development.
- Promote dialogue between countries, partners and developers through needs assessments, evaluation, piloting and scale up, to ensure rapid access to safe and effective products that meet national needs.
- Identify key bottlenecks in new product approval and implementation, and develop new strategies to overcome them.
- Continue to prioritize capacity building and coordination of national regulatory authorities, including regulatory harmonization to expedite introduction of WHO pre-qualified vaccines.
- Promote early consideration of the broad implications of novel interventions nearing practical application, to identify possible implementation enablers/barriers and potential acceptability issues.
- Ensure that the lessons learned from successful vaccine introductions are documented and shared.
- Promote the development of regional and national research capacity to support more locally relevant evidence generation.

6. Promote use of data to stimulate and guide action and to inform decision-making

- Prioritize collection of data specifically required to monitor and improve national programme performance.
- Encourage closer linkage between data collection and action, to drive forward continuous quality improvements.
- Enhance national programme capacity for data collection and use.
- Encourage greater data transparency and sharing of data, in the right format, for the right people to use at the right time.
- Ensure programmes have the flexibility to halt collection of data of limited value and to add useful new data sources.
- Encourage collection of qualitative data, to aid understanding of underlying causes.
- Ensure that national immunization programmes are able to draw upon and contribute to integrated infectious disease surveillance data systems.
- Encourage national immunization programmes to prepare for the likely widespread and potentially transformative frontline implementation of new data technologies in the next decade.
- Promote collaborations with data scientists and informatics experts in other fields to ensure effective use of data.
- Ensure lessons are learned from SDG and UHC/PHC information management strategies and plans and data collection experience.

7. Strengthen monitoring and evaluation at the national and sub-national level to promote greater accountability

- Ensure that implementation and monitoring and evaluation (M&E) are fully integrated to ensure that the latter is better able to promote accountability.
- Ensure that targets and milestones are set at the country level, informed by agreed global targets.
- Use data-driven processes to establish global, regional and national targets and milestones.
- Ensure that progress towards milestones and targets is reviewed at least annually, to underpin corrective action, with more in-depth programme reviews conducted periodically (e.g. five-yearly).
- Build capacity for M&E at national and sub-national levels.
- Explore the potential for NITAGs to play a larger role in M&E and programme oversight.
- Recognize the risks of overloading frontline/programme staff; an M&E framework should be lean and fit for purpose, with all national data collection having a clear purpose.
- Ensure that regional- and global-level data requests are only for clearly defined purposes; wherever possible, global data analysis should be based on data routinely collected to inform national activities.

- Ensure that, wherever possible, data collection serves multiple purposes (e.g. SDG as well as M&E reporting).
- Build some flexibility to adapt goals, targets and indicators (e.g. regionally, over time) into the M&E framework.
- Recognize that some important data generation will occur outside the M&E framework (e.g. qualitative research, root cause analysis in countries).
- Encourage countries and regions to identify specific subsets of country data required for advocacy/political reporting.
- Ensure that the monitoring and evaluation reporting schedule for research reflects the different pace of research, and provides separate reporting opportunities for new product development and for implementation/operational research.

Annex 1 Contributors

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Annex 2 Supplemental Information available electronically

This summary draws on the following source documentation available at: www.who.int/entity/immunization/global_vaccine_action_plan/GVAP_review_lessons_learned/en/

- Report on GVAP review and lessons learned: Methodology, analysis and results of stakeholder consultations
- The GVAP Monitoring, Evaluation and Accountability (M&E/A) Framework: Review and lessons learned
- Global Vaccine Action Plan - Monitoring, evaluation & accountability - 2019 report
- Global Vaccine Action Plan - Progress towards GVAP-RVAP goals – 2019 regional reports
- National Immunization Coverage Scorecards 1999-2018

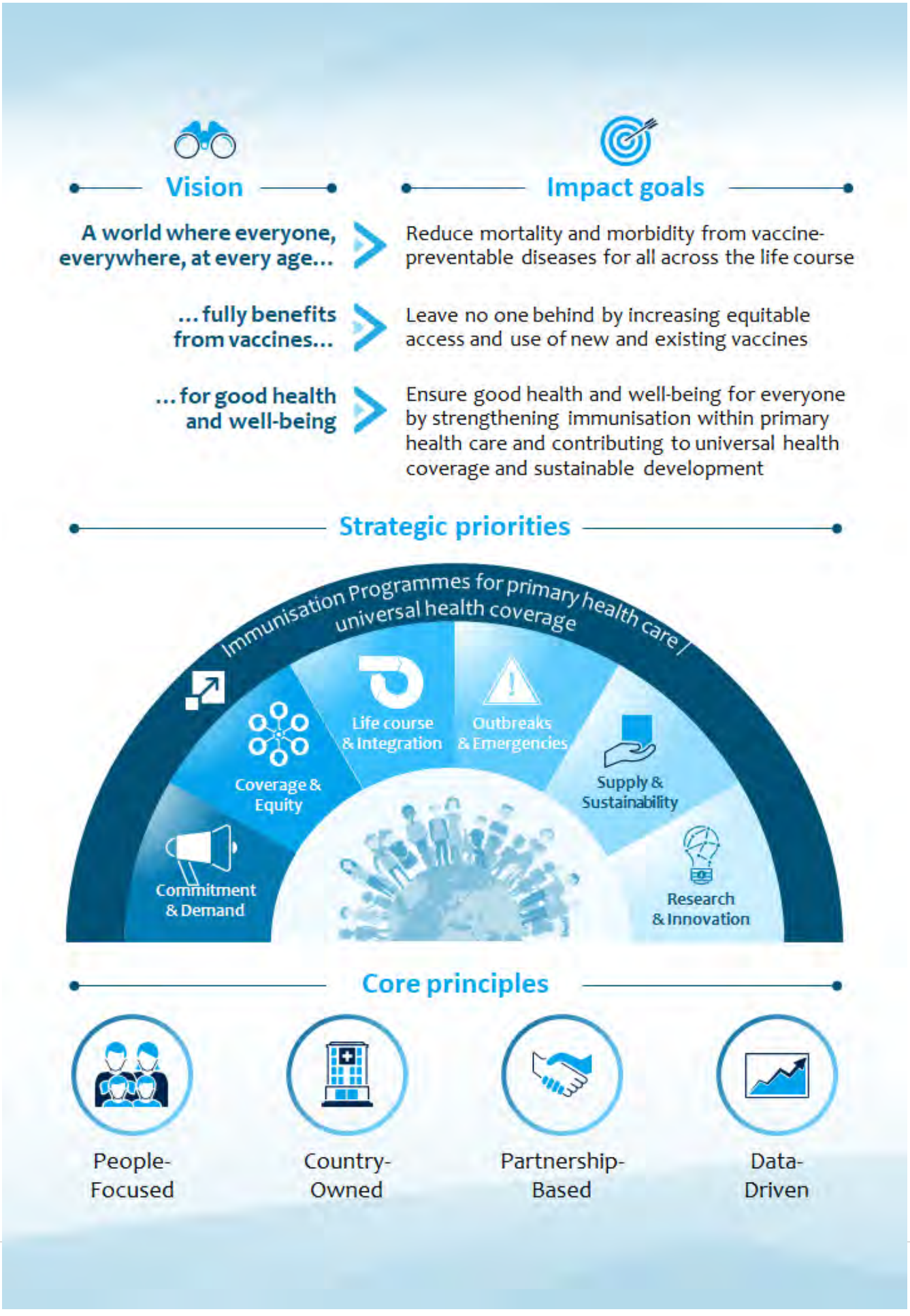
Immunisation Agenda 2030

A Global Strategy To Leave No One Behind

Draft for SAGE

Contents

At a glance


Vision
A world where everyone, everywhere, at every age...
... fully benefits from vaccines...
... for good health and well-being
Impact goals
Reduce mortality and morbidity from vaccine-preventable diseases for all across the life course
Leave no one behind by increasing equitable access and use of new and existing vaccines
Ensure good health and well-being for everyone by strengthening immunisation within primary health care and contributing to universal health coverage and sustainable development
Strategic priorities
Immunisation Programmes for primary health care / universal health coverage
Coverage & Equity
Life course & Integration
Outbreaks & Emergencies
Supply & Sustainability
Commitment & Demand
Research & Innovation
Core principles
People-Focused
Country-Owned
Partnership-Based
Data-Driven

Introduction

Immunisation is a global health and development success story, saving millions of lives every year. Between 2010 and 2017, 21 million deaths were averted by measles vaccination alone.[1] The number of infants vaccinated annually – more than 116 million, 86% of all babies born – has reached the highest level ever reported. More than 20 life-threatening diseases can now be prevented by immunisation[2]. Since 2010, 116 countries have introduced new vaccines that they were not previously using[3], including vaccines against major killers, such as pneumonia, human papillomavirus, rotavirus, typhoid and cholera.

Furthermore, this is an era of much innovation in vaccine development. The first vaccines have been developed for malaria, dengue and Ebola, and promising vaccines for respiratory syncytial virus, universal influenza vaccines and tuberculosis are in the pipeline. Promising new research on broadly neutralizing antibodies and therapeutic vaccines has the potential to open new horizons. Increasingly, vaccines are protecting health beyond infancy – in adolescence, adulthood, during pregnancy and in older age groups.

Innovative new ways are being developed to distribute and administer vaccines, and to improve immunisation services. Digital tools, new technologies for needle-free vaccine administration and more robust vaccine storage and supply chains promise to transform immunisation programmes over the next decade. Ready access to reliable data will provide exciting new opportunities for national programmes to monitor and continually improve their performance, reach and efficiency.

Immunisation is a key component of primary health care and is making a huge contribution towards universal health coverage. Vaccines are critical to the prevention and control of infectious disease outbreaks, underpinning global health security, and will be a vital tool in the battle against antimicrobial resistance.

Nevertheless, there are important challenges to overcome. The benefits of immunisation are unevenly shared: vaccine coverage levels vary markedly between and within countries, with some populations having poor access to immunisation services – often the poorest, the most marginalised or the most vulnerable in fragile and conflict-affected settings. Each year, 20 million infants do not enjoy the benefits of a full course of even basic vaccines, and many more miss out on newer vaccines.

In some countries, progress has stalled or even reversed, and there is a real risk that complacency will undermine past achievements. Measles and vaccine-derived poliovirus outbreaks are stark reminders that strong immunisation programmes and effective disease surveillance are needed to sustain high levels of coverage and achieve disease elimination and eradication. Due to its high infectiousness, measles can serve as an indicator ('the canary in the coalmine') of inadequate immunisation coverage and gaps in the system. Measles vaccination and surveillance is therefore a key pathfinder for improving immunisation services and strengthening primary health care systems.

If all people are to gain access to immunisation services, vaccines must be delivered to geographically and/or culturally isolated and marginalised populations, to displaced people and migrants, and to those affected by conflict, political instability and natural disasters. The causes of low vaccine uptake must be understood and

[1] Dabbagh A, Laws RL, Steulet C, Dumolard L, Mulders MN, Kretsinger K, Alexander JP, Rota PA, Goodson JL. Progress Toward Regional Measles Elimination - Worldwide, 2000-2017. *Morbidity and Mortality Weekly Report* 2018;67:1323-29.
[2] https://www.who.int/immunization/diseases/en/
[3] 2018 Assessment Report of the Global Vaccine Action Plan, WHO (https://www.who.int/immunization/global_vaccine_action_plan/sage_assessment_reports/en/)

addressed, to boost people's demand for immunisation services. New approaches are needed to reach older age groups and to deliver integrated, people-centred immunisation alongside other primary health services.

The **Immunisation Agenda 2030 (IA2030)** capitalises on new opportunities to meet the continuing challenges posed by infectious diseases. It positions immunisation as a key contribution to people's fundamental right to the highest attainable physical and mental health, as well as an investment for the future, creating a healthier, safer and more prosperous world for all. IA2030 aims to ensure that we maintain our hard-won gains, but also achieve more – leaving no one behind, in any situation or at any stage of life.

IA2030 sets an overarching vision and the direction and global goals for the decade 2021–2030. This document is just the beginning – it will be followed by regional strategies and a monitoring and evaluation framework that will guide country implementation. These will complement existing strategies and immunisation plans, including those of disease-control, elimination and eradication programmes. IA2030 provides a long-term strategic framework, which will guide a dynamic operational phase, responsive to changes in country needs and global context.

IA2030 is intended to inspire and align the activities of community, country, regional and global stakeholders – national governments, regional bodies, global agencies, development partners, health care professionals, academic and research institutions, vaccine developers and manufacturers, the private sector and civil society. Success will depend on building and strengthening partnerships with others both within and outside the health sector, as part of coordinated efforts to achieve universal health coverage and accelerate progress towards the 2030 Sustainable Development Goals.

Through the collective endeavours of all stakeholders, we can achieve the vision for the decade: *A world where everyone, everywhere, at every age, fully benefits from vaccines for good health and well-being.*

The Case for Immunisation

Immunisation reaches more people than any other health and social service and is a key component of primary health care systems. Immunisation benefits individuals, communities, countries – and the world as a whole. It is an investment in the future that benefits all.

1. **Saving lives and protecting population health:**
   Immunisation saves lives. Deaths from infectious diseases have fallen dramatically thanks to immunisation. Vaccines also prevent disabilities that impair child growth, leading to better growth and cognitive development – giving children the opportunity not just to survive but also to flourish.

   Between 2010 and 2017, under-5 mortality declined by **24%**, thanks in large part to immunisation[4]

   Vaccines are similarly beneficial for older age groups, from adolescents to those in their later years. Vaccines can prevent infection-related cancers and protect the health of the elderly and the vulnerable, further enabling people to live longer, healthier lives. In addition, fewer infections mean less risk of disease transmission to relatives and other members of the local community.

   In less than 10 years, HPV vaccination has reduced HPV prevalence by **83%** in girls aged 13–19 and reduced the prevalence of precancerous lesions by **51%** among girls aged 15–19 in countries which have introduced the vaccine[5]

   In many countries, out-of-pocket payments on health care can have a catastrophic impact on household finances, potentially plunging households into poverty. Preventing infection by immunisation can reduce families' expenditure on health care, contributing to financial protection, a core component of universal health coverage.

   Vaccines will help prevent an estimated **24 million** people slipping into poverty by 2030[6]

2. **More productive and resilient countries:**
   Immunisation is the foundation for a healthy and productive population. Preventing infections reduces the burden on health systems, while a healthier population is a more productive one. Children protected against infectious disease benefit more from schooling and contribute more to national development and prosperity.

   Vaccination against measles in 94 low- and middle-income countries returned an estimated **US$58** for every US$1 invested in vaccination[7]

   Disease outbreaks are disruptive and costly to halt. Outbreaks of measles and other infectious diseases can overwhelm public health programmes and health services. They can profoundly disrupt health systems, and also affect trade, travel and development. For seasonal diseases such as influenza, treatment costs and lost productivity are borne repeatedly. Well-

   The full economic impact of the 2014–16 West Africa Ebola outbreak has been estimated at **US$53.2bn**[8]

[4] Global Burden of Disease, Institute for Health Metrics and Evaluation, IHME, 2017
[5] Drolet M, Bénard É, Pérez N, Brisson M; HPV Vaccination Impact Study Group. Population-level impact and herd effects following the introduction of human papillomavirus vaccination programmes: updated systematic review and meta-analysis. Lancet. 2019;394(10197):497–509
[6] Chang AY, Riumallo-Herl C, Perales NA, Clark S, Clark A, Constenla D, Garske T, Jackson ML, Jean K, Jit M, Jones EO, Li X, Suraratdecha C, Bullock O, Johnson H, Brenzel L, Verguet S. The equity impact vaccines may have on averting deaths and medical impoverishment in developing countries. Health Aff (Millwood). 2018;37(2):316–324
[7] Ozawa S, Clark S, Portnoy A, Grewal S, Brenzel L, Walker DG. Return on investment from childhood immunisation in low- and middle-income countries, 2011-20. Health Aff (Millwood). 2016;35(2):199–207
[8] Huber C, Finelli L, Stevens W. The economic and social burden of the 2014 Ebola outbreak in West Africa. J Infect Dis. 2018;218(suppl_5):S698–S704

immunised communities are resistant to infectious disease outbreaks, while strong health systems and immunisation programmes can detect and respond rapidly to outbreaks, limiting their impact.

3. **A safer, healthier and more prosperous world**:

Vaccines are a critical component of the battle against emerging and re-emerging infections. Pathogens are not bound by national borders – local and international movement of people can rapidly spread infections. Increasing urbanisation creates large and dense populations in urban areas, increasing the likelihood of infectious disease transmission and outbreaks. In addition, climate change exposes new populations to vector-borne diseases, and may alter patterns and intensity of seasonal diseases. Detecting, preventing and responding to infectious disease threats are therefore key to **global health security**.

Between 2030 and 2050, malaria is expected to cause **60,000** additional deaths per year[9]

In all parts of the world, bacterial and parasitic infections are increasingly developing resistance to antibiotics and other antimicrobials. Prevention of infections by immunisation not only protects against drug-resistant infections, but also reduces the need for and use of antibiotics, thereby contributing to the battle against **antimicrobial resistance**.

Without action, antimicrobial resistance will be causing an estimated **10 million** deaths by 2050[10]

Immunisation and disease surveillance are core capacities of International Health Regulations (IHR), contributing to resilient and sustainable health systems that can respond to infectious disease outbreaks, public health risks and emergencies.

Furthermore, immunisation plays a critical role in **achieving the Sustainable Development Goals (SDGs).** Most directly, it contributes to SDG3 – to ensure healthy lives and promote well-being for all at all ages – but it directly or indirectly contributes to 13 of the other SDGs (Fig. 1).

[9] World Health Organization. (2014). Quantitative risk assessment of the effects of climate change on selected causes of death, 2030s and 2050s. World Health Organization.

[10] Review on Antimicrobial Resistance. Tackling Drug-Resistant Infections Globally: Final Report and Recommendations. 2016. London: Review on Antimicrobial Resistance.

	Immunisation **protects people from being forced into poverty** by out-of-pocket health care expenditure and loss of income.		Immunisation promotes a **healthy and productive workforce** contributing to the economy.
	Infectious disease prevention increases the impact of food security and **reduced hunger** on child development and maternal health.		Vaccine manufacturing contributes to national industrial **infrastructure** in low- and middle-income countries.
	Immunisation is one of the most cost-effective ways to save lives and promote good **health and well-being**.		Immunisation prevents diseases affecting **the most marginalised**, especially in urban poor or remote rural settings and in conflict areas.
	Protecting against illnesses that could impair cognitive development enables **quality education** to provide greater benefits.		Immunisation protects urban public health and interrupts disease transmission, providing a platform for **sustainable cities and communities**.
	Due to its significant reach, addressing gender-related barriers to immunisation contributes to **gender equality**.		Vaccines are critical to building people's resilience to and mitigating the risk of disease outbreaks tied to **climate change** such as yellow fever and cholera.
	Immunisation and **water, sanitation and hygiene** act synergistically to prevent diarrhoeal diseases – a leading cause of child mortality in low-income countries.		Good health through immunisation is a critical determinant of **peace and well-being** in society.
	Immunisation logistics systems are increasingly using cleaner and more sustainable technologies reliant on solar and other **renewable energies**.		Immunisation broadens **partnerships** and multi-sectoral approaches with civil society, communities and the private sector working towards common goals.

Fig. 1 – Immunisation's contributions and relevance to 14 of the 17 Sustainable Development Goals[11].

[11] Gavi - Immunisation and the sustainable development goals https://www.gavi.org/library/publications/gavi-fact-sheets/immunisation-and-the-sustainable-development-goals/

Shaping a Strategy for the Future

Immunisation Agenda 2030 envisions ***"A world, where everyone, everywhere, at every age, fully benefits from vaccines for good health and well-being"***.

To achieve this ambitious vision, we have drawn the lessons from the past and identified the factors that contribute to success in the future.

Learning from the Global Vaccine Action Plan

The Global Vaccine Action Plan (GVAP) was the global immunisation strategy during the Decade of Vaccines between 2011 and 2020. Developed through extensive global consultations, GVAP brought together existing disease eradication and elimination goals, and set new global goals across the full spectrum of immunisation functions. A review of GVAP in 2019 identified important lessons to be carried forward into the next decade to 2030[12].

GVAP successfully brought multiple global, regional and national stakeholders together to develop a **shared vision and strategy** for the future of immunisation. The health and immunisation community agreed to aspirational goals to catalyse action, and although many GVAP goals were not met, much progress has nevertheless been made.

GVAP enhanced the visibility of immunisation and helped to build high-level **political will for immunisation**. It provided a common framework for establishing priorities, aligning activities and assessing progress. It created a platform that can be built on – GVAP was a comprehensive strategy, and most of its **goals and objectives** remain relevant.

Implementation of GVAP was anticipated to be through national immunisation programmes, with the support of partners. However, GVAP was only partially successful in influencing actions at a country level, and partner activities were not always fully coordinated at the global or national level. To achieve the enhanced country ownership critical to the success of IA2030 vision, tailored strategies will be needed, taking into account significant differences between countries of varying sizes, resources and contexts, including sub-national differences. IA2030 will also focus on strengthening existing partnerships and building new relationships, for example with a wider range of civil society organisations (CSOs) and the private sector.

In GVAP implementation, **Regional Vaccine Action Plans** provided a mechanism for translating global strategies into regional planning. Regional plans will be revised to align with IA2030, which will be a critical step in the implementation of the IA2030 vision and strategies.

GVAP also struggled to influence national and global responses to issues that grew in importance during the decade, such as high levels of conflict, migration and urbanisation, and growing public reluctance to use vaccination services. For implementing IA2030, greater flexibility may be needed at the national and sub-national levels to account for local context, in order to respond more effectively to **emerging challenges**.

GVAP created the first global **monitoring and evaluation framework** for immunisation, defining roles and responsibilities for stakeholders. This provided a wealth of data on progress, and raised awareness of the need for

[12] The Global Vaccine Action Plan and the Decade of Vaccines, Review and Lessons Learned, Draft 13 September 2019 for SAGE

quality data. However, the framework was unable to ensure that this abundance of data drove improvements in national programme performance and national-level accountability.

IA2030 will build on these lessons, establishing greater clarity on roles and responsibilities for implementation at national, regional and global levels, and improving the use of data to drive action and ensure accountability.

Lessons learned from disease-specific initiatives

GVAP drew together pre-existing disease-focused eradication and elimination goals for polio, measles and for maternal and neonatal tetanus. Disease-specific initiatives were inspired by the landmark smallpox eradication achievement. They have the advantage of focusing on a single clear objective, with stakeholders aligned around common approaches and agreed timelines. After the endorsement of GVAP, additional disease-specific targets have been endorsed at the World Health Assembly (Table 1).

Existing disease-specific goals are enduring global commitments, endorsed by the World Health Assembly, and will continue as an important component of IA2030. Nevertheless, revisions may be made during the development of the IA2030 monitoring and evaluation framework, especially for goals where target dates have passed.

Polio: Enormous progress has been made towards polio eradication. Wild poliovirus is now circulating in only two countries, where insecurity and lack of access, cross-border population movements and health infrastructure weaknesses are major obstacles to immunisation. In many countries, the Global Polio Eradication Initiative (GPEI) has helped to build an infrastructure that supports immunisation functions beyond polio. Effective planning for an immunisation setting without the GPEI infrastructure and resources is therefore vital to ensure that functions essential for shared disease-prevention goals – vaccine-preventable disease surveillance, strong immunisation services, and outbreak responses – are sustainably integrated into national immunisation programmes. Continuing outbreaks of vaccine-derived poliovirus are a reminder of the importance of maintaining high levels of population coverage to sustain eradication.

Measles: Before measles vaccines were introduced in the 1960s, measles was a leading global cause of child morbidity and mortality, responsible for more than two million deaths annually. From 2000 to 2017, global measles mortality has declined by about 80%. However, regional elimination has not been achieved and sustained, and recent years have seen an alarming resurgence in measles cases and deaths across the globe. As measles is so contagious, very high levels of vaccine coverage (95%) are required to prevent its spread. Global coverage of the first dose of measles vaccine has plateaued around 85% over the past decade and although coverage of the second dose has increased to 69%, this is not sufficiently high to remove the need for supplementary means of delivering vaccine, through planned campaigns, periodic intensification of routine immunisation and other strategies. Measles vaccination, and effective surveillance for rapid outbreak detection, is therefore the foundation of effective immunisation programmes and primary health care systems. Responding to the measles challenge will also drive immunisation programmes to achieve enhanced equity, since it is the disease that highlights immunity gaps and requires every child, everywhere to be reached.

Maternal and neonatal tetanus: Maternal and neonatal tetanus elimination (MNTE) has been achieved in three-quarters of priority countries, although greater efforts are needed to achieve elimination in those remaining. Achieving MNTE will reduce neonatal mortality, which has declined more slowly than under-5 mortality. While addressing inequities, current MNTE strategies only target pregnant women and women of reproductive age, leaving older male children, male adults and elderly males unprotected. The implementation of strategies aimed at vaccinating all populations with a life-course approach will help overcome these gender disparities. Maternal

and neonatal tetanus is also strongly associated with poverty, so its incidence can be used as a marker of the quality of health services being delivered to marginalised and underserved populations, and of care seeking by these groups.

Strengthened systems for integrated disease control: Controlling key infectious diseases equitably, efficiently and sustainably requires both strong immunisation programmes and targeted disease-specific approaches. Strong disease surveillance and immunisation programmes as an integral component of primary healthcare provide the essential method to raise immunity, reduce disease risk, and prevent morbidity and mortality. However, supplementary immunisation activities may sometimes be needed to rapidly boost immunity in targeted populations and to provide a rapid response to outbreaks. Deciding on the blend and balance between these two approaches depends on disease epidemiology, context and the ability of health systems to deliver vaccines to those who need them most.

Elimination and eradication goals that have not been achieved over the past decade are more likely to succeed when building upon a strong national immunisation infrastructure integrated into primary health care systems.

Disease-specific goals (initiatives)	Targets
Polio eradication (Polio Endgame Strategy 2019-2023)[i]	Interrupt transmission of all wild poliovirus (WPV) by 2020
	Stop circulating vaccine derived poliovirus (cVDPV) outbreaks within 120 days of detection
	Certify eradication by 2023
Measles and rubella elimination (Global Measles and Rubella Strategic Plan 2012-2020)	Eliminate measles in at least five WHO regions by 2020
Neonatal tetanus elimination (GVAP)	Eliminate rubella in at least five WHO regions by 2020
	Reach neonatal tetanus elimination in the last 40 countries by 2015
Cholera control (Ending Cholera – A Global Roadmap to 2030)	Achieve 90% reduction of cholera deaths by 2030
Elimination of viral hepatitis as a major public health threat (Global Health Sector Strategy on viral hepatitis 2016-2021)	Achieve 90% reduction new cases of chronic viral hepatitis B (and C) infections by 2030
	Achieve 65% reduction of viral hepatitis B (and C) deaths by 2030
Vector-borne diseases (incl. Japanese encephalitis) control (Global Vector Control Response 2017-2030)	Reduce mortality due to vector-borne diseases by at least 75% by 2030
	Reduce case incidence due to vector-borne diseases by at least 60% by 2030
	Prevent epidemics of vector-borne diseases in all countries by 2030
Elimination of yellow fever epidemics by 2026	Reduce yellow fever outbreaks to zero by 2026
Elimination of meningitis epidemics and reduction of cases and deaths (Meningitis Roadmap)	Eliminate meningitis epidemics by 2030[ii]
	Reduce cases and deaths from vaccine preventable meningitis by 80% by 2030
	Decrease the impact of sequelae by 50% by 2030
Reduction of seasonal influenza burden (Global Influenza Strategy 2019-2030)	(No disease-specific targets)
Zero deaths from dog-mediated rabies by 2030 (Rabies Global Strategic Plan "0 by 30")	Reduce deaths from dog-mediated rabies to zero by 2030

i. Target dates dependent on epidemiological situation
ii. As of September 13th, 2019

Table 1: Existing goals and targets of disease-specific initiatives

Changing context and challenges

As well as learning lessons from the past decade, IA2030 has been shaped by a review of the changing global context.

Inequities: The benefits of immunisation are not spread equitably, either among or within countries. As of 2018, 70% of unvaccinated children live in **middle-income countries.**[13] Reaching all people will require increased national vaccine coverage but, importantly, also reduced **sub-national inequities**. Success will depend on interventions that take account of poverty, education, socio-economic and cultural factors, and gender-related barriers hindering access to immunisation.

Population movements: Continuing **urbanisation** will pose a major challenge, creating large and dense urban populations at high risk of infectious disease. **Migration** has the potential to create communities of unprotected individuals at risk of infection. Migrants and mobile populations are often difficult to reach and track.

Conflict and political instability: Civil conflict can rapidly lead to loss of health service infrastructure and shortages of trained health workers, often for extended periods, disrupting immunisation service delivery. Affected populations are often also at increased risk of infectious diseases, due to the breakdown in national infrastructure and mass displacement into temporary settlements.

Climate change and natural disasters: The world's changing climate will have significant implications for infectious disease. New populations will be exposed to vector-borne diseases such as malaria and dengue, and increased risks of flooding will create new opportunities for the spread of water-borne diseases such as cholera. Climate change also disrupts seasonal disease patterns, potentially shifting the timing, duration and pattern of their transmission, and has the potential to alter the endemicity of infectious diseases. Climate-informed surveillance and response systems will be an essential part of national preparedness for infectious disease outbreaks.

Outbreaks: The world continues to experience outbreaks of measles, yellow fever, diphtheria, other vaccine-preventable diseases, and of emerging infections such as Ebola. Immunisation and **disease surveillance** will be critical for the prevention, detection and control of infectious disease outbreaks. Disease surveillance provides insight into the effectiveness of immunisation programmes, informs the optimisation of vaccine approaches and serves as early warning of potential outbreaks. Comprehensive preparedness and response strategies, including the capacity to carry out research in outbreak situations, will limit the impact of outbreaks on people's health and national finances.

Sustaining trust: Uptake of immunisation services is affected by multiple factors, from the convenience and quality of facilities and services to the spread of misinformation about the safety and effectiveness of vaccines. These factors need to be understood and addressed, in order to build and sustain trust in vaccines and immunisation services within communities and to enhance resilience to misinformation about vaccines. To tackle the harms being caused by anti-vaccination messaging – especially through social media channels – there is a need to understand the specific context and the reasons for the lack of trust, with robust efforts to build and sustain this trust, especially in the face of falsehoods. Strategic investments to build trust and confidence in vaccines can increase community support for vaccines and assure that immunisation is viewed as a social norm.

[13] WHO/UNICEF coverage estimates 2018 revision, July 2019, https://www.who.int/immunization/monitoring_surveillance/data/en/

Ensuring immunisation for all ages: Expanding the benefits of vaccination to other age groups along the **life course** offers tremendous opportunities, but more effort is needed to do it effectively. As more vaccines become available for older age groups, new approaches are needed to reach populations other than infants and to deliver integrated and people-centred health services. The world is also experiencing significant **demographic shifts**. Regions such as Africa are undergoing rapid population growth and a resultant 'youth bulge', while others are experiencing significant population ageing. These shifts will have a major impact on the need for immunisation services at different ages.

Optimising and sustaining supplies: Achieving the IA2030 vision will require a **reliable global supply of appropriate, innovative and affordable vaccines and other immunisation products of assured quality**. Every year, many countries experience disruptions in the supply of vaccines, often because of a mismatch between global production levels and the combined needs of countries. Attention needs to be given to achieving and sustaining healthy market dynamics for vaccines and immunisation products over the long term, at both the global and regional levels. Reliable forecasts of national vaccine needs and priorities will continue to be important enablers in improving healthy market dynamics and optimising and sustaining supplies. The **price of vaccines** is another key barrier to access, and can delay the introduction of new vaccines in low- and middle-income countries. Countries also have markedly different procurement processes, which may need adjustments to respond to changes in the vaccine market and in quality assurance requirements.

What's new in IA2030?

Recognising these lessons from the past and the changing context, IA2030 differs from its predecessor – the Global Vaccine Action Plan – in several marked respects:

- **Bottom-up co-creation:** IA2030 has been developed through an co-creation process, with close engagement of countries to ensure that the vision, strategic priorities and goals are aligned with country needs.
- **Tailored implementation adapted to country context:** The IA2030 framework is more flexible, enabling countries to tailor the global strategy according to their local context, and partners to provide differentiated, targeted and tailored support.
- **Adaptability to changing needs:** The IA2030 strategic framework is designed to be adapted to changing needs and new challenges that emerge over the course of the decade.
- **Targeted ways to address inequities:** IA2030 aims to ensure that the benefits of immunisation are equitably shared both among and within countries, prioritising those not currently being reached, particularly the most marginalised communities within countries, and the most vulnerable communities living in fragile and conflict-affected settings.
- **Stronger systems focus:** IA2030 positions sustainable immunisation programmes, embedded within primary health care, as the basis for achieving high coverage and advancing universal health coverage.
- **Measles as the key pathfinder:** IA2030 places measles vaccination as the driver that will help to build strong immunisation programmes and primary healthcare systems, and the indicator identifying where to focus to find every last unimmunised child.
- **Life-course approach:** The growing numbers of new vaccines administered beyond childhood open new frontiers for national immunisation programmes and require new methods to deliver them. IA2030 has a stronger focus on expanding the benefits of immunisation throughout the life course.
- **Strengthening partnerships beyond health:** The future of immunisation will increasingly be based on integration and collaboration with stakeholders within and beyond health. IA2030 focuses on greater

collaboration with existing and new partners. This enhanced collaboration will have mutual benefits, extending the benefits of immunisation, while at the same time helping others to achieve their goals.

- **Accelerating innovation:** A more nimble and robust research agenda brings new opportunities to meet unknown future challenges. IA2030 focuses not only on new vaccine development but also on accelerating innovations to improve programme performance and to enhance the delivery of immunisation, drawing on lessons learned from other sectors.
- **Better use of existing resources for self-sustainability:** IA2030 has a strong focus on maximising the impact achieved with existing resources. Efficient, effective and resilient national immunisation programmes delivered as a part of primary healthcare, backed up by strong political commitment and popular support, hold the key to future progress and long-term sustainability. Partners have a key role to play in supporting countries on this pathway to self-sustainability.

These shifts in emphasis do not, however, lessen the importance of other still-relevant priorities identified by the Global Vaccine Action Plan, which have been incorporated into IA2030's framework for action.

A Framework for Action

IA2030 is based on a conceptual framework of **seven strategic priorities** (Fig. 2). Each strategic priority has defined **objectives and goals**, and outlines the **key areas of focus** for future efforts. Actions towards these inter-related strategic priorities are needed to achieve the overall vision and impact goals of IA2030, and to ensure immunisation fully contributes towards the strengthening of primary health care and achievement of universal health coverage.

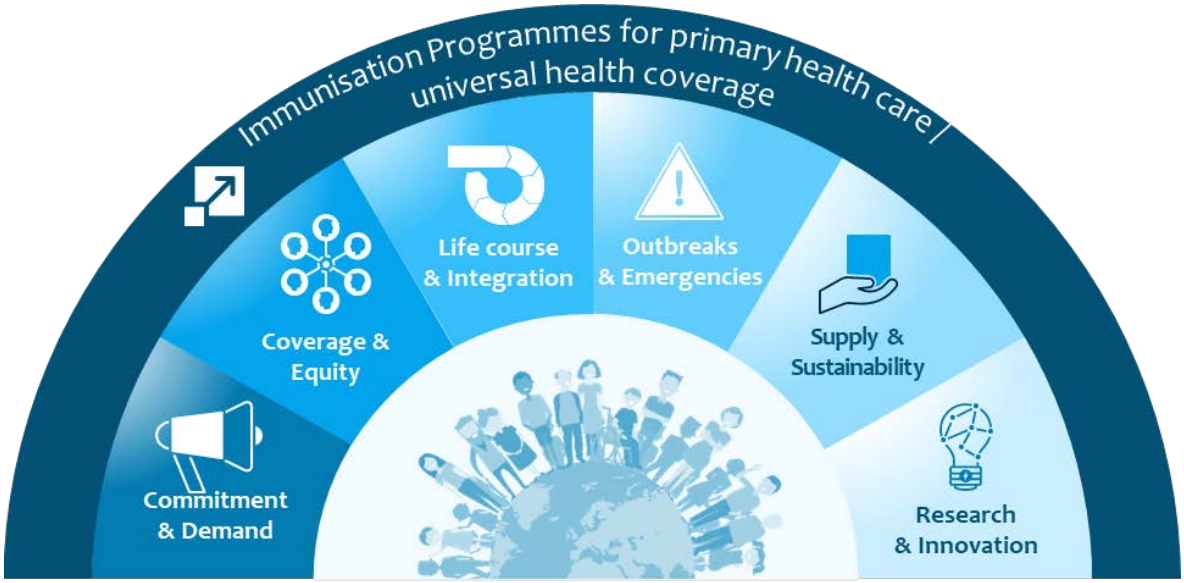


Fig. 2 – The seven strategic priorities of the Immunisation Agenda 2030.

The **first strategic priority is overarching**, to ensure that the immunisation programmes are an integral part of a primary health care system and aligned to the ambition of universal health coverage. The second relates to commitment and community demand. Together, these first two strategic priorities focus on the **fundamentals of an immunisation programme** needed to deliver people-centred and demand-driven services to individuals and communities.

The next three strategic priorities focus on ensuring the **delivery of immunisation services** along the life course to all, and in the context of population growth, continuing urbanisation, rising migration and displacements of people, and in places affected by conflict, political instability, natural disasters and climate change.

The remaining two strategic priorities are **enablers of success** through continued investments in research to combat important infections for which no vaccines exist, and in innovations to improve immunisation programme performance and to enhance the delivery of immunisation services to underserved populations. Likewise, assuring a reliable global supply of affordable vaccines and dedicated efforts to ensure the financial sustainability of national programmes worldwide are critical enablers of success.

The seven strategic priorities are reinforced by a set of **four core principles** that will shape the nature of actions undertaken to achieve every strategic priority objective and goal (Fig. 3). The four core principles are the threads that weave together the strategic priorities and provide guidance on the translation of a high-level strategy into

practical actions. They also convey key messages to all partners within and outside of the immunisation community on the values and guiding principles that underpin mutually beneficial partnerships and alignment of activities.

People-focused – *Ensuring responsiveness to populations needs*
The design, management and delivery of immunisation services should be shaped by and be responsive to the needs of individuals and communities.

Country-Owned – *Driving progress from the bottom up*
Countries should establish targets that are shaped by local contexts and be held accountable for achieving them.

Partnership-Based – *Aligning efforts to maximise impact*
Immunisation partners will align and coordinate actions to increase efficiencies and build on complementarities, and reach out to sectors beyond immunisation for mutual benefit.

Data-Driven – *Promoting evidence-based decision-making*
Reliable and timely data will be used to track progress, drive improvements in programme performance, and underpin decision-making.

Fig. 3 – The four core principles of the Immunisation Agenda 2030.

[SP 1] Immunisation programmes for primary health care/universal health coverage

Objective:

Effective, efficient and resilient immunisation programmes to safely deliver immunisation services as part of national primary health care systems, contributing to universal health coverage.

Goals:

- Ensure adequate health workforce availability
- Build and strengthen comprehensive vaccine-preventable disease surveillance supported by strong and reliable laboratory-based systems
- Secure high-quality supply chains and effective vaccine management to facilitate equitable coverage in immunisation and establish synergies with other primary health care supply chains where possible
- Generate fit-for-purpose immunisation data for evidence-based decision-making
- Ensure functional vaccine safety systems in close collaboration with national regulatory agencies

Key areas of focus:

Immunisation in primary health care

Ensure immunisation is an integral part of national primary health care strategies and operations, and national strategies for universal health coverage.

Health workforce

Develop health workers who are motivated, skilled, available, resourced and knowledgeable to plan, manage, implement and monitor immunisation programme performance at all levels and locations.

Supply chain and logistics

Strengthen supply chains to ensure that high-quality vaccines are always available in the right quantity, in the right presentation, at the right time and in the right place. Promote integration with other supply chains for a more effective delivery of primary health care.

Vaccine-preventable disease surveillance

Enhance the efficiency, responsiveness and comprehensiveness of disease surveillance (including epidemiology and laboratory capacity) in order to: inform vaccine introductions, optimise immunisation programmes; measure vaccine impact; monitor disease control, elimination and eradication; and detect, investigate and respond to outbreaks. These efforts should build on existing surveillance infrastructure, such as that for polio and measles.

Health information systems

Ensure that health information systems enable decision-makers to use high-quality immunisation data to effectively manage immunisation programmes and are linked to other primary health care data systems.

Vaccine safety monitoring

Ensure that national immunisation programmes are able to detect and respond to potential vaccine safety concerns, through continuous monitoring and coordination across relevant stakeholders (e.g. immunisation programmes, national regulatory agencies).

Disease control initiatives

Ensure that vaccine-preventable disease control, elimination and eradication efforts are implemented in ways that strengthen national health systems.

Applying the core principles:

People-focused	Country-owned	Partnership-based	Data-driven
Immunisation strengthening will be designed and tailored to the needs and social and cultural preferences of people and communities.	National strategies and plans to strengthen immunisation programmes will be aligned with broader health systems strengthening and primary health care development for the attainment of universal health coverage.	Public and private partnerships will be forged with joint and coordinated efforts to strengthen immunisation programmes, including with partners beyond the health sector, with the private sector and with CSOs.	Strengthening immunisation programmes and improving their design and performance for universal health coverage will be guided by data, evidence, and lessons learnt on best practices.

[SP 2] Commitment & Demand[14]

Objective:

Everyone values immunisation and actively seeks out and receives immunisation services, and immunisation is positioned as a key contributor to the right to health, with accountability and ownership at all levels.

Goals:

- Build and sustain strong social, political and financial commitment for immunisation
- Strengthen leadership, management and coordination for immunisation at all levels
- Ensure people and communities value, actively support and seek out immunisation services

Key areas of focus:

Commitment

Ensure key groups, champions and stakeholders advocate for greater commitment and ownership of immunisation programmes, including sustained domestic financing, at national and sub-national levels. Encourage leaders to prioritise immunisation in their strategic and operational planning and in their policy, fiscal and legislative instruments. Strengthen evidence-based decision making, with technical input from groups such as National Immunisation Technical Advisory Groups (NITAGs).

Sub-national support

Build support for immunisation and capacity for leadership, management, coordination at the national and sub-national levels in large countries and in those with devolved health systems. Establish mechanisms for stakeholder coordination and participation in planning, implementation and monitoring.

Accountability

Establish accountability frameworks involving all stakeholders at all levels, incorporating platforms for engagement and dialogue. Ensure that communities and CSOs are better equipped to hold national and sub-national authorities

[14] For the context of this strategic priority, "demand" refers to the actions of individuals and communities to seek, support and/or advocate for vaccines and vaccination services. Demand is dynamic and varies by context, vaccine, vaccination services provided, time and place. Demand is fostered by governments, immunisation programme managers, public and private sector providers, local leadership and civil society organisations hearing and acting on the voices of individuals and communities. (Source: Final Report from the informal Working Group on Strategic Objective 2 (SO2) of the Global Vaccine Action Plan (GVAP) to the Strategic Advisory Group of Experts (SAGE) of the World Health Organization GVAP Working Group (April 2017)).

accountable for the equitable delivery and quality of immunisation services. Ensure access to information and develop frameworks for joint monitoring.

Leadership, governance and management
Create an enabling environment for effective coordination, financial management and performance monitoring at every level of the immunisation programmes.

Public trust and confidence
Develop a better understanding of community attitudes, behaviours and social norms, and use communication technologies, social media, social behaviour change and gender responsive approaches to engage communities and encourage greater use of immunisation services.

Public knowledge and understanding
Include immunisation in education curricula, develop public education tools, including those that meet the specific needs of vulnerable or marginalised groups, provide educational opportunities for the health workforce, and develop information resources for advocacy groups.

Acceptance, trust and value of immunisation
Use local data to understand underlying causes of low uptake of services and tailor approaches to address them. Based on the evidence, address convenience, service availability, confidence and complacency issues. Proactively implement plans for prevention and response for adverse events, rumour and hesitancy and to strengthen resilience.

Approaches to address reluctance to vaccinate
Address concerns and develop robust strategies to target sources of vaccine misinformation and reduce the risk of its propagation.

Applying the core principles:

People-focus	Country-owned	Partnership-based	Data-driven
Community engagement will be at the heart of building people's trust, acceptance and use of vaccines and vaccinations with an emphasis on dialogue, service quality, caregiver respect, user convenience and accountability.	Political leaders, civil society and immunisation champions will be identified to ensure countries commit to immunisation of their people as a right and to ensure that communities are protected against vaccine-preventable diseases.	New partnerships will be built to communicate knowledge and raise awareness of the value of immunisation, and to overcome gender barriers to build relationships and trust with communities.	Behavioural and social research, data and evidence will be collected locally and nationally for use in developing locally appropriate interventions and acceptable communication technologies will be deployed to increase commitment and demand for immunisation.

[SP 3] Coverage & Equity

Objective:
Everyone has access to safe and effective vaccines irrespective of their geographical location, age, socioeconomic status or any gender-related or other obstacle impeding their opportunity to gain the full benefits of vaccination.

Goals:

- Reach high equitable immunisation coverage at national level and in all districts
- Increase coverage of vaccines among the most disadvantaged populations
- Reduce the number of children not reached through the immunisation programme ("zero-dose" children)

Key areas of focus:

Disadvantaged populations

Identify and address low levels of coverage across the life course among the poorest and most disadvantaged individuals and communities.

Barriers to immunisation

Identify barriers to uptake of immunisation services based on age, location, social, cultural or gender-related factors (of recipients, health workers and caregivers), and use evidence-based approaches to overcome these barriers to achieve high equitable coverage.

Measles as a pathfinder

Use measles as a key 'pathfinder' for immunisation programmes by identifying zero-dose children, weaknesses in immunisation programmes and evidence of low vaccine uptake.

Learning from disease-specific initiatives

Use the experience learned from disease eradication and elimination initiatives in reaching the most marginalised populations, integrating successful strategies for delivery and accountability into the full immunisation programmes.

Context-specific interventions

Develop, evaluate and scale up innovative, locally tailored, evidence-based and people-centred approaches to reach poorly served populations.

Implementation research

Strengthen local capacity to conduct implementation research to identify factors affecting the equity of immunisation coverage and promoting use of the results to develop locally tailored and context-specific interventions and innovations to address inequalities.

Applying the core principles:

People-focused	Country-owned	Partnership-based	Data-driven
Coverage and equity gaps will be addressed – especially among marginalised and disadvantaged communities – by actively engaging representatives of local communities and local health providers in the design of interventions tailored to these groups.	National immunisation programmes will need to implement strategies to overcome immunisation barriers based on proven and innovative approaches and local research into effective ways to deliver services to underserved groups.	Partnerships with local communities, representatives of marginalised groups, and organisations that work with them will be built for implementation of local initiatives to address inequalities and with a solid understanding of the obstacles to their access to vaccination (including gender barriers of recipients caregivers and health workers).	Immunisation data systems will be expanded to map and track unimmunised and under-immunised populations at the sub-national level and specific marginalised groups to ensure they are reached by the immunisation programme.

[SP 4] Life course & Integration

Objective:

- Everyone benefits from new and underused vaccines recommended across the life course
- Delivery of vaccinations is integrated with other appropriate health opportunities

Goals:

- Strengthen policies and service delivery to provide new and underused vaccines and appropriate catch-up vaccination across the life course
- Establish integrated delivery touchpoints for immunisation and other public health interventions across the life course

Key areas of focus:

Mobilising support
Raise awareness of the benefits and public demand for vaccines beyond childhood through adolescence and in priority adult groups such as pregnant women, health workers and older adults.

New delivery methods
Identify and use successful delivery strategies for scaling up coverage of new and underused vaccines recommended across the life course.

Missed opportunities
Implement proven approaches to reduce missed opportunities by integrating immunisation with other primary health care planning, health registers and other record systems, and community- and facility-based service delivery for all ages.

Cross-sectoral collaborations
Develop collaborative initiatives to integrate age-appropriate and catch-up vaccination with public and private health services. Establish collaborations beyond healthcare to develop context-specific programmes incorporating immunisation in areas such as education, nutrition, water and sanitation, care of older people, and women's empowerment.

Policy environment
Promote enabling changes in legislation or policy (of immunisation and other programmes), to expand national focus beyond childhood immunisation. Develop new collaborations and private sector partnerships to mobilise additional financing to expand service provision to specific older age groups.

Tracking vaccination status
Develop approaches that enable vaccination coverage to be monitored at different ages and for vaccinations administered across the life course.

Evidence-based practices
Evaluate new approaches for reaching populations beyond infancy and integrating services, and share lessons learned to encourage adaptation and wider uptake.

Applying the core principles:

People-focused	Country-owned	Partnership-based	Data-driven
Life-course vaccinations will be provided through people-centred touch points integrated with other health care services to meet the needs of different age groups.	NITAGs will guide country programmes to expand vaccines beyond infancy and contact points throughout the life course that reflect their specific national and sub-national contexts.	Partnerships with other health interventions and with non-health actors will be built (including with education, water, sanitation and hygiene (WASH) and nutrition) to develop comprehensive life-course approaches for disease control and elimination including for pneumonia, diarrhoea and cervical cancer.	Implementation, social and behavioural research will be conducted to generate data and evidence on effective ways of deliver integrated and coordinated packages of services with immunisation and to identify new vaccination contact points throughout the life course.

[SP 5] Outbreaks & Emergencies

Objective:

- Capacities to prepare for, prevent, detect and rapidly respond to vaccine-preventable disease outbreaks are maintained and strengthened.
- Those affected by conflict, political instability, acute emergencies and humanitarian crises continue to receive immunisation services, adapted to their specific needs.

Goals:

- Decrease the number and magnitude of outbreaks of epidemic-prone vaccine-preventable diseases
- Ensure timely, well-organised responses to outbreaks of epidemic-prone vaccine-preventable diseases
- Establish timely and appropriate vaccination services in acute emergencies and humanitarian crises

Key areas of focus:

Coordination and integration
Strengthen coordination and implementation of outbreak preparedness, detection, and response and vaccination activities – in the contexts of the overall humanitarian response, international health regulations, and health systems development programming.

Local capacity
Invest in and sustain local capacities and health systems to ensure timely detection of and response to outbreaks; identify and address the underlying causes of outbreaks; and ensure communities affected by outbreaks, other emergencies, and humanitarian crises have continuous access to immunisation services; and ensure immunisation recovery plans are embedded into outbreak and emergency response.

Comprehensive health response
Ensure global, regional, national, and sub-national coordination and governance mechanisms can effectively support equitable, transparent, and timely decision-making on the allocation of essential supplies and vaccines and mobilisation of trained human resources.

Integrated surveillance
Re-build national, regional and local capacity to conduct integrated surveillance for priority diseases rapidly following an emergency or humanitarian event, maximising opportunities to monitor and characterise multiple pathogens to ensure early detection of outbreaks.

Tailored approaches and innovation
Develop, implement and evaluate innovative, tailored approaches and relevant frameworks and tools to safely, ethically and equitably vaccinate populations during outbreaks and in humanitarian settings and initiate reestablishment of immunisation services following acute emergencies along with broader early recovery efforts and in line with disaster risk reduction principles.

Community engagement
Prioritise two-way communication and engagement with communities and health workers during outbreaks and in humanitarian settings to promote participation in decision-making; ensure access to and use of services; and identify and address unmet health needs.

Applying the core principles:

People-focused	Country-owned	Partnership-based	Data-driven
Outbreak and emergency preparedness and response will adapt interventions to meet the full range of needs of affected individuals and draw upon local knowledge to tailor interventions to the context.	National authorities will coordinate efforts to address emergencies and outbreaks with local authorities and services will be delivered using trained local staff and community mobilisation networks.	Partnership will be built for coordinated action to provide an integrated package of health services, including vaccination, in ways that support ongoing health systems and surveillance strategies during outbreaks, other acute emergencies and in humanitarian settings.	Research and evaluations will be conducted to generate evidence on novel approaches to deliver vaccinations and health services during outbreaks, other acute emergencies and in humanitarian settings

[SP 6] Supply & Sustainability

Objective:
- All countries have a reliable supply of appropriate, innovative and affordable vaccines of assured quality
- Adequate and predictable financing is available for immunisation, through a health financing system that ensures efficient use of resources and universal and equitable access.

Goals:
- Build and sustain healthy markets across all antigens at the global level
- Safeguard access to quality-assured vaccines in a timely fashion in all countries
- Ensure sufficient financial support for immunisation programmes across all countries to achieve universal health coverage
- Increase immunisation expenditure from domestic resources for aid-dependent countries, and when transitioning away from aid, secure government domestic funding to sustain coverage of all vaccines after transition

Key areas of focus:

Innovation and affordability
Ensure development, supply and access to new vaccines meet country needs, and that vaccines are introduced in a timely manner irrespective of the wealth of the country, and are priced affordably to sustain supply.

Vaccine supply and demand
Enhance national and global forecasting capabilities and strengthen relationships with manufacturers to ensure that vaccine production and supply meets national needs across all countries.

Sources of assured quality vaccines
Strengthen regulatory capacity across all countries to enhance timely access to vaccines of assured quality and to allow diversification of manufacturing sources.

Supply for emergency situations
Strengthen mechanisms for rapid access in emergency, outbreak, pandemic or humanitarian situations.

Sufficient and predictable resources
Ensure funding from all sources is sufficient to procure and deliver recommended vaccines universally.

Immunisation financing
Ensure good governance, stewardship and accountability of immunisation programme financing to achieve high performance and best value for money.

Partner alignment
Streamline and align partnerships that provide immunisation or primary health care/integrated financing, and ensure effective global collaboration where the roles, responsibilities and accountability of all partners are clearly defined, transparent and monitored.

Sustainable transitions
Ensure mechanisms exist so that countries transition smoothly out of programmes supported by donors, maintaining and enhancing their immunisation programmes.

Applying the core principles:

People-focused	Country-owned	Partnership-based	Data-driven
A strong focus on developing local human capacity for governance and management of immunisation financing, and to build understanding of people's choices to inform better forecasting of current and future vaccine markets.	Country capacity to plan for and secure the required financing for their programme will reduce their reliance on external support. Countries can plan, forecast, budget, and procure vaccine requirements and ensure the quality of vaccines used by their populations.	Enhanced partnerships will be built to plan for and ensure long-term sustainable financing, with clear roles, responsibilities and accountability of all partners. Enhanced collaboration among key stakeholders to support healthy vaccine markets.	Data systems will be expanded to better allocate resources within national immunisation programmes, to monitor the use of these resources, and to better forecast vaccine demand, supply and pricing.

[SP 7] Research & Innovation

Objective:

- Evidence is developed and generated on the benefits of new and improved vaccines, technologies and vaccine manufacturing platforms.
- Data is also generated for other innovations to improve disease prevention, immunisation service delivery and programme management, and on promotion of their implementation at scale.

Goals:

- Establish and strengthen country capacity to identify, create and manage innovation
- Develop new vaccines and technologies and improve existing products and services for immunisation programmes
- Introduce and scale up new and underused vaccines and improved technologies, services and practices

Key areas of focus:

Needs-based innovation
Strengthen mechanisms to identify research and innovation priorities based on the needs of communities, particularly the underserved, and ensure they inform innovations in immunisation products, services and practices.

New and improved products
Develop new vaccines and technologies and improve existing products and services while ensuring continued progress on vaccines for HIV, TB, malaria and other priority diseases.

Development and implementation
Accelerate the pathway to impact, including through evidence generation, operational and implementation research, innovative immunisation management processes and practices, improved regulatory capacity, and greater knowledge sharing.

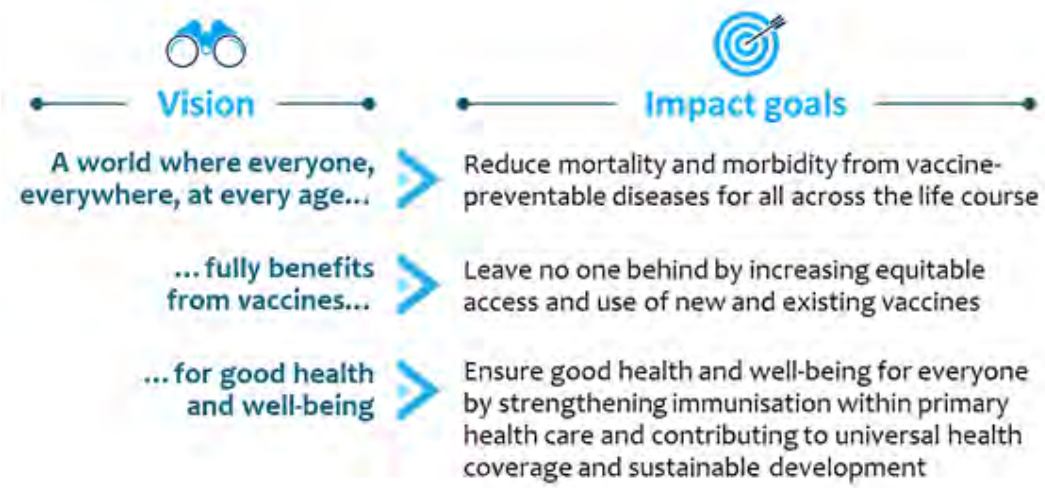
Local innovation
Build local capacity to use innovation to solve programmatic challenges so that innovations are closer to the problem, created and demanded by local managers, and can be rapidly brought to scale.

Applying the core principles:

People-focused	Country-owned	Partnership-based	Data-driven
Innovations in products, services and practices should address community and provider needs and preferences.	Countries should have the capacity to identify and manage innovation, including identifying, documenting and communicating their own priorities and evaluating and implementing innovations. Country priorities should inform the global innovation agenda. Global partners should research, document and communicate country needs to industry.	Partners should develop mechanisms to support the development, evaluation, implementation and sustainability of suitable solutions, drawing on the complementary expertise of national and global stakeholders.	Evidence on unmet needs and the effectiveness of innovations across all aspects of immunisation should be rigorously collected and shared to promote evidence-based research, development, implementation and scale-up.

Impact and Strategic Priority Goals

Realising the IA2030 vision will involve achieving the following "impact goals":



In addition, each strategic priority will have specific strategic priority goals, as the basis for evaluation of progress. These goals will complement the existing disease-specific goals, and the broader health and SDGs. The strategic priority goals mirror the ambition of these existing commitments and aim to galvanise efforts to achieve important gains in immunisation over the coming decade.

As an adaptive and flexible strategy, the IA2030 framework allows for the revision of goals throughout the decade in response to major contextual changes. These goals will be further refined in the monitoring and evaluation framework and will include indicators, targets and methods for tracking progress.

IA2030 goals will inspire action for implementation. For countries, this could mean setting country-specific targets and milestones for the decade toward those goals. For regions, this could mean contextualising global goals and setting specific targets and milestones in Regional Vaccination Action Plans. For partner organisations, this could mean aligning organisational strategies and indicators to support the attainment of IA2030 goals.

Goal and target setting at the global, regional and country level should be[15]:

- Aligned with the vision of IA2030.
- Responsive to changing trends and contexts.
- Aligned with the broader health agenda (SDG3/primary health care/universal health coverage).
- Ambitious, but with achievable and measurable to enable accountability.
- Linked to an action and a work plan.
- Reinforcing previous commitments (e.g. disease-specific goals; Table 1).

[15] Definitions of key terms: a goal is an ambitious commitment to address a single challenge; an indicator is a metric used to measure a goal; a target is a specific (and sometimes time-bound) outcome of an indicator to identify a goal's achievement.

Strategic priorities	Strategic priority goals
Immunisation Programmes for primary health care / universal health coverage	• Ensure adequate health workforce availability
	• Build and strengthen comprehensive vaccine-preventable disease surveillance supported by strong and reliable laboratory-based systems
	• Secure high-quality supply chains and effective vaccine management to facilitate equitable coverage in immunisation and establish synergies with other primary health care supply chains where possible
	• Generate fit-for-purpose immunisation data for evidence-based decision-making
	• Ensure functional vaccine safety systems in close collaboration with national regulatory agencies
Commitment & Demand	• Build and sustain strong social, financial and political commitment for immunisation
	• Strengthen leadership, management and coordination for immunisation at all levels
	• Ensure people and communities value, actively support and seek out immunisation services
Coverage & Equity	• Reach high equitable immunisation coverage at national level and in all districts
	• Increase coverage of vaccines among the most disadvantaged populations
	• Reduce the number of children not reached through the immunisation programme ("zero-dose" children)
Life course & Integration	• Strengthen policies and service delivery to provide new and underused vaccines and appropriate catch-up vaccination across the life-course
	• Establish integrated delivery touchpoints for immunisation and other public health interventions across the life course
Outbreaks & Emergencies	• Decrease the number and magnitude of outbreaks of epidemic-prone vaccine-preventable diseases
	• Ensure timely, well-organized responses to outbreaks of epidemic-prone vaccine-preventable diseases
	• Establish timely and appropriate vaccination services in acute emergencies and humanitarian crises
Supply & Sustainability	• Build and sustain healthy markets across all antigens at the global level
	• Safeguard access quality assured vaccines in a timely fashion in all countries
	• Ensure sufficient financial support for immunisation programmes across all countries to achieve universal coverage
	• Increase immunisation expenditure from domestic resources for aid dependent countries, and when transitioning away from aid, secure government domestic funding to sustain coverage of all vaccines after transition
Research & Innovation	• Establish and strengthen country capacity to identify, create and manage innovation
	• Develop new vaccines and technologies and improve existing products and services for immunisation programmes
	• Introduce and scale up new and underused vaccines and improved technologies, services and practices

Table 2: Immunisation Agenda 2030 impact goals and strategic priority goals

Operationalisation

IA2030 is an **umbrella strategy** intended to establish a shared vision and strategic priorities on immunisation to guide the activities of countries and stakeholder organisations.

This document does not exist in isolation. It is backed up by technical documentation, and complements the strategies of stakeholder organizations, disease-specific initiatives and other global health and development programmes to guide the development of national strategies and plans for immunisation.

Furthermore, creating IA2030 is planned as a **multi-step process**, with agreement of a vision, strategic priorities and high-level goals as a first step. Equally important is the second step – translating the strategy into concrete actions. This will take place through the development of operational plans, an IA2030 governance mechanism, and a monitoring and evaluation framework.

IA2030 is designed to be adapted to regional and national contexts. Countries will be able to prioritize their efforts towards the focus areas of each IA2030 strategic priority, depending on local context. It enables partners and stakeholders at all levels to align their work, ensuring that all efforts reinforce one another in pursuit of common goals.

Operational Plans

The global strategy will be operationalised at national, regional and global levels, shaped by IA2030's seven strategic priorities and four core principles.

At the **national level**, countries can incorporate the IA2030 vision and strategies into their National Vaccination Action Plans, as a part of their national health planning process. According to their individual contexts, countries will define their own targets and timelines to achieve IA2030 goals. Where support is needed, it will be tailored to country context and integrated, as much as possible, into processes to strengthen primary health care and achieve universal health care and the SDGs.

At the **regional level**, existing **Regional Vaccination Action Plans** will be updated to align with IA2030's vision and strategic priorities. Tailored support will be provided to countries according to the different needs of national immunisation programmes. Regional collaboration will involve stakeholders within and outside of immunisation to leverage synergies and promote integration.

At the **global level**, the operationalisation of IA2030 vision and strategy will focus on strategic priorities with a strong global element, regional and country support best coordinated at a global level, and alignment among global stakeholders. This will include communications and advocacy to maintain momentum, mobilize global support for IA2030 and immunisation more generally, and to promote buy in to IA2030's principles and priorities.

Governance mechanism

A governance mechanism will be established to ensure implementation and accountability, defining the roles and responsibilities of all stakeholders delivering the IA2030 vision and strategies. This will be a key objective of the second phase of the IA2030 development process.

Monitoring and evaluation framework

Drawing upon the lessons learned from the Global Vaccine Action Plan, a robust monitoring and evaluation framework will be developed to measure progress towards the vision and goals. It will closely align with operational plans to promote greater transparency and accountability.

The approach to achieving the IA2030 vision will be dynamic and responsive. While this document serves as a constant throughout the decade, operational plans at the national, regional and country level will evolve as circumstances change. Just as the battle against infectious disease requires agile and flexible immunisation programmes, so too a global immunisation strategy must be sensitive to rapid shifts, constantly evolving according to changing needs.

Strategic Advisory Group of Experts (SAGE) on Immunization

Interim Recommendations on Vaccination against Ebola Virus Disease (EVD)

7 May 2019

Over the last four weeks, the Ebola outbreak in the Eastern Provinces of the Democratic Republic of Congo (DRC) has deteriorated with a large increase in the number of cases[1]. A major factor in this rise is an increase in critical security incidents that have dramatically affected the ability to identify, follow up and vaccinate contacts successfully. This context challenges the implementation of ring vaccination based on the identification of contacts and contacts of contacts, as recommended by SAGE in April 2017 and confirmed by SAGE during its April 2019 meeting.[2] Further, a potential vaccine shortage may manifest in case the outbreak expands further and/or is prolonged.

SAGE expressed grave concern about the current worsening outbreak epidemiology and completeness of ring vaccination noting that disease transmission continues to occur notably in locations where ring vaccination cannot be implemented and that a large proportion of new cases continue to arise among unknown contacts. SAGE further acknowledged the work of those involved in the Ebola outbreak response in a very challenging context.

SAGE deliberated on the following recommendations on implementation of novel strategies and adjusted dose regimes:

1. **Implementation of innovative operational strategies.**

Innovative operational approaches are being implemented to address security concerns and community tensions. These innovative operational approaches to implement ring vaccination include:

(i) **Pop-up vaccination** – In this approach, already successfully implemented to address security issues and tensions with the community, rather than setting the vaccination site at the residences of contacts and contacts of a given case (which is how ring vaccination is typically done), vaccination is implemented at an agreed and temporary, protected vaccination site, at a distance from the residence of the contacts, often a health facility) and;

(ii) **Targeted geographic vaccination** – In this approach, already successfully implemented to address security issues, all the contacts and contacts of contacts of all cases reported in a given village or neighbourhood are enumerated and invited for vaccination simultaneously. Again, this is done at a fixed location where security to the teams is provided. Besides addressing the security issues, this strategy allows

[1] WHO Ebola Virus Disease. Democratic Republic of the Congo External Situation Report 39. http://newsletters.afro.who.int/icfiles/1/46425/184054/6134450/97816cb57ede15249d4eb5b5/sitrep_evd_drc_20190430-eng.pdf?ua=1, accessed 7 May 2019

[2] The report of the SAGE April 2019 will be published in the WHO Weekly Epidemiological Record (www.who.int/wer/en/) on 30 May 2019.

the teams to catch up with the increased number of cases without vaccination rings in certain locations.

In view of the implementation challenges, SAGE agrees with the proposed innovative operational approaches, tailored to the local situation, should be implemented to address security concerns.

2. Revised vaccination strategy to adjust the target population for ring vaccination to include a second and third barrier of immunized individuals around each incident case.

In order to contribute to interrupting the chain of transmission within the current outbreak, SAGE recommends adjusting the target population for ring vaccination to include a second and third barrier of immunized individuals around each incident case with onset of symptoms within the previous 21 days as follows:

(i) Continue to offer as a priority rVSV-ZEBOV-GP vaccine and vaccinate those at higher risk of Ebola including contacts and contacts of contacts and health care workers (HCWs) and front line workers (FLWs) in affected Aires de Santé.

(ii) Offer rVSV-ZEBOV-GP and vaccinate to those who can potentially be involved in the tertiary generation of cases (e.g. 3rd level of contacts) to create a barrier around the contacts of contacts in affected Aires the Santé. This approach also addresses community requests to offer vaccination to additional members of the community that they consider to be at high risk as they believe this is likely to increase overall community acceptability and;

(iii) Offer a vaccine other than rVSV-ZEBOV-GP to those at some risk of Ebola in Aires de Santé with cases, although at a lower risk than those described in (i) and (ii) above. In order to determine suitability of Ebola vaccines for clinical studies, WHO reviewed data generated by Ebola vaccine manufacturers on two candidate vaccines: the adenovirus 26 vectored glycoprotein / MVA-BN (Ad26.ZEBOV/ MVA-BN) vaccine developed by Johnson & Johnson, and the CanSino-Beijing Institute of Biotechnology (Ad5-EBOV) vaccine.[3] SAGE recommends that these lower risk populations would be vaccinated with the J&J vaccine with informed consent. The latter ideally implemented as per the SAGE recommendation from April 2019 which outlines that studies using other candidate vaccines should be done in this context: "*Proposed studies should be scientifically and epidemiologically justified, have appropriate approvals including from all African and other regulatory and ethics authorities, and have defined endpoints including for safety which can contribute to licensure.*" [2,4]

[3] WHO Ebola Vaccines Decision framework. April 12, 2019. www.who.int/blueprint/priority-diseases/key-action/ebola-vaccine-candidates/en/, accessed 07 May 2019

[4] WHO Meeting summary for the SAGE meeting of April 2019 www.who.int/immunization/sage/meetings/2019/april/SAGE_April_2019_meeting_summary.pdf?ua=1, accessed 07 May 2019

3. Alternative dosing for the rVSV-ZEBOV-GP vaccine.

To ensure vaccine continues to be available and offered to individuals at greatest risk of Ebola during this outbreak and in order to secure the availability of the rVSV ZEBOV-GP in the mid-term, SAGE revised the following proposal, based on an analysis undertaken by the U.S. Food and Drug Administration (Appendix 1), to exceptionally adjust the vaccine dose for the currently available lots of rVSV-ZEBOV-GP being used in DRC:

(i) For those at higher risk of Ebola including contacts and contacts of contacts including HCWs and FLWs in the affected areas: offer a vaccine dose with a similar potency to that used in the Guinea Ebola ça suffit trial (i.e. 2×10^7 pfu).

(ii) For those who can potentially be involved in the tertiary generation of case (e.g. 3rd level of contacts), a 5-fold dose adjustment compared with the current dosing of the vaccine is recommended (in relation to the potency of the vaccine lots being used in DRC). The 5-fold dose reduction in the broader population was motivated on immunological considerations related to dose-response analysis using a 4.8-fold dose reduction in various subpopulations and seroconversion rates in those groups at 28 days after vaccination and later, noting this dosing regimen provides a reasonable risk-benefit trade-off for protection.

SAGE supports the adjusted dosing administration as proposed above. SAGE acknowledges, that since the vaccine is available in 10-dose vials at 1 ml/dose, that a 2-fold and a 5-fold reduction in dose could be readily implemented by injection of 0.5 mL and 0.2 mL, respectively.

SAGE stresses that the terminology used should be determined with caution to avoid the impression that the proposed dosing is sub-standard. Training for vaccinators and adequate standard operating procedures (SOPs) and equipment are needed to ensure the success of delivery of the adjusted dosing.

Research needs

SAGE requests that it would be helpful to determine the duration of protections conferred by the adjusted dosing. The response of adjusted dosing used in special risk groups, such as HIV infected needs to be assessed.

Immunogenicity studies of the different adjusted doses head-to-head with full dose of rVSV-ZEBOV-GP vaccine should be conducted preferably in Africa. Further, immunogenicity head-to-head studies between the rVSV-ZEBOV-GP vaccine and other available products would be useful.

Further, all possible efforts in such challenging circumstances should be continued to regularly collect and review safety and effectiveness data, particularly for pregnant women and infants 6-12 months.

4. **Proposal to further adjust the protocol to incorporate alternative individual informed consent forms.**

SAGE was presented with a proposal to further adjust the protocol to incorporate alternative individual informed consent forms that while complying with Good Clinical Practice (GCP) guidelines can expedite the vaccination process. These have been adapted to facilitate the consent process while complying with Good Clinical Practice and simplifying the safety follow up by focusing on passive reporting of serious adverse events by phone. Only pregnant women will be actively followed up until delivery date or end of pregnancy, and a single visit at day 21 will take place for infants 6-12 months of age. Plans are also underway to train additional ring vaccination team members who are from the affected areas and speak the local languages.

SAGE approves the proposal of the adjusting the protocol, highlighting that the adjusted dosing will need to be reflected in the protocol.

5. **Implementation of a mass communication campaign.**

Implementation of a mass communication campaign is proposed, targeting community knowledge, attitudes and behaviours regarding Ebola. In particular, this campaign will communicate the evidence on effect on reduced mortality if admitted early to an Ebola treatment unit, the preventative effectiveness of vaccination and the emerging evidence on the reduced mortality due to Ebola among vaccinated individuals.

SAGE supports the recommendation to undertake a mass communication campaign targeting community knowledge, attitudes and behaviours regarding Ebola. The need for ongoing communication efforts is obvious and investment in social sciences is needed to understand how trust can be built.

Appendix 1: Summary of data relevant to consideration of adjusted dosing of VSV-ZEBOV (rVSVΔG-ZEBOV-GP) Ebola vaccine

Introduction

To increase the supply of the rVSVΔG-ZEBOV-GP Ebola vaccine in order to provide broader vaccine coverage to at risk individuals, manufacturing data, animal protection data, and immunogenicity data from Phase 1 and 2 clinical studies conducted in various subpopulations were analyzed to inform considerations of adjusted immunizing doses. Adjustment of dosing is associated with potential risk of reduced vaccine effectiveness. However, tolerance for any risk to effectiveness should be informed by risks associated with other options and the number of vaccine doses projected to be needed.

Manufacturing data

Potency data for the currently available vaccine lots could support an adjustment in dosage of 2-fold, while still on average approximating the dose that was used in the Guinea Ebola ca suffit ring vaccination clinical endpoint efficacy study (referred to as the "Guinea dose").

Of note, this calculation may be subject to revisions pending release potency data of future rVSV-ZEBOV-GP lots.

Animal and human immunogenicity data

Human immunogenicity data derived from six clinical studies (all of which followed subjects for 6 months to one year) in which both the "Guinea dose" and a 6.7-fold adjusted lower dose were evaluated suggest a trend towards higher immune responses with the "Guinea dose;" however, in most of these studies the differences in antibody titers were modest. In two of these studies a dose-response relationship was not observed, moreover vaccination at a lower dose resulted in higher immune responses compared to vaccination with one or more higher doses.

In the two larger studies a major difference in immune responses induced by the "Guinea dose" and the 6.7-fold adjusted lower dose was not observed, while in the four smaller studies, two had results consistent with a difference in immune responses, and two did not show a clear difference.

Since protective response soon after vaccination is critical for ring vaccination, the kinetics of response may be especially important. The trend (albeit with overlapping confidence intervals) towards higher GMTs when using the "Guinea dose" compared to the 6.7-fold adjusted lower dose is also observed at 14 days after vaccination in three studies where this time point was evaluated. This trend in GMT response was consistent with reduced day 14 seroconversion rates at the 6.7-fold lower adjusted dose, which was observed in 2 of the 3 studies. At times 28 days or later post vaccination, human immunogenicity data from these small studies suggest a modest to negligible dose-response relationship in this dose range.

While the relationship between immunogenicity and effectiveness is not established in humans or animals, data from non-human primate challenge studies are generally consistent with immune response and protection being insensitive to immunizing dose.

This also is consistent with the mechanism of action of replicating live-virus vaccines, for which protection is usually considerably less sensitive to immunizing dose than it is for other types of vaccines.

Together, the clinical immunogenicity data and non-human primate challenge study data could support a 2 to 5-fold adjustment in immunizing dose with some uncertainty about using the limited clinical data to support adjustment of potency in settings where rapid immune response is critical (e.g., ring vaccination).

While linearity of the immune response has not been demonstrated, a 2-fold reduction in immunizing dose might be expected to yield immune responses closer to the "Guinea dose", while a 5-fold reduction would still be expected to yield immune responses greater than the 6.7-fold adjusted dose.

In summary, adjustment of rVSV-vectored Ebola vaccine (rVSVΔG-ZEBOV-GP) dosage in the above-described ranges is unlikely to be associated with a reduction in vaccine effectiveness in the context of outbreak control. This assessment is based on the data analyzed. If feasible additional data (for example, from the field) addressing the impact of using adjusted doses of rVSVΔG-ZEBOV-GP should be obtained. Based on a review of the potency data for currently available rVSVΔG-ZEBOV-GP vaccine lots, vaccine could reasonably be considered for ring vaccination at potency adjustment reduction of 2-fold compared to the current dose in use in DRC (so it is comparable to the "Guinea dose"). For more general use (e.g., when rapid evolution of immune response is less critical), based on an analysis of a combination of manufacturing, clinical, and animal data, potency reduction of 5-fold (or half of the "Guinea dose") could be considered.

The following is important in considering adjustment of rVSVΔG-ZEBOV-GP dosing:

1. Use of an adjusted dose is associated with potential risk that effectiveness may be reduced.
2. The more modest the adjustment in dose, the more modest the risk to effectiveness.
3. Tolerance for any risk to effectiveness should be informed by risks associated with other options and the number of vaccine doses projected to be needed (i.e., a critical factor in making decisions about potential vaccine dosage adjustment should be the number of vaccine doses needed and the projections for the availability of additional full-dose vaccine, see 4).
4. Weighing of risks associated with vaccine dosage adjustment should consider the likelihood of vaccine shortages and the potential public health benefits of having greater numbers of doses of vaccine available.
5. This analysis is restricted to animal and clinical data, so there may be other operational considerations in dosage adjustment. For example, adjustment of dosing may require use of different syringes than are used in the current protocol or modification of consent forms currently in use.

SAGE Working Group on Quality and Use of Immunization and Surveillance Data:

Executive Summary

Material included in the Yellow Book

1. Updated Executive Summary of the "Report of the SAGE Working Group (WG) on Quality and Use of Immunization and Surveillance Data" and table with WG recommendations with timeframe and responsibilities
2. Immunization Data: Evidence for Action (IDEA) Precis
3. India Case Study: Utilization of Immunization Data to Improve Evidence-based Decision-Making
4. Excerpt from the draft 2019 Western Pacific Region 28th Technical Advisory Group Meeting report summarizing presentations on the draft "Regional strategic framework for vaccine-preventable diseases and immunization in the Western Pacific, 2021-2030"

Supplemental material on the SAGE website

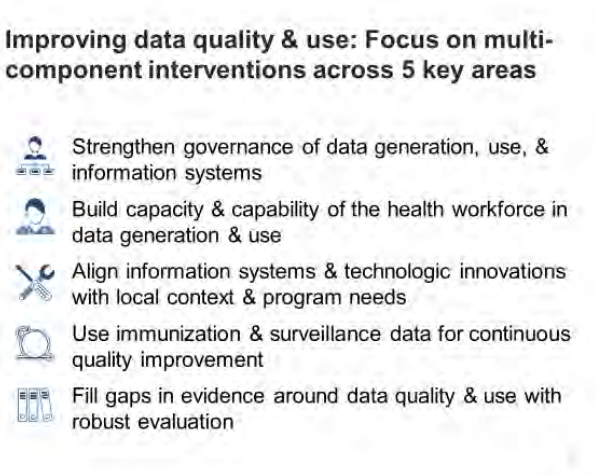
5. An updated version of the "Report of the SAGE Working Group on Quality and Use of Immunization and Surveillance Data" that was presented in the April 2019 Yellow Book, including the Executive Summary and References
6. All previously presented annexes reference in the Report: literature reviews, case studies, white papers

Purpose of session: propose recommendations for SAGE endorsement. The session will include a recap on the major findings for the work of the WG and discuss a way forward for the proposed recommendations, including a country example from India on how data has been used to improve programme performance and a presentation from the WHO Western Pacific Region on data and surveillance for their regional immunization strategy.

Specific questions for SAGE: for SAGE to discuss high-level recommendations and next steps, including:

- Endorsing WG report and recommendations
- WHO to incorporate recommendations into Immunization Agenda 2021–2030
- Regions and countries to incorporate recommendations into 2021–2030 strategies, including multi-component interventions for improving data quality and use across 5 key areas:
    - Strengthen governance of data generation, use, & information systems
    - Build capacity & capability of health workforce in data generation & use

- Align information systems & technologic innovations with local context & program needs
- Use immunization & surveillance data for continuous quality improvement
- Fill gaps in evidence around data quality & use with robust evaluation



Target outcomes: SAGE to consider and endorse WG report and high-level recommendations:

1. Endorsement for the WG report, framework and included recommendations
2. A call for the Immunization Agenda (IA) 2030 to take into account Data as a key enabler and the recommendations from the WG
3. A call to integrate data activities under the broader umbrella of Universal Health Coverage (UHC) and Primary Health Care (PHC)
4. A call to actions to regions and countries, through their regional immunization technical advisory groups (RITAGs) and national immunization technical advisory groups (NITAGs), to take the recommendations and implement activities aimed at improving data quality and use.

Background

Concerns about the quality and use of immunization and vaccine-preventable disease (VPD) surveillance data have been highlighted on the global agenda –including by the SAGE – for more than two decades. The demand for accurate data and their use in programme management and decision-making has only increased as countries strive to meet the ambitious vaccination coverage and disease elimination goals of the Global Vaccine Action Plan (GVAP). These agreed upon goals require new, more precise and finer types of measurements than have often been used in many low- and middle-income countries. Improved information systems and data quality will also be critical to measuring progress in achieving the Sustainable Development

Goals (SDGs) and Universal Health Coverage (UHC), such as improvements in equity of service delivery and in reaching under-served, marginalized, and migrant populations.

Recent efforts by countries and immunization partners to improve immunization-related data have resulted in successes in a number of countries. However, poor quality and under use of data remain a persistent problem in many, affecting the ability of countries and partners to monitor progress against the GVAP and other global goals as well as to support optimal changes to immunization programmes. In fact, SAGE assessment reports of GVAP implementation stated that poor data quality was impeding programme improvement, and recommended that improving data quality should be a top priority for national immunization programmes.

As a concrete measure to address this ongoing problem, the SAGE Working Group (WG) on the Quality and Use of Global Immunization and Surveillance Data was established in August 2017. Its mandate was to:

- Take stock of data availability and determine if there are unmet immunization monitoring and evaluation data needs at global and regional level, and suggest revisions for reporting processes;
- Review existing and new draft standards and guidance on immunization monitoring and vaccine-preventable disease (VPD) surveillance data to identify gaps, revisions, and areas that require updates;
- Review and assess the current 'state' of immunization and VPD-surveillance data quality and use at country, regional, and global level;
- Review evidence on:
    - factors that may cause and/or limit access to quality and use of immunization and VPD-surveillance data for decision-making at different levels;
    - effectiveness (including where possible, cost-effectiveness) of interventions for improving access to, improving quality of, or promoting the use of data at national and subnational levels;
- Review the status of information systems that collect immunization and VPD-surveillance data, the availability of modern information technologies, and their current and potential future role in supporting the collection, management, analysis and use of immunization and surveillance data;
- Identify knowledge gaps & create prioritized research agenda around data quality and use.

Methods and definitions

The WG considered data within the scope of their review as vaccine coverage, immunization programme process indicators (e.g., vaccination sessions), vaccine supply, and VPD surveillance data. A series of landscape analyses (involving key informant interviews and document

reviews), literature reviews, country case studies and data analyses (data triangulation exercises) were conducted by the WG, consultants and partners to fulfill the terms of reference of the WG and prepare the Data WG report. Detailed reports for many of these reviews and analyses can be found in the Annexes, along with full versions of the case studies.

The WG used a definition of data quality as *data that are accurate, precise, relevant, complete and timely enough for the intended purpose (or "fit-for-purpose")*, such as to monitor programme performance, support efficient programme management or provide evidence for decision-making. The structure of the report presents the current landscape and is based on a simplified theory of change, which identifies five pillars − Governance, People, Tools, Processes for Continuous Quality Improvement, and Evidence required to produce data that are available, fit-for-purpose and used for action.

Major findings and key points

The availability, quality and use of immunization and surveillance data, data-related guidance and assessment methods

There is a considerable amount and variety of immunization and surveillance-related data available nationally, regionally, and globally, though the data are not always accessible to those that need them the most. However, when evaluated, the quality of these data is still often poor, especially in low- and middle-income countries, with inaccuracies in denominators used to calculate immunization coverage or disease incidence rates being particularly pronounced. The WHO-UNICEF Joint Reporting Form (JRF) and WHO-UNICEF estimates of national immunization coverage (WUENIC) remain key sources of immunization data available internationally. There is also increased demand for the collection of disaggregated data for immunization and VPD surveillance (e.g., subnational; individual-level) to support achieving programme objectives. The new global electronic platforms and strategies, including the WHO Immunization Information System (WIISE) (which will include an e-JRF), the WHO Immunization Data Handbook and related Immunization Monitoring Academy and the global Comprehensive VPD Surveillance Strategy, should help improve the quality and use of immunization and surveillance data.

In recent years, a plethora of global and regional guidance documents and standards have been developed to address issues related to monitoring, data quality and use. However, awareness of these tools among people working in immunization and VPD surveillance and their ability to find and access these tools needs to improve. In addition, the review found a continued lack of practical guidance and tools for a number of technical areas. Tools for countries to assess data quality – such as the Data Quality Self-assessment (DQS) and Data Quality Review (DQR) tools – have improved over the years and have had a positive impact on country ownership and interest in making data improvements in a number of countries, with some evidence of positive impact on data quality and use as well. More work is needed to define a common lexicon of

definitions around data and a standard set of indicators to measure data quality and use, as part of comprehensive programme monitoring.

The factors limiting and the effectiveness of interventions to improve access, quality and use of immunization and surveillance data

The possible sources of data quality loss or failure to share and use data are many and can occur at all levels of the health system. Data quality loss can result from failure to record properly, errors in transcribing/calculation, inaccurate denominator data, poor/missing/outdated forms, procedural gaps (e.g., not including private sector), lost/damaged records, or intentional falsification. Types of barriers to sharing data locally and internationally include technical (inadequate interoperability, standards, archiving procedures), motivational (lack of incentives, trust between data providers and users, or resources/time needed), economic (e.g., potential negative economic effects), political (bureaucratic hurdles, lack of political will), and legal and ethical barriers. Failure to use data can result from lack of confidence in the quality of available data, lack of basic/advanced data analysis and interpretation skills, or lack of understanding on how to use data to monitor and improve the immunization programme, as well as lacking a culture of information use.

Systematic reviews have found that multicomponent interventions are most prevalent and often more effective for improving health data quality and use. For example, no impact has been observed from technological interventions alone, without the related capacity building. Training combined with supervision or group problem solving or certain multifaceted strategies were found to be more effective than single strategies. Further, a health systems approach was found to be more likely to succeed and be sustained over long-term. An example of this would be implementing data review meetings, creating national guidelines and protocols on data use, and hiring data managers at all levels. For this reason, it is relevant to consider implementing multi-component interventions within and across the five key areas of Governance, People, Tools, Processes for Continuous Quality Improvement, and Evidence towards improving data quality, access and use as part of a health systems approach.

Strengthening governance of data collection, access, and use

Having strong policies and mechanisms in place that govern all key aspects of data collection, access, and use is important to develop immunization and VPD surveillance information systems that produce high-quality, credible data that are useful to monitor and improve programmes. Data can be used for programme planning, performance accountability, implementing evidence-based interventions to improve vaccine uptake, and informing policy decisions. Coordination and collaboration between different units dealing with data (e.g., immunization programme, labs, surveillance units), between partners and the government, as well as across the entire health care system is crucial to establish efficient, sustainable information systems, and to avoid systems that are fragmented and duplicative. Strong

leadership within national governments and the political will to improve data quality — even if it initially leads to lower reported performance —are also critical to ensure the sufficient resources, key policies and regulations, and development of a "data use culture" needed for improvements. Also, key is the establishment of national standards governing all stages of data generation and use and having policies and mechanisms in place for sharing data both within countries (e.g., data from the private sector and Non-Governmental Organization-NGOs/Civil Society Organizations-CSOs) and internationally, while also taking issues of privacy and confidentiality into account.

Building capacity and capability of the health workforce in data collection and use

The lack of adequate person-time equivalents and skills in data collection, analysis, interpretation and use among health workers are key factors limiting the quality and use of immunization and VPD surveillance data. This report recognizes that data quality at all levels ultimately depends on the quality of data collection at the health facility level, and thus data quality interventions, including workforce planning and capacity-building must specifically target the local level. In addition, data-related activities often compete with clinical duties for health workers' time, thus impacting the quality, completeness and timeliness of reporting. Improving this situation requires a multi-pronged approach — including pre-service and in-service training, with regular reinforcement through supportive supervision, and feedback — as well as adequate resourcing and dedicated person-time for data-related tasks taking into consideration in workforce planning. Some countries have dealt with the issue by creating a cadre of health information personnel specifically trained and dedicated to managing and analyzing data.

The reviews found that current pre-service training programmes often do not adequately prepare health workers to carry out data-related tasks, even in high-income countries, nor has most in-service training around data had a major impact in improving the skills and practices of health workers. Governments therefore need to make a dedicated effort to provide continuous and effective competency-based training on the generation and use of health data, incorporating adult learning theory and based on the data-related responsibilities required at all levels of the health system. The WG has developed a framework that defines the roles and responsibilities of health workers in collecting, analyzing and using immunization data from the facility to the global level in order to assist countries in planning their capacity-building activities related to immunization data and information systems.

Align information systems and technological innovations with local context & programme needs

Health workers need user-friendly tools (either paper or electronic) that make their jobs easier and more efficient. Recent advances in information and communication technology (ICT) have led to a multitude of innovative tools developed with the aim of improving data quality,

availability and use. Immunization information systems are currently either immunization-specific tools or part of an integrated health management information system, such as DHIS2, and challenges with both approaches exist. Innovative “e-Health” tools used in immunization and disease surveillance programmes range from electronic immunization registries (EIRs) to decision-support tools (such as dashboards), mobile technologies to enable real-time data collection, reporting and monitoring; geospatial-based tools (e.g., GIS) and predictive analytics to improve coverage and population estimates.

While there is evidence that some of these tools improve data quality and use, many — with the exception of electronic information systems, such as DHIS2 and some EIRs —never get rolled out nationally, nor thoroughly evaluated. Some innovations have failed because they ignored country context, user requirements, and issues of interoperability with existing systems. This highlights the fact that technologic solutions are not a magic bullet for solving all data problems, but rather the successful use and scale-up of these innovations depends to a large extent on other key elements being in place, including a skilled and motivated workforce, strong governance, sustainable financing, adequate infrastructure, such as computers, connectivity, and technical support, as well as clear operating procedures and processes. Global guidance is also needed on how and when to scale up innovations to ensure a sustained, long-term benefit on data quality and use.

Using immunization and surveillance data for continuous quality improvement

There is evidence to suggest that improving the quality of immunization and VPD surveillance data on a periodic basis can only go so far, and that using a continuous quality improvement (CQI) approach has the potential for greater and longer-lasting improvements. This approach should start with an assessment of the root causes of poor data quality extending down to the lowest level of the health system. Limited evidence also indicates that increasing the use of data can improve data quality, though not necessarily the other way around. However, gaps in data use and data use capacity abound at all levels.

Solutions proposed as part of a continuous quality improvement approach include a shift from periodic data quality assessments to routine monitoring of data quality, including automated data validation checks and analyses on electronic information systems; and the better use of existing, under-utilized data, such as surveillance, rapid coverage monitoring, and vaccine supply data, to create a fuller picture of programme performance. They also include the “triangulation” of data to synthesize evidence across different data sources to address relevant questions for programme planning and decision-making (e.g., checking data quality, prioritizing areas for intervention, estimating coverage/denominator, evaluating programme impact/effectiveness). Such data triangulation analyses should be the default for public health analysis.

In line with the goals of improving equity of services across populations and geographic areas, better measures, tools and indicators need to be developed to monitor equity on a regular basis. Similarly, current methods for measuring and estimating vaccination coverage must be adjusted to accommodate the shift towards a life-course vaccination approach. Methods for improving estimates of target populations, including dealing with migration, remain among the needs that are most critically felt at the local programme level.

Filling gaps in evidence around data quality and use

This report identifies and maps out gaps in evidence and knowledge concerning key aspects affecting the quality and use of immunization and VPD surveillance data and proposes a research agenda based on these gaps, structured according to the pillars for improving data quality and use. In general, the Working Group found a need for more robust evaluation of the impact of various data quality and use interventions (e.g., tools, capacity building approaches), their cost-effectiveness, and their impact on staff time and efficiencies.

The Working Group has outlined high-level and specific recommendations for countries (national and subnational), regional and global levels with a timeline in the Table below.

Table of SAGE Immunization Data Working Group recommendations by level, WHO role and time horizon[1]

Recommendation area	Specific recommendation	Countries	Regions	Global	WHO-specific unit & topic-area	Time horizon[2]
1. Embed monitoring of data quality and use into global, regional and national monitoring of immunization and vaccine-preventable disease (VPD) surveillance	WHO to develop a common definition, attributes, and indicators of data quality (i.e., small panel of indicators corresponding to the different data quality attributes), using those identified in this report as a starting point			x	EPI – see previous experience with GVAP, propose for eJRF	+
	Integrate ongoing monitoring of data quality indicators alongside other routine programme performance (e.g., coverage) and impact indicators	x	x	x	EPI – Guidance, Supporting implementation	+/++
	Develop and utilize data quality assessment approaches for immunization programme data other than coverage (i.e., VPD surveillance, stock data, etc.)	x	x	x	EPI – Guidance, Supporting implementation	++
	Evaluate the impact, cost and sustainability of interventions which aim to improve data quality, management, and use to inform decisions on scale-up	x	x	x	IVB, EPI – Convening, guidance, advocacy - Collaboration with HSS	++/+++
2. Increase workforce capacity and capability for data quality & use starting at lowest level, where data collection occurs	Develop and disseminate data-related competencies guidance and capacity building tools to implement assessment of workforce at country-level	x	x	x	EPI – Guidance, advocacy (building on work on functions & competencies) - Collaboration with HSS	++/+++
	Ensure data functions (collection, analysis, and use) are accounted for & resourced in workforce management plans, e.g., devoting adequate person-time equivalents, staff recruitment, and retention	x			- Collaborate with HSS	+++
	Build data capabilities across various levels and career stages (pre-service, refresher, supportive supervision, etc.), considering new approaches (e.g., e-Learning) potential efficiencies created by coordination across programmes	x	x	x	- Collaborate with HSS	+++

[1] Acronyms: eJRF – Electronic WHO/UNICEF Joint Reporting Form on Immunization; EPI – Expanded Programme on Immunization; GVAP – Global Vaccine Action Plan 2011-2020; HSS – Health Systems Strengthening; IVB – Department of Immunization, Vaccines and Biologicals at WHO

[2] Time horizon represents a proxy for priority and feasibility. Code is: + short term or within two years; ++ medium term or 2-5 years; +++ long term or 5 or more years.

Recommendation area	Specific recommendation	Countries	Regions	Global	WHO-specific unit & topic-area	Time horizon[2]
3. Take actions to improve the accuracy of immunization programme targets (denominators)	WHO and UNICEF to revise and finalize the draft guidance on Assessing and Improving the Accuracy of Target Population Estimates for Immunization Coverage (2015), including proposing practical and evidence-based solutions			x	IVB, EPI – Convening, guidance, advocacy - Collaborate with HSS - Beyond health sector	++
	Increase immunization programme coordination with national statistics office, birth/civil registration offices, and other relevant programmes/ organizations for improving the quality of denominators	x				++/+++
	Identify and attempt to address the technical (e.g., resident vs non-resident) and non-technical barriers (e.g., political) to accurate denominators in countries, including the use of operational denominators	x	x	x		+++
	Document best practices & country experiences about using different sources (birth cohorts, vital registries & census estimates) or methods for improving denominators	x	x	x		++
4. Enhance use of existing data for tailored action, including immunization programme planning, management and policy-change	At all levels, increase the use of data sources beyond administrative coverage for monitoring, planning and decision-making (e.g., numerators, denominators, surveys, surveillance, vaccine supply, service delivery, serosurveys)	x	x	x	EPI – Guidance, Supporting implementation	+/++
	Develop /incorporate guidance and training on data triangulation for immunization and surveillance programmes at the national and subnational level	x	x	x	EPI – Guidance, Supporting implementation	+/++
	Support the development and use of decision-support tools (e.g., monitoring charts, dashboards), as needed, for better planning and programme management	x	x	x	EPI - Guidance-Supporting implementation - Polio team - Health info systems (e.g, DHIS-2)	+/++
	Further work on defining the role of serosurveys for immunization programme management at different levels, across different diseases and different epidemiological contexts			x	IVB – Convening, guidance	++

Recommendation area	Specific recommendation	Countries	Regions	Global	WHO-specific unit & topic-area	Time horizon[2]
5. Adopt a data-driven continuous quality improvement (CQI) approach as part of health system strengthening	Shift from identifying data quality issues to root cause analysis and improvement planning, as outlined in the draft *Handbook*	x	x	x	EPI - Guidance - Supporting implementation	++
	Monitor the implementation and impact of previous recommendations to improve accountability and inform new recommendations (e.g. create data-driven improvement cycles)	x	x	x	EPI - Supporting implementation - Collaborate with HSS	+/++
	Tailor multi-component strategies for strengthening data collection & use, which may include capacity-building activities, tools, supportive supervision, actionable feedback, staff recognition (e.g. certificates, awards) & accountability mechanisms	x	x	x	EPI - Supporting implementation - Collaborate with HSS	++
	Recognize that perverse incentives may have led to overestimation in reported coverage, and ensure that data quality improvements leading to lower coverage are not penalized (i.e., promote accurate reporting)	x	x	x	EPI - advocacy - Collaborate with HSS - Beyond health sector	+++
	Develop a vision and strategic framework for a CQI approach for EPI, including measuring relative changes alongside absolute indicator targets	x	x	x	EPI - Supporting implementation - Collaborate with HSS	++/+++
6. Strengthen governance around piloting & implementation of new information, communication, & technology (ICT) tools for immunization & surveillance data collection & use	Design systems and tools based on needs, user requirements, and local context (e.g., sustainability)	x	x	x	EPI – convening, guidance - Collaborate with HSS - Digital health	+++
	Review existing evidence on cost, impact and effectiveness when considering pilot or scale up new tools for data collection/ management	x	x	x	EPI – convening, guidance - Collaborate with HSS - Digital health	++
	Plan for and ensure integration & interoperability of any newly introduced tools within the existing information system	x	x	x	EPI – convening, guidance - Collaborate with HSS - Digital health	+++
	Ensure new information systems include historical data, support all data management functions (archiving, security, and linkage of relevant data), and are accompanied by guidance, standards and specification	x	x	x	EPI – convening, guidance - Collaborate with HSS - Digital health	+++

Recommendation area	Specific recommendation	Countries	Regions	Global	WHO-specific unit & topic-area	Time horizon[2]
7. Improve data sharing and knowledge management across areas and organizations for improved transparency and efficiency	Include best practices on data management (archiving, migration, sharing, and security) in immunization monitoring and surveillance guidance and training	x	x	x	EPI - Guidance - WHO Monitoring - Digital Health	++
	Make data, guidelines, documentation, and reports readily available and accessible to relevant users by building and maintaining user-friendly websites, mobile apps and other communication tools	x	x	x	IVB - knowledge management - WHO in general	++
	Improve routine coordination between stakeholders (epidemiologic surveillance, laboratory, and immunization units; private providers, civil society organizations, and partners) with regards to reporting/sharing of relevant data and information	x	x	x	EPI – Guidance, Supporting implementation	+++
8. WHO & UNICEF to continue strengthening global reporting and monitoring of immunization and surveillance data through a periodic needs assessment and revision process	Continue development and implementation of global (WHO Immunization Information System-WIISE) and regional information systems, including electronic JRF		x	x	EPI - implementing	+ Ongoing
	Collect and monitor disaggregated coverage (e.g., subnational) and surveillance data (e.g., by age, vaccination, lab confirmation)	x	x	x	EPI - Guidance	+ Ongoing
	Develop approaches for data collection & routine monitoring of emerging immunization issues, e.g., coverage equity, life-course, migrants / mobile populations, qualitative data		(x)	x	EPI - Guidance	++
	Collaborate to convene new research & validate existing research for improving denominators & national/ subnational coverage (e.g., spatial modelling), including use of data sources beyond coverage (e.g., stock), to inform guidance for programme use			x	EPI – Convening, Guidance, Supporting implementation	++
9. WHO & SAGE should periodically review the implementation status of the WG recommendations, lessons learned, and the gaps to be addressed.				x	- Coordinate with SAGE	Every 2-3 yrs

IDEA

IMMUNIZATION DATA:
EVIDENCE FOR ACTION

A Realist Review of What Works to Improve Data Use for Immunization

Evidence from low- and middle-income countries

PRÉCIS

Introduction

Within global health, it is widely acknowledged that a cornerstone of well-functioning health systems is data of high enough quality to guide decision-making. Yet despite international efforts to improve the quality of health data, including in the immunization field, increasing data use for making decisions remains a challenge, especially at the level of health care delivery.[1] There is a need to take stock of the evidence from existing efforts to strengthen immunization data and identify effective and ineffective approaches, as well as any knowledge gaps.

The goal of the Immunization Data: Evidence for Action (IDEA) project is to identify, review, synthesize, and disseminate *what works* to improve use of immunization data and *why* it works. To this end, we conducted a realist review with these objectives:

- *Articulate a Theory of Change (TOC) that illustrates key mechanisms and outcomes related to strengthening data use.*
- *Synthesize existing evidence (published and unpublished) related to strengthening the use of immunization data, and evidence on strengthening data quality in relation to data use.*
- *Provide information and evidence so that various stakeholders may select approaches with the highest potential for improving the use of routine immunization data.*

This review was a collaborative effort between PATH and the Pan American Health Organization (PAHO). The review team included health systems researchers with expertise in immunization, measurement and evaluation, and evidence-informed policymaking from PATH's Health Systems Analytics team, as well as immunization and data use experts from PAHO. To ensure the review's relevance for multiple agencies, countries, and decision-making bodies, a steering committee of ten global and regional senior leaders in the areas of immunization, data quality, and use guided the work of the review team.

1 Karuri J, Waiganjo P, Orwa D, Manya A. DHIS2: The tool to improve health data demand and use in Kenya. J Health Inform Dev Ctries [Internet]. 2014 Mar 18 [cited 2018 Sep 9];8(1). Available from: http://www.jhidc.org/index.php/jhidc/article/view/113

Methods

The review sought to answer two principal research questions:

01. *What are the most effective interventions to improve the use of data for immunization program and policy decision-making?*
02. *Why and how do these interventions produce the outcomes that they do?*

Realist Review Approach

To answer our research questions, we conducted a realist review of the evidence on what works to improve data use. This approach allowed us to include multiple types of evidence, such as experimental and nonexperimental study designs, grey literature, project evaluations, and reports.

Much of the immunization sector's knowledge on data quality and use interventions has not been rigorously evaluated or published. In addition to including studies and evaluations that applied scientific research methods or evaluation design in our review, which we referred to as "evidence," we considered grey literature that did not qualify as a study or evaluation but had strong theoretical plausibility of improving data use, as judged by our TOC. We referred to these records as "promising strategies": strategies that have not yet proven successful but have potential for future success.

Realist reviews are typically driven by a theoretical understanding of how the context and causal mechanisms interact to produce certain outcomes.[2] By providing explanations for why interventions may or may not work and under what circumstances, realist reviews can lead to more pragmatic, actionable conclusions. The approach also gave us the flexibility to orient our data collection iteratively to fill gaps.

Review Process

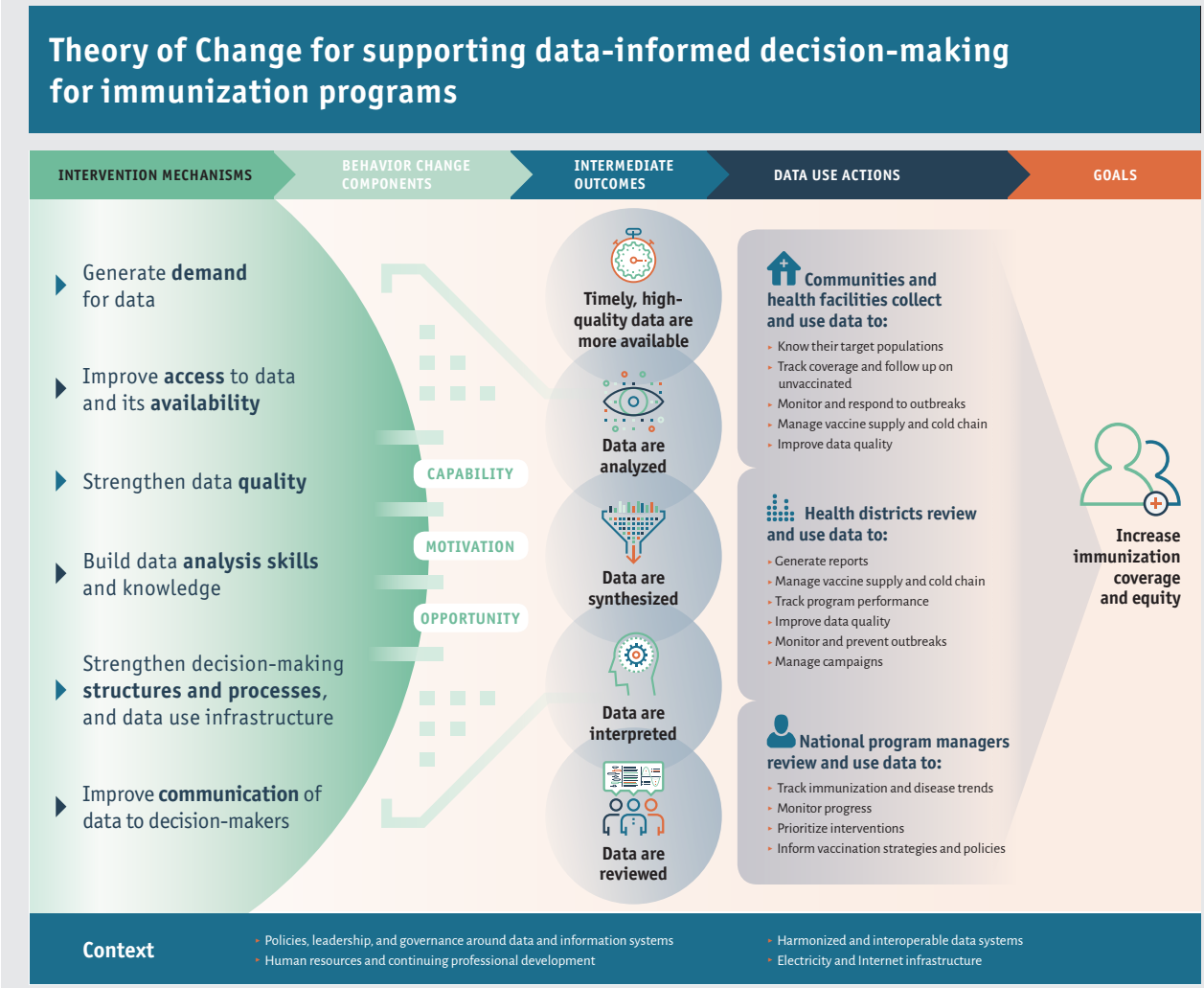
The review included eight steps:

01. *Develop a TOC based on our analysis of systematic reviews and related literature.*
02. *Conduct a systematic review of effectiveness (peer-reviewed and grey literature).*
03. *Review promising strategies to inform why and how the interventions work.*
04. *Extract and code text data based on the TOC.*
05. *Conduct a quality assessment of studies and evaluation of effectiveness.*
06. *Synthesize preliminary data and validate findings with the IDEA steering committee and other immunization stakeholders.*
07. *Conduct a second round of data collection and review literature on data use interventions in other health sectors.*
08. *Synthesize the final data and develop an evidence gap map.*

To guide the review, we developed a TOC (see Figure 1) based on our analysis of existing health information and data use frameworks and logic models, as well as reviews on topics related to health information system strengthening and evidence-informed decision-making. The TOC framed our hypothesis of the theorized mechanisms and contextual factors that work together to help decision-makers translate data into information and, ultimately, action. In order to be effective, we hypothesized that any intervention must incorporate one or more of these mechanisms: demand, access and availability, quality, skills, structure and process, and communication. We also included behavioral drivers: capability, motivation, and opportunity.

2 Pawson R, Greenhalgh T, Harvey G, Walshe K. Realist review--a new method of systematic review designed for complex policy interventions. J Health Serv Res Policy. 2005 Jul;10 Suppl 1:21–34.

FIGURE 1.



We identified intermediate outcomes as the necessary precursors to data use: data quality and availability; and analysis, synthesis, interpretation, and review of data. The ultimate outcomes of interest are the data use actions, which are based on the World Health Organization's Global Framework to Strengthen Immunization and Surveillance Data for Decision-making.[3] The TOC guided our analysis of how interventions led to improved data use and, ultimately, to increased immunization coverage.

The review focused on studies, evaluations, reports, and descriptions of interventions to improve use of routine data by an immunization program for service delivery (which excluded surveillance, financial, and human resources data). We excluded documents that were not specific to a particular intervention or where the outcome examined was something other than data use. We considered health care professionals to be the principal users of routine health data and did not examine use of data by recipients of health care services. We primarily focused on interventions implemented in low- and middle-income countries (LMICs); however, in a limited number of cases, we considered relevant publications from high-income countries (n=7). Much of the literature we collected had been published within the last 15 years.

Although we primarily focused on evidence related to strengthening the use of immunization data, we also examined interventions to strengthen data quality in relation to improving data use. Our TOC recognizes data quality as both a driving mechanism of data use and a measurable intermediate outcome of data use interventions. We therefore included literature on data quality that allowed us to examine these relationships.

3 World Health Organization. Global Framework to Strengthen Immunization and Surveillance Data for Decision-making. Geneva, Switzerland: WHO; 2018 Jan.

We searched PubMed, POPLINE, CABI (Centre for Agriculture and Biosciences International) Global Health, and African Journals Online for published evidence. We obtained grey literature by searching vaccine and digital health conference, implementer, and technical agency websites, as well as through targeted outreach to entities such as TechNet-21, the Global Digital Health Forum, BID Learning Network webinars, other key stakeholders, and members of the steering committee to identify projects and interventions. We assessed the quality of records that qualified as evidence using the Mixed Methods Appraisal Tool (MMAT), a checklist for systematic literature reviews.[4]

We examined the characteristics of the interventions: designs and strategies; targeted types of health care professionals and levels of the health system; implementation settings; and outcomes. We looked at how the interventions functioned and what mechanisms made them successful. We also sought to understand the reasons why interventions did not show evidence of effectiveness.

We presented a synthesis of our preliminary findings to the IDEA steering committee and other immunization stakeholders in May 2018 and identified gaps in the literature. For intervention categories that had limited evidence and were applicable outside of immunization, we expanded the review to include evidence from other health sectors, specifically HIV and maternal and child health. We coded the included records, synthesized the evidence according to outcomes in the TOC, and rated the certainty of evidence.

Assessing Certainty of Evidence

Realist reviews generally do not exclude evidence based on study design or quality. We took this approach but adapted various methods of quality appraisal. We considered certainty of evidence of the evaluated intervention's effect on data quality and use by analyzing (1) design and (2) quality of the included studies, (3) number of studies and their agreement, and (4) context dependence of the evidence. The certainty of evidence rating of high, moderate, low, or very low was a subjective estimation based on these four constructs.

Literature Findings

We initially reviewed 426 documents from published and grey literature and in the second round of data collection reviewed another 123 documents. Ultimately, we included 103 of these documents in the full-text review. We determined that 69 of the articles were research evidence, as they reported results from a study or evaluation, and 34 were promising strategies. Most included literature came from LMICs, although seven pieces of literature were from high-income countries. Africa was the most represented region in the review, and electronic immunization registries were the most reported primary intervention type.

- *48% of reports from Africa*
- *13% from the Americas*
- *9% from South East Asia*
- *6% from Western Pacific*
- *5% from Eastern Mediterranean*
- *2% from Europe*
- *17% of reports were not related to a single region*

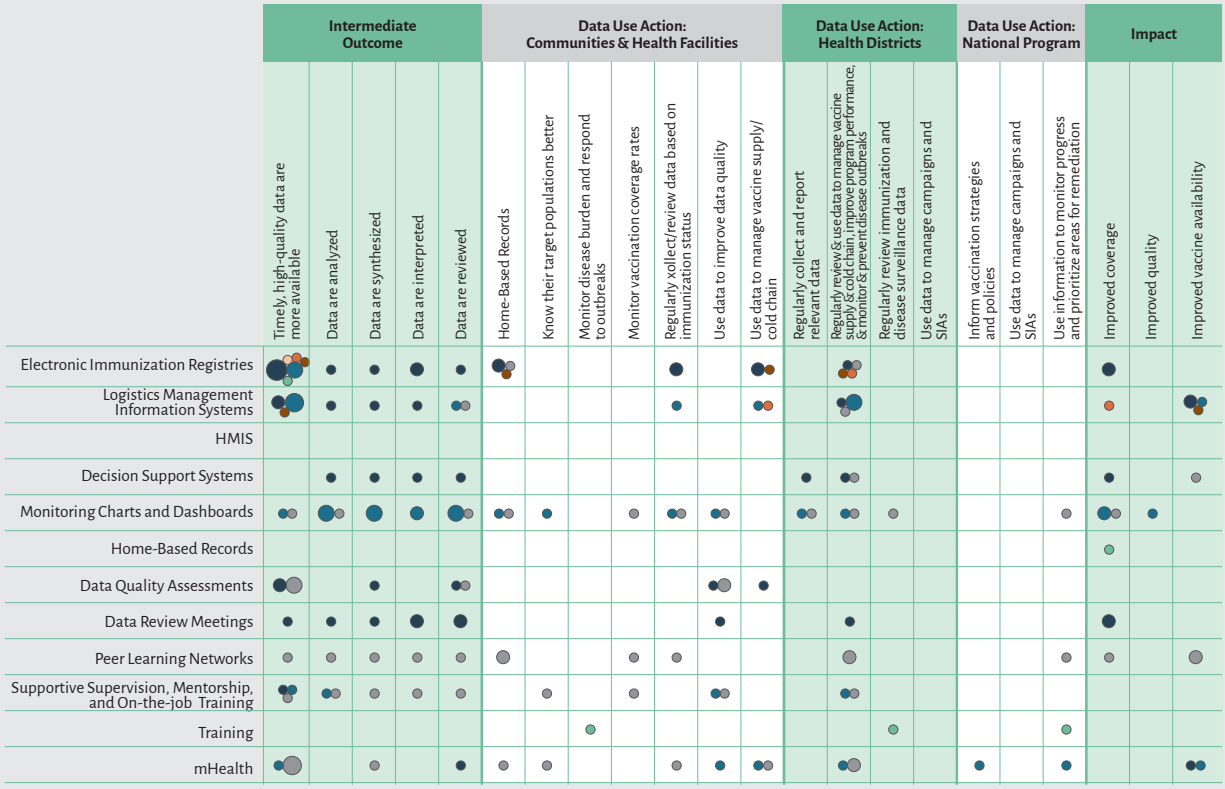
Most documents described projects with multiple intervention components and tended to report on multiple intermediate outcomes and data use actions.

We developed a gap map to visualize all the pieces of evidence and promising strategies included in the review, which illustrates the relatively small number of records pertaining to many data use actions and impact indicators (see Figure 2). Many gaps exist regarding national-level data use actions.

4 Pace R, Pluye P, Bartlett G, Macaulay AC, Salsberg J, Jagosh J, et al. Testing the reliability and efficiency of the pilot Mixed Methods Appraisal Tool (MMAT) for systematic mixed studies review. Int J Nurs Stud. 2012 Jan;49(1):47–53.

FIGURE 2.

Evidence Gap Map



Evidence presented in the gap map includes studies and evaluations of immunization data use interventions that applied scientific research methods or evaluation design, as well as literature that did not qualify as a study or evaluation but had strong theoretical plausibility of improving data use, as judged by our TOC. We referred to these records as promising strategies, which we define as strategies that have not yet proven successful, but have potential for future success.

Strong, Moderate, and Weak categories apply only to the study quality. Reviewers appraised each study using the Mixed Methods Appraisal Tool (MMAT) checklist, which translates into a percentage score. 'Strong'-quality studies scored 75-100%; 'Moderate'-quality studies scored 50-74%; 'Weak'-quality studies scored 0-49%.

To access the interactive gap map, please visit public.tableau.com/profile/path5412#!/vizhome/IDEAgapmap/FORPUBLICPUBLISH

The color of a circle indicates the strength and directionality of the evidence

- Strong quality evidence
- Moderate quality evidence
- Weak quality evidence
- Promising strategy
- Weak quality counterevidence
- Moderate quality counterevidence
- Strong quality counterevidence

The size of a circle indicates the amount of evidence available

- One piece of evidence reviewed
- Two pieces of evidence reviewed
- Three pieces of evidence reviewed

A blank square on the gap map indicates no evidence from immunization data use interventions was identified

Categories of Data Use Interventions

We grouped the interventions into ten primary intervention categories, as well as multicomponent interventions (see Table 1). Although not all interventions were digital, we aligned most of the intervention categories with the WHO Classification of Digital Health Interventions.[5]

TABLE 1.

Descriptions of immunization data use intervention categories

Intervention Category	Description
Electronic immunization registries (EIR)	Store data on administered vaccine doses in computerized, individual-level databases
Logistics management information systems (LMIS)	Collect data on vaccine inventory and demand to support managing the vaccine supply chain; often computerized
Health management information systems (HMIS)	Store aggregated health data and can facilitate converting data into useful information for decision-making; we focused on computerized HMIS
Decision support systems	Help users interpret data and use data for decision-making; include computerized decision support systems (CDSS) and noncomputerized tools (e.g., monitoring charts, dashboards, and home-based records)
Data quality assessments	Range from interventions that train program managers how to routinely audit data quality to external audits of data quality
Data review meetings	Employ adult-learning techniques (e.g., peer learning and knowledge sharing) to build skills in data analysis
Peer learning networks	Connect health workers so they can share information and discuss data; increasingly accessed through social networking platforms online
Supportive supervision, mentorship, and on-the-job training	Build health workers' skills, foster performance and motivation, and identify and resolve problems
Training	Strengthen the capacity of health workers responsible for managing and using data at all levels of the health system through workshops, classroom-based learning, and hands-on approaches
Multicomponent interventions	Leverage many of the intervention categories but lack a clearly identifiable primary intervention type

5 World Health Organization. Classification of Digital Health Interventions v1.0 [Internet]. Geneva, Switzerland: WHO; 2018. Available from: http://apps.who.int/iris/bitstream/handle/10665/260480/WHO-RHR-18.06-eng.pdf?sequence=1

Results

We identified data use actions at the community and health facility, district, and national levels and analyzed the effects of interventions on those actions, as well as on intermediate outcomes according to our TOC.

Intermediate Outcomes

Timely, high-quality data are more available. Computerized interventions (EIR, LMIS, and HMIS) improved data quality, especially when combined with other data use activities. While evidence suggested that these systems made data more available, inconsistent use undermined this availability. Tools used to digitize paper immunization records and mHealth solutions applied to LMIS interventions helped increase data availability. Countries that conducted repeat data quality assessments or that held data review meetings as part of broader efforts to develop health information infrastructure saw improved data quality. These efforts were more effective when combined with supportive supervision and other forms of feedback, so that health workers developed the skills to address issues.

Data are analyzed, synthesized, interpreted, and reviewed. Health workers reported increases in their ability to synthesize and interpret routine data as a result of using computerized systems (EIR, LMIS, HMIS, and CDSS), especially at the district and provincial levels. Simple paper-based monitoring charts and dashboards increased tracking of immunization coverage; these tools are most effective when integrated within established data review and decision-making processes (such as monthly review meetings) and when reinforced through supportive supervision and other forms of feedback. Evidence suggests that peer learning networks increase collaborative data review and problem-solving by health workers.

Data Use in Communities and Health Facilities

There was little evidence that health facilities used data from computerized data collection and management systems (EIR, LMIS, and HMIS) to make decisions and take action, especially when implemented as stand-alone interventions with no support mechanisms. At this level, improving data quality was often emphasized more than improving data use. Challenges such as additional data-entry burdens, poor infrastructure, and workers' lack of motivation contributed to inconsistent use. Digitizing paper immunization records helped improve data quality and relieve the burden of manual data entry. Peer learning networks, training, and decision support interventions (monitoring charts) bolstered facility performance. Data quality assessments prompted health facilities to improve data quality, and such improvements in turn generated more data use in facilities.

Data Use at the District Level

When used consistently, computerized data collection and management systems had more impact on using data to make decisions at the district level than at the facility level, likely as a result of fewer operational challenges. LMIS interventions in particular improved vaccine stock management. Health districts used monitoring charts and dashboards to strengthen facility performance and data quality, but the effect of computerized decision support systems that employed algorithm-based software was uncertain. Data review meetings at the district level increased the use of data to understand and solve issues. Training of district monitoring and evaluation personnel also improved the quality and use of data.

Data Use at the National Level

There was little evidence on how interventions improved data use by national programs. However, anecdotal evidence suggested that a data quality assessment led to the use of data to inform national vaccine strategies and policies. Evidence also suggested that training contributed to more use of data at the national level to strengthen systems and implement policies. National-level participants in peer learning networks reported becoming more data oriented in their work and making decisions based on data. Peer learning networks are likely most effective when they bring together individuals from across departments and levels of the health system and adopt structured approaches for continuous quality improvement.

Impact on Overall Immunization Programs

Few evaluations and studies measured improvements in immunization coverage, equity, and vaccine availability resulting from data use interventions. Among the evaluations and studies that measured overall impact on the immunization program, the results were difficult to attribute to improvements in data use because other interventions were often implemented at the same time.

Improved coverage: Some interventions, such as EIRs, contributed to increased vaccination rates, however it was difficult to assess the EIR's effectiveness in isolation since complementary activities such as text message immunization reminders may have contributed to the improvements. Decision support systems (monitoring charts) contributed to improvements in coverage in low-performing regions. Data review meetings and supportive supervision also contributed to increases in coverage.

Improved vaccine availability: Both use of LMIS and participation in peer learning networks improved vaccine stock management, leading to more consistent stock availability.

Improved equity: We found no evaluations that examined whether or how data use interventions led to improvements in immunization equity.

Key Findings

Summarizing across all evidence and promising strategies, and informed by our TOC, we reached the following broad conclusions:

- **(1) Multicomponent interventions were the most prevalent and were often more effective.** Nearly all the interventions we reviewed used more than one strategy. More comprehensive strategies that addressed barriers at various stages of data use were more likely to achieve results.
- **(2) Interventions that took a health systems approach to institutionalizing data use were more likely to succeed and be sustained over the long term.** This occurred by routinely conducting data review meetings, creating national guidelines and protocols on data use, hiring data managers at all levels of the health system, and incorporating training in data use in national curricula.
- **(3) Although we found limited evidence on the effectiveness of health management information systems (HMIS), including electronic immunization registries (EIR), on data use, they remain promising interventions when accompanied by complementary activities.** Transitioning from paper to computerized HMIS across all levels of the health system has made higher-quality data more available to decision-makers. Phasing in computerized systems incrementally after establishing reliable infrastructure and human resource capacity improves their likelihood for success.
- **(4) Computerized logistics management information systems (LMIS) have made higher-quality data more available to decision-makers to improve supply chain management, especially at district levels and higher.** Although implementing computerized LMIS as a single intervention improves data quality and use, even greater gains were made when other data use activities complemented the LMIS.
- **(5) There is a dynamic, cyclical relationship between data quality and data use.** Although results of this review confirm that data quality is a necessary precursor to data use, we found limited evidence that single-component interventions increased data quality and improved data use. Conversely, we found stronger evidence that data quality improved as a result of increased use of data. More data use generated demand for higher-quality data, which in turn drove actions to improve data quality; as data quality improved, users were able to better trust the data, thus reinforcing data use.

Discussion

The state of the evidence around what works to improve data use is still nascent. Few data use interventions have been rigorously studied or evaluated. We found more evidence on intermediate outcomes within our TOC, such as improved data quality and availability, but less evidence on what works to support decision-making informed by data, particularly at the facility level. More emphasis on building skills and a culture of data use at the facility level may have a greater effect, but this should be tested in future research.

Many of the HIS interventions pointed to challenges with operational barriers and administrative burdens on health workers. Health workers' concerns about sustainability and data loss also limited their acceptance of these systems. We propose additional research and suggest considering the human transaction costs associated with the intervention, as well as any potential unintended consequences for service delivery.

We recommend that data use interventions be designed to address multiple mechanisms in the TOC. Implementers should define the specific data use actions that the intervention will reinforce. Monitoring and evaluation strategies should measure whether data are being used as defined by the data use actions. To strengthen data use throughout the health system, national guidelines for data collection, analysis, and use should be developed and effective support, tools, and training provided to health workers at the facility and district levels. Especially at the facility level, efforts to improve data quality should be balanced with strategies to improve data use. To reduce administrative burdens, health facilities should be equipped with sufficient human resources, including dedicated staff to perform data-related tasks.

Both monitoring and evaluation of interventions could be strengthened: monitoring primarily through better indicator definitions and evaluation through more appropriate evaluation designs. There is a need to develop better measures for assessing data use in decision-making to better understand the effectiveness of these interventions. Measuring data use is possible but requires a firm understanding of the mechanisms that drive data use behaviors and actions and how the use of data may change health outcomes. Evaluations should consider the cost-effectiveness of interventions. Supplementing long-term evaluations with iterative approaches to improving effectiveness of interventions will enable problems and their solutions to be identified more quickly.

Strengths of the Review

The strengths of this review were its inclusiveness and methodological flexibility, afforded by the realist review approach, its focus on data use interventions in LMICs, and its emphasis on understanding how the interventions functioned, what made them successful, for whom, and under what conditions. A majority of the evidence we reviewed was from the non-peer-reviewed literature; although of lesser quality, it provided important evidence and learnings that more traditional systematic reviews would overlook.

Limitations of the Review

Several factors limited this review. Our findings relied on what the literature reported, which sometimes did not thoroughly describe the factors that contributed to an intervention's success or failure and may have caused us to miss important contextual considerations. We likely missed some interventions, especially in regions where English is not the dominant language. Our focus on routine immunization data helped contain the scope of the review but risks further isolating immunization programs or missing lessons from surveillance, financial, and human resource data use interventions that were excluded from the review. Although we expanded the review to include literature from other health sectors, these efforts likely failed to capture all the available evidence. Few studies and evaluations analyzed cost-effectiveness, so we were unable to examine the cost-effectiveness of interventions included in this review. Likewise, we did not find any examination of the outcomes of data use interventions over the long term, which makes it challenging to determine how to ensure lasting results.

Conclusion

By synthesizing the evidence and learnings from 69 studies and evaluations and the promising strategies from 34 papers, this review contributes to our understanding of what interventions improve the quality and use of routine immunization data and why. Although presented primarily through the lens of using data to make decisions in immunization programs, our findings are relevant for other health sectors. The evidence on the most effective practices detailed in this review will help program implementers, policymakers, and funders choose approaches with the highest potential for improving vaccine coverage and equity. We anticipate that these findings will also be of interest to researchers and evaluators to prioritize gaps in the existing knowledge. However, the state of the evidence does not lend itself to recommending which specific interventions or packages of interventions are most effective. Improving immunization data use greatly depends on designing a package of interventions that is theoretically sound and contextually driven, addresses technical and behavioral barriers, and can be sustained outside a project setting.

Suggested citation: Immunization Data: Evidence for Action. A Realist Review of What Works to Improve Data Use for Immunization, Evidence from Low- and Middle-Income Countries [précis]. Seattle: PATH, Pan American Health Organization; 2019.

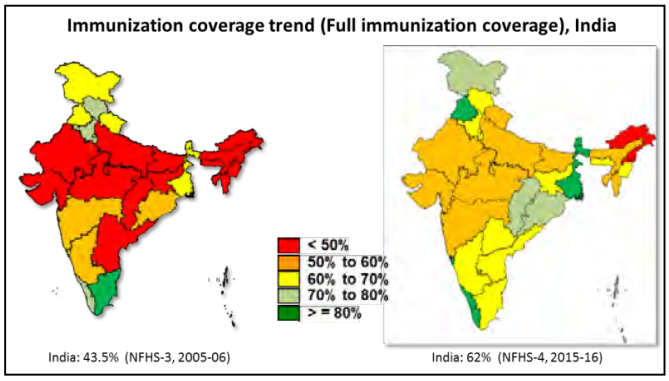
India Case Study

Utilization of Immunization Data to Improve Evidence-based Decision-Making

Background

India's Universal Immunization Programme (UIP) has been one of the largest public health programmes targeting to annual cohorts of around 26 million infants and 29 million pregnant women. UIP has greatly contributed to reducing the burden of vaccine-preventable diseases (VPDs), and saving the lives of millions of children as is evident from the decline of annual under-five mortality, from 3.3 million in 1990 to 1.2 million deaths in 2015, a significant proportion of this decline has been a result of immunization against vaccine preventable diseases.

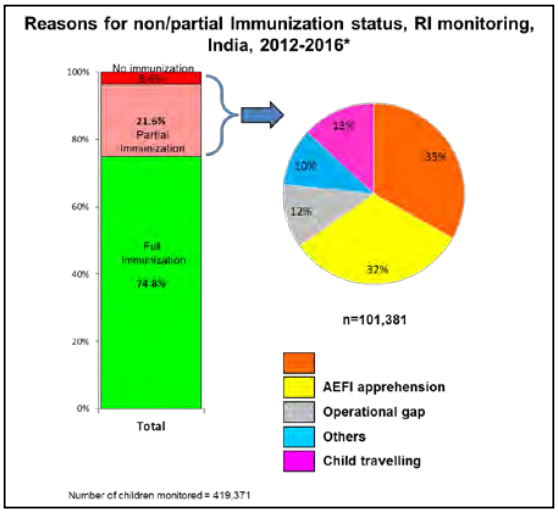
Challenges



Despite steady progress through a variety of improved strategies, the full immunization coverage (FIC) (coverage of all antigens up to one year of age) had improved at a slow rate, with only 1% average increase each year among children aged 12-23 months .i.e. from 35.5% in the first National Family Health Survey (NFHS-1) (1992-93) to 62% in the 4th NFHS-4 (2015-16). Health system strengthening through National Health Mission has provided a major thrust in improvement as is evident from 1.8% annual increase in FIC between NFHS-3, 2005-06 (43.5%) and NFHS-4 (62%) which was only 0.6% between NFHS-1 (35.5%) and NFHS-3 (43.5%).

Although vaccines under UIP are provided free of cost across public health facilities & outreach sessions, still nearly 8 million children in the country do not receive all available vaccines due to demand-supply inequities among different population groups that limit vaccination coverage.

Data for better health outcomes



A more comprehensive review of the NFHS-4 data highlights considerable inequity in full vaccination coverage in different states/union territories, with Puducherry having 91% coverage and Nagaland having as low as 35% coverage, while other factors like gender, birth order, area of residence, wealth, parental education), topography, demography etc. also contributed to inequity. It was also noticed that the improvement in full immunization coverage was more in rural areas (from 39% NFHS-3 to 61% NFHS-4), as compared to urban areas.

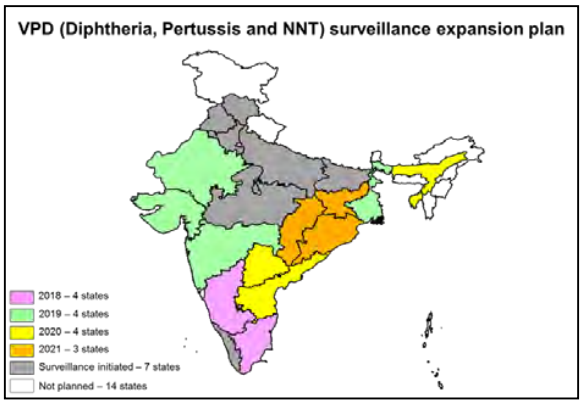
WHO- National Polio Surveillance Project's (NPSP) routine monitoring data also provided information on immunization coverage with some insights into reasons for partial and non-immunization, which shows that lack of information about immunization accounts for two-thirds of these children, and 12% due to operational gaps.

In response to improving immunization coverage and addressing the equity agenda, the Prime Minister and the Ministry of Health & Family Welfare launched a focused and systematic immunization drive 'Mission Indradhanush' (MI) in December 2014 with the objective of rapidly raising national full immunization coverage to 90% by 2020, timeline of which was later advanced to 2018.

MI has been an excellent example of how data plays a crucial role at every stage of implementation of an intervention. MI aimed at covering unimmunized and partially immunized children and pregnant women in pockets of low immunization coverage, hard-to-reach and high-risk areas. A total of 537 districts were covered in the five phases of MI covering 33.4 million children and 8.6 million pregnant women with immunization services. Initially, the districts were identified on the basis of latest available Rapid Survey of Children (RSOC 2013-14) and were categorized as high priority and medium priority on the basis of estimated no. of missed children and were covered in phase-1 and 2 of MI respectively. For the 3rd and 4th phase of MI, triangulation of data was done using WHO concurrent monitoring and national survey data to identify districts to be covered in MI. In the last phase of MI also known as Intensified Mission Indradhanush (IMI), a more elaborate districts wise exercise was conducted where best estimate of coverage of DPT3 was used instead of FIC used in previous phases. This best estimate was arrived at using methodology of 'WHO and UNICEF estimates of immunization coverage' (WUENIC) that utilized administrative data, survey data and monitoring data. On this basis districts fulfilling the following criteria were selected: 1) at least 13,000 children were estimated to have missed DPT3/Pentavalent-3 or; 2) DPT3/Pentavalent 3 coverage was estimated to be less than 70%. These datasets were further analyzed in consultation with the states and partners (WHO, UNICEF, etc.) to further add any districts having weak health systems or those districts from where outbreaks of vaccine preventable diseases had been reported.

In all the phases, daily reporting of coverage was ensured right from session site up to national level (through district followed by state) which was analyzed at all levels on a daily basis to identify the challenges encountered and address the same. Further, more than 2000 monitors from WHO-NPSP, supervisory cadre of govt. and Medical Officers did monitoring of session sites as well as house to house monitoring. IT based monitoring tool was used which is based on of Android-based Open Data Kit (ODK) tool so that the monitoring data was available without delay and could be actually used of corrective action during the ongoing activity.

Using immunization and surveillance data for better decision-making



Despite huge infrastructure for the delivery of vaccines, the programme lacks systems to generate reliable laboratory-supported disease surveillance data to measure the impact of this programme and effectively guide public health interventions.

To assess the overall performance and impact of the immunization programme, laboratory supported case-based surveillance for diphtheria, pertussis and neonatal tetanus is established in seven states, between 2015 and 2018, through joint efforts of the government and WHO. Plans to expand case-based vaccine preventable disease surveillance to other states are ongoing. In addition, nationwide laboratory supported AFP surveillance and measles rubella surveillance is ongoing.

Analysis of the data of VPD surveillance provided valuable inputs on changing epidemiology of diphtheria to higher age-group that helped National Technical Advisory Group on Immunization (NTAGI) to recommend replacement of Tetanus toxoid (TT) with Tetanus and adult diphtheria (Td) vaccine for routine immunization by December 2018.

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Excerpt from the draft 2019 Western Pacific Region (WPR) 28th Technical Advisory Group (TAG) Meeting report summarizing presentations on the draft "Regional strategic framework for vaccine-preventable diseases and immunization in the Western Pacific, 2021-2030"

1.1 Strategic Objective 2. Managing health intelligence on vaccine-preventable diseases and immunization

Strategic objective 2 (SO2) is focusing on health intelligence needed to support the Strategic Goal of Accelerated Control and Elimination of Vaccine-Preventable Diseases (VPD) and to strengthen immunization programmes. SO2 includes 4 focus areas: i) VPD surveillance, which includes epidemiological and laboratory surveillance; ii) laboratory capacity and networks that address building and maintaining laboratory capacity at country level or through international networks; iii) monitoring and evaluation (M&E), which address the need to identify suitable programme performance indicators and collect quality data through various sources to monitor them; and iv) data for action which emphasize the need to analyze and disseminate all the information collected through surveillance and M&E to guide decision making as adequate at all levels. SO2 also contributes to strengthen overall health system and supports efforts towards Universal Health Coverage (UHC) by providing information to identify underserved populations as well as successful service delivery approaches; some Expanded Programme on Immunization (EPI) indicators are included in UHC, International Health Regulations (IHR) and Sustainable Development Goal (SDG) monitoring frameworks. SO2 also contributes to strengthen health security through detection of outbreaks, critical information to guide response, and identification of risks for VPDs transmission.

For M&E some of the strategic directions in 2021-2030 are: to improve quality of data, with disaggregation at subnational level, through approaches that could be undertaken by EPI or in coordination with other health system stakeholder, including integration of EPI data in broader health information systems, and capacity building of health workforce on data-related capacities relevant to each level; engage EPI in understanding and shaping national eHealth strategies and support implementation of Information and Communication Technology (ICT) solutions adequate to country context.

For data for action some of the strategic directions in 2021-2030 are: to build capacity of health workforce on epidemiology and data analysis through approaches that could include pre-service training, on-the-job training, continuous education opportunities; build capacity for critical appraisal of data by systematically including analysis of available data in programme performance reviews and evaluations; conduct rregularly national risk assessments and develop improvement plans accordingly; high-level advocacy and support the national authorities to conduct evidence-based decision making processes, and secure funding and resources to implement mitigating measures/actions as suggested by data.

1.2 VPD surveillance systems: regional goal 2030 and strategic direction

Based on findings from VPD surveillance reviews, observations during outbreak response, analysis of data reported to WHO, and a survey conducted in 2017 survey, all countries in WPR have a surveillance system for measles, rubella and polio, but not all have systems for other VPDs; systems often do not comply with minimum requirements for quality surveillance, as defined by WHO guidelines. While some countries are integrating surveillance for different diseases, VPDs surveillance is often fragmented, vertically organized, leading to excessive cost and workload, and data discrepancies. Overall, across countries in WPR there is large variability of VPD surveillance maturity and performance. Capacity for surveillance is often limited and resources are inadequate. Strategic directions to address these challenges in 2021-2030 include: expansion of quality surveillance to additional VPDs (polio/acute flaccid paralysis, measles, rubella, congenital rubella syndrome, diphtheria, neonatal tetanus and Japanese encephalitis in all countries and additional VPDs based on country context); ensure that integration or optimization of use of resources for VPD surveillance is achieved for one or more of surveillance functions (i.e. specimen transportation, data management, surveillance review, etc.); ensure adequate legal/regulatory frameworks and allocate adequate resources; build capacity through effective pre-service and on-the-job training, including mentoring programmes, distance learning, Field Epidemiology Training Programs (FETP); strengthen laboratory support capacity, particularly for bacterial diseases; support development of ICT solutions adequate to each country context; ensure availability, dissemination and use of surveillance data for action at all levels.

1.3 VPD laboratories and networks: regional goal 2030 and strategic direction

WPRO/EPI coordinates five regional VPD laboratory networks consisting of 500 public health laboratories for polio (43) since 1992, measles and rubella (385) since 2001, Japanese encephalitis (20) since 2009, rotavirus (32) and invasive bacterial-vaccine preventable diseases (20) since 2010. These VPD laboratory networks are facing challenges including, still depending on WHO support; reduced funding that may affect elimination and eradication programmes; funds allocated for specific surveillance programmes; lack of integrated VPD surveillance systems; high workload during outbreaks (e.g., measles), and risk of complacency in polio laboratories due to the absence of poliovirus.

A regional strategy aims to maintain functional and sustainable laboratory surveillance for VPDs through (i) providing technical and financial support to VPD laboratories of priority countries; (ii) implementing Quality Management System (QMS) continuously; iii) promoting the shift of funding from specific diseases to integrated VPD surveillance to allow testing for differential diagnosis; and (iv) improving epidemiological and laboratory surveillance collaboration for VPDs in routine and outbreak situations; applying correct case definition criteria; collecting adequate specimens, and using appropriate laboratory resources.

Executive Summary: Polio

Background

In 2019, the polio eradication program has experienced an increase in detections of paralytic cases caused by Wild Poliovirus Type 1 (WPV1) as well as an unexpected increase in number of outbreaks and cases of circulating vaccine derived polioviruses (cVDPVs). Despite these setbacks, the program has been able to keep Africa free of WPV1 for >3 years; and WPV type 3 is now considered eradicated globally.

As of 21 August 2019, there have been 66 wild poliovirus (WPV) cases, compared with a total of 33 in the whole of 2018. WPV cases have been located in Afghanistan: 13 cases in 2019 (compared with 11 for the same period in 2018), and Pakistan: 53 cases in 2019 (compared with 3 for the same period in 2018). Additionally, there is wide-spread detection of WPV in environmental surveillance in both Pakistan and Afghanistan; and repeated environmental detections of WPV1 in Iran, most likely a result of importations from Pakistan. Further, there have been 53 cases of circulating vaccine-derived poliovirus (cVDPV), vast majority of them detected in sub-Saharan Africa. Most of these new cVDPV2 outbreaks were seeded by monovalent OPV2 (mOPV2) which had been used to respond to preceding cVDPV2 outbreaks. Thus, there is an urgent need for a new type 2 vaccine.

Because of the ever-expanding outbreaks of cVDPV2 in Africa, the world is running out of mOPV2. While sufficient supplies of mOPV2 are absolutely critical in the next 12-18 months, the best approach to deal with cVDPV2, is the development and regulatory approval of a novel OPV2 (nOPV2) that is currently in phase II clinical trials. Clinical data demonstrated that nOPV2 provides equal or better immunogenicity compared with mOPV2, and a substantially lower risk of seeding new VDPV2 due to higher genetic stability. The results of these trials will be used to apply for WHO's Emergency Use Listing (EUL) in early 2020. Any delay in EUL approval will seriously delay addressing the cVDPV2 problem and could undermine donor confidence.

To overcome an acute shortage of mOPV2, we explored strategies to stretch current mOPV2 supply, including using one instead of two drops as an immunizing dose. A clinical trial was conducted in Mozambique to assess immunogenicity of one drop of mOPV2.

Purpose of the session and summary

This session will consist of three presentations: (1) global epidemiological overview including presentation of the main areas of concern and new strategies for outbreak control, (2) brief summary of preliminary clinical results from nOPV2 trials; and (3) report from deliberations of SAGE Polio Working Group which will include brief presentation of results from mOPV2 one-drop trial.

For this SAGE meeting, there are two items for decision/endorsement: endorse call for acceleration of clinical development and licensing of nOPV2 vaccine; and endorsement of one-drop mOPV2 strategy if mOPV2 supply should further deteriorate.

In addition, SAGE members will be invited to comment on the progress of polio eradication and on challenges and strategies to overcome the remaining obstacles to achieving final eradication.

Background documents in the yellow book

- Report from meeting of SAGE WG on polio (held on August 21-22, 2019)
    - This report provides summary of the deliberations of the SAGE Working Group

- Summary of preliminary results from clinical trials on safety and immunogenicity of novel OPV2 (nOPV2) [SAGE will be asked to deliberate and endorse acceleration of nOPV2 clinical development and licensing]
    - This summary will provide information on the clinical data from nOPV2 trials that show its immunogenicity, safety, and genetic stability

- Summary of preliminary results from clinical trial on safety and immunogenicity of one-drop mOPV2 administration [SAGE will be asked to deliberate on and endorse use of one-drop mOPV2 in times of supply scarcity]
    - This summary will provide information from a trial in Mozambique

Background documents on the web

    - None

21-22 August 2019

18th Meeting of the SAGE Polio Working Group

Conclusions and recommendations

Note for the Record

World Health Organization

Background

The 18th face-to-face meeting of the SAGE Polio Working Group (WG) was held on 20-21 August, 2019 at the World Health Organization HQ in Geneva, Switzerland.

Dr. Ilesh Jani and Dr. Peter Figueroa co-chaired the meeting. Agenda and the List of Participants are attached as Annexes. This note presents a summary of the discussions and recommendations.

Context and topics

1. To review the GPEI programme update, including the WPV and VDPV epidemiology.
2. To take note of the specific challenges of eradicating WPV1 in Afghanistan and Pakistan and discuss potential solutions for acceleration of eradication.
3. To review scenarios for cVDPV2 outbreak response including OPV2 vaccine restart in routine immunization.
4. To review options for IPV only vaccination schedules in polio free regions.
5. To review results from one-drop mOPV2 study and, if positive, consider endorsing its use.

Summary of the meeting conclusions and recommendations

The WG expressed serious concerns with the status of the eradication program and the inadequacy of currently available tools, specifically: the ever-expanding outbreaks of circulating vaccine derived poliovirus 2 (cVDPV2) in Africa in the context of decreasing population immunity with sustained cVDPV2 transmission (>6 months) in Nigeria, Niger, Democratic Republic of Congo and Somalia; and the limited supply of mOPV2 vaccine to control these outbreaks. WG agreed that there is urgent need for a more genetically stable OPV2 vaccine (the novel OPV2 vaccine (nOPV2)) and agreed with the imperative to accelerate its clinical development and licensure.

The increased circulation of wild poliovirus 1 (WPV1) in Pakistan and Afghanistan, bans on vaccinations, and increasing community resistance to vaccination constitute another serious challenge to the program. These developments run the risk of undermining the entire polio eradication effort. There is an urgent need for the development of new strategies and tools.

The WG acknowledged the positive developments in polio eradication. There has been no WPV3 detected globally since November 2012, and no WPV of any serotype detected in the Africa continent since September 2016 while increased surveillance sensitivity in Nigeria was achieved. The introduction of at least one dose of IPV into routine immunisation of all OPV-using countries has been completed, with catch-up vaccination starting for the approximately 43 million children that did not receive IPV due to supply constraints. The WG noted the significant decrease in the estimated incidence of vaccine-associated paralytic poliomyelitis (VAPP) cases since the introduction of IPV and switch from tOPV to bOPV (a decrease estimated at 244 VAPP cases annually). Lastly, there is continued support from Gavi, The Vaccine Alliance, for the inactivated poliovirus vaccine (IPV) and in the future for IPV-containing whole-cell pertussis hexavalent vaccine.

Summary of key WG recommendations from 18th Meeting:

WG took an unprecedented step to brief WHO's Director General and ask him for immediate actions based on the recommendations below.

1) **The WG was extremely concerned over the deterioration of the program in Afghanistan and Pakistan. Polio eradication must be prioritized in these countries**. The number of WPV1 cases in Afghanistan and Pakistan has already surpassed 2018 totals, and will likely increase in the second half of 2019. There is an immediate risk of WPV1 exportation to neighboring countries (as demonstrated by repeated detections of WPV1 in environmental samples in Iran). High-level advocacy and immediate action to ensure government and community commitment is required in Pakistan and Afghanistan as well as in the neighbouring countries.

2) **The WG was extremely concerned over the cVDPV2 outbreaks in sub-Saharan Africa. An effective response to cVDPV2 outbreaks is essential.** The quality and time of the response by countries in Africa to outbreaks of cVDPV2 must improve. The WG agreed with the Cessation Risk Task Team (CRTT) on the necessity of changes to the Standard Operating Procedures (SOPs), which will be revised, on scope, quality and timeliness of the mOPV2 response.

3) **Recommended steps to secure adequate mOPV2 supply**. The WG stated that it is essential to ensure an un-interrupted supply of mOPV2, for short-term use to control outbreaks and contingency plans. The WG recommend:
   a) Urgently identify sites capable of Fill and Finish of existing mOPV2 bulk for utilisation.
   b) Restart bulk production of mOPV2, given the 15-18-month lead time required by manufacturers.

   The WG acknowledge that these activities are off-budget and the GPEI needs to come up with the resources/funding.

4) **Clinical development and Emergency Use Licensure (EUL) of nOPV2.** While sufficient supplies of mOPV2 are critical in the next 12-18 months, the ultimate solution to deal with cVDPV2 is the development and licensure of nOPV2. Current phase I/II clinical data demonstrate that nOPV2 is safe, immunogenic and genetically stable. The WG support the accelerated clinical development of nOPV2 and endorsed the accelerated assessment of nOPV2 under Emergency Use Listing (EUL). The WG acknowledged that at this stage of clinical development there are still some risks for nOPV2 development, which are estimated to be small, including the risk of reversion and immunogenicity in an outbreak setting, and that there are contingency plans in place with mOPV2 production. The WG emphasise that new serotype 1, 2 and 3 OPVs will not replace IPV in routine immunisation and is ultimately still not compatible with eradication of all polioviruses due to the very low but likely not zero risk of reversion of these more stable OPV strains.

5) **One vs two drop of mOPV2.** The WG recommended that the preference is to use two-drops (the standard dose) of mOPV2 vaccine. However, in the event that mOPV2 supply deteriorates to levels inadequate to cover the required population, the off-label use of one drop mOPV2 could be considered. This is based on data from a single, small clinical trial in Mozambique which showed a minor decrease in immunogenicity of one vs two-drop administration but given the small sample size, the 10% non-inferiority margin could not be statistically confirmed.

6) **The WG is concerned that bOPV SIAs are being cut due to budget limitations**. The WG recommends countries experiencing cVDPV2 outbreaks do not forget about the importance of SIAs with bOPV to prevent poliovirus type 1 and 3. To improve type 1 and type 3 immunity, combined administration of bOPV and mOPV2 during campaigns should be considered.

7) **IPV allocation criteria**. The WG recommended an updated prioritization order for IPV allocation:
   a) Ensure routine immunization needs in all countries are met.
   b) Allocate to the populations that are IPV-unvaccinated since the switch, due to IPV supply shortages, based on risk assessment.
   c) Ensure requirements for the acceleration of the interruption of wild poliovirus transmission are fully met (requests from endemic countries for SIAs to interrupt WPV).

Minutes of the meeting and SAGE WG recommendations

Day 1
21 August 2019

Welcome and opening remarks
WG Chair

The WG and WHO secretariat announced that Dr Jacob John has withdrawn as a WG member. The group acknowledged the substantial contribution that Dr Jacob John made to polio eradication in India and globally over his career.

Programme update
M. Zaffran, WHO

On 14 May 2019, polio was reconfirmed as a Public Health Emergency of International Concern (PHEIC), ongoing since May 2014.

As of 21 August 2019, there have been 66 wild poliovirus (WPV) cases, compared with a total of 33 in 2018. WPV cases have been located in Afghanistan: 13 cases in 2019 (compared with 11 for the same period in 2018), and Pakistan: 53 cases in 2019 (compared with 3 for the same period in 2018). Additionally, there is wide-spread detection of WPV in environmental surveillance in both Pakistan and Afghanistan. As of 21 August 2019, there have been 53 cases of circulating vaccine-derived poliovirus (cVDPV). There has been continued detection of cVDPV2 in sub-Saharan Africa, with multiple emergences of new cVDPV2 outbreaks seeded by monovalent OPV2 (mOPV2) outbreak response campaigns.

Priority activities for the Global Polio Eradication Initiative (GPEI) were outlined as:

Global
- Mobilise resources to rapidly and fully finance the program

Endemic countries (WPV)
- High level Political advocacy with Pakistan to reset the program
- Fully staff and operationalize Pakistan/Afghanistan hub
- Resume vaccination in Afghanistan

Outbreak Countries (cVDPVs)
- Radically improve speed and quality of vaccination responses
- Secure sufficient quantities of mOPV2 for stockpile (identify new Fill and Finish capacity)
- Accelerate development and EUL of nOPV2
- Further improve surveillance in all outbreak countries and beyond
- Collaborate with EPI to build capacity to mitigate risks

IPV Supply update and update on mOPV stockpile
A. Ottosen, I. Lewis

IPV supply:
At the 16th meeting of the WG in September 2018, the prioritization order for IPV allocation was recommended as follows:

I. *Ensure that routine immunization needs in all countries are met. At the same time, ensure national and sub-national monitoring of IPV stocks.*
II. *Ensure requirements for interruption of wild poliovirus transmission are fully met (requests from endemic countries for SIAs to interrupt WPV).*
III. *After these 2 requirements, excess doses should be allocated to populations that are IPV-unvaccinated since the switch, based on risk assessment.*

As of 2019, at least one dose of IPV has been introduced into routine immunization (RI) in all countries. The overall availability of IPV is increasing: in 2019, supply fully meets requirements for RI, supplementary immunization activities (SIAs) in endemic countries, and for catch up campaigns in 5 priority countries. It is forecasted that there will be sufficient supply for the majority of countries to be offered IPV for catch-up campaigns in 2020, and a gradual move from 1 dose to 2 doses in RI in countries can start from 2021.

mOPV2 supply:
A total of 303 million doses (Mds) of mOPV2 have been deployed since April 2016. Current stock levels are at 58Mds, with +200Mds for supply secured for the next 12 months. Due to on-going cVDPV2 outbreaks, the projected mOPV2 demand can't be met in 2020 with current suppliers. Securing filling, licensure and prequalification of mOPV2 from alternative supplier(s) in 2020 of 160-295Mds would achieve the goals. The decision and funding are urgently needed to ensure timely availability in 2020.

- The mOPV2 bulk in the stockpile – in the understanding funded by GPEI and kept under contract – which is not currently in process of being converted into finished product against awards, amounts to 220Mds
- mOPV2 bulk outside of the stockpile – available to be procured for addition to the stockpile, released by the NRA of producing country – is 500Mds.

Discussion:

- There was consensus in the WG that the prioritization order for IPV allocation recommended in September 2018 should be updated, based on the evolving cVDPV2 epidemiology, program experience and time since OPV2 withdrawal.
- The WG recommended an updated prioritization order for IPV allocation:
    a) Ensure routine immunization needs in all countries are met.
    b) Allocate to the populations that are IPV-unvaccinated since the switch, due to IPV supply shortages, based on risk assessment.
    c) Ensure requirements for the acceleration of the interruption of wild poliovirus transmission are fully met (requests from endemic countries for SIAs to interrupt WPV).

- The WG stated that it is essential to ensure an un-interrupted supply of mOPV2, for short-term use to control outbreaks and contingency planning. The WG recommend immediate action on:
    1. Fill and Finish of existing mOPV2 bulk for utilisation.
    2. Restart the bulk production of mOPV2 for contingency plans, given the 15-18-month lead time required by manufacturers.

  The WG acknowledge that these activities are off-budget and the GPEI needs to come up with the resources/funding.
- There was a discussion on the containment of PV2 and the implications on mOPV2 vaccine production. It was emphasised that containment is a key strategy developed by the GPEI, with significant progress made over the past few years, and something that is essential for eradication. Containment is not inflexible and is developed to minimize polio risks, which can accommodate and advise on the best approach for mOPV2 production. However, containment is not just about vaccine production facilities, but all poliovirus-containing facilities, and is a global issue. The GPEI containment management group, the containment working group and the containment advisory group have been working together to achieve bio-risk management and ensure that mOPV2 can be produced to meet programmatic needs, in a secure environment.

Update on IPV catch-up campaigns
A. Ramirez Gonzalez

Globally, approximately 42 million children were missed in 36 countries due to supply shortages. Analyses showed that coverage of one dose of IPV through RI tends to improve following the first 1-2 years of introduction. However, on average it continues to be low compared to coverage of DTP3 (diphtheria, tetanus toxoids and pertussis vaccine third dose) and might have resulted in approximately 98 million children missed in the last 3 years. This was not due to vaccine shortage but due to poor EPI performance.

Based on a risk assessment by Imperial College London, prioritization and allocation of available supply for catch-up immunization has started in 2019. Doses have been made available for Angola, Liberia, Sudan, Iran, Tanzania, and Zambia and additional countries have conducted catch ups without global support. Therefore, 35% of the cohort missed due to IPV shortage could be completed by end 2019.

Discussion:
- The WG welcomed the fact that catch-up campaigns have started in countries with prioritization based on the risk assessment.
- The WG stated that it is important that every child receives at least one dose of IPV.
- The WG also welcomed that the IPV catch-up campaign in Tanzania was combined with a measles vaccination campaign.
- It was noted that Angola is considering an IPV/mOPV2 combined campaign, as they are conducting both catch-up IPV campaigns and responding to cVDPV2.
- It was highlighted that when introducing a new vaccine into RI, it often takes a couple of years to reach the coverage levels achieved by reference, established

vaccines. However, if we continue to see low coverage of IPV compared to DTP3 in the next few years, specific initiatives to improve coverage may be required.

Presentation on challenges in last WPV1 endemic areas
J. M. Olivé/ Ch. Maher (absent)

Following a request at the 17th SAGE WG meeting, a more in-depth review of the program challenges in Pakistan and Afghanistan was presented to the WG.

In Afghanistan, there has been a ban on house-to-house campaigns from May 2018 and a ban in May 2019 on WHO activity in the country. The first SIA campaign after the WHO activity ban, conducted in August 2019 had 50.6% target missed, due to issues of access. However, the number of detected WPV1 cases has not yet increased despite surveillance even in compromised areas.

In Pakistan, there have been significant challenges in 2018-2019 resulting in vaccine resistance at the community level. Following an increasing number of security incidents involving health-care workers, there is a pause in SIAs from April to November 2019. The opportunity presented by the SIA pause should not be missed to regain and improve on the capacity in Pakistan from 2014-2018 and correct identified gaps.

Discussion:

- The WG expressed serious concern over the program in Afghanistan and Pakistan.
- It was discussed that the pause of SIAs in Pakistan until November 2019 provides an opportunity for rebuilding the program and community engagement.
- The WG highlighted the risk of exporting WPV1 to neighboring countries, demonstrated by the recent exportation to Iran. An exportation to Yemen, Syria or Iraq, could lead to WPV1 outbreaks due to the weak healthcare systems in those countries.
- The WG recommend it is essential to ensure polio eradication is prioritized in Afghanistan and Pakistan. High-level advocacy and immediate action to ensure the community commitment is required in the endemic countries as well as in the neighbouring countries.

Update from the Cessation Risk Task Team (CRTT)
J. Wenger

This presentation provided an Update from the Cessation Risk Task Team (CRTT), who met on 19-20 August 2019 to discuss current cVDPV2 epidemiology, potential future scenarios for cVDPV2 outbreaks, methods to control outbreaks including the potential role of new, more stable oral vaccines (nOPVs) and criteria for the restart of tOPV production and use. The summary of the CRTT meeting, and areas to discuss with the SAGE polio working group, were outlined:

1. Communication of emergency cVDPV2 situation
2. Accelerating development, licensure and production of nOPV2
3. Innovation required to implement effective outbreak response now

a. Change mOPV2 response strategy
b. Studies of simultaneous mOPV2/bOPV administration
c. Evaluation of single drop mOPV

4. mOPV2 supply (need to restart bulk production and filling)

Discussion:

- The SAGE WG stated that the cVDPV2 situation is an emergency of unprecedented nature. The current strategy is not working and current tools are inadequate.
- There was consensus amongst the WG that the main conclusions and action points presented by the CRTT were comprehensive and appropriate.
- The WG recommended that changes in strategy of outbreak response will be reflected in revised standard operating procedures (SOPs).
- It was highlighted that simultaneous mOPV2/bOPV administration may cause confusion amongst vaccinators and could have a risk of interaction between vaccines. CDC is planning a trial to study simultaneous mOPV2/bOPV administration. In the study design, the field team composition will change to include an additional vaccinator and 2 finger markings will be used. Within the study CDC also intend to do a clinic-based investigation with seroprevalence to see if there is any interaction effect when vaccines are administered concomitantly.

Reducing Outbreak Risks Associated with Oral Polio Vaccine Withdrawal
J. Vertefeuille

A pathway to mitigate cVDPV1 and cVDPV3 risks in advance of bOPV withdrawal was proposed, incorporating the lessons learnt from the 2016 OPV2 withdrawal. The budget cuts in SIAs to medium-high risk countries could result in emergent cVDPV1 and 3 in the near or medium term and increased vulnerability to WPV1. Risk mitigation efforts through rigorous preventative SIAs should target the highest risk districts in highest risk countries. These efforts should be combined with broader vaccine-preventable disease gains.

- The WG welcomed the proposed pathway to reducing outbreak risks, through focusing on the highest risk geographies. The WG agreed with the critical need to learn from post-switch experience to better prepare for OPV cessation.
- The WG was concerned over the reduction in preventative SIAs leading to a risk in cVDPV1 and cVDPV3 outbreaks and WPV1 vulnerability. The WG recommended that those countries effected by cVDPV2 and conducting mOPV2 campaigns do not overlook bOPV SIAs.
- The WG approved of the approach to combine preventative SIAs with vaccines or other health interventions in these vulnerable populations that are often hard to reach.

Consideration for IPV only schedules for polio-free regions
R. Sutter

The continued use of OPV has a risk of VAPP and VDPV emergence and therefore, some polio-free regions are considering regional implementation of IPV-only schedules. Since 2016, SAGE guidance is available for countries moving to IPV-only schedules. This raises the

question whether there should be criteria to guide Regions/Sub-Regions to adopt all IPV schedules. In addition, it was highlighted that SAGE could update guidance on IPV-only schedules for pre-cessation of all OPV use and post-cessation.

Discussion points:

- In WPRO there has been no WPV for almost 20 years; however, the cVDPV1 outbreak in Papua New Guinea in 2018 cost more than USD 30 million to control. This has started discussions in WPRO over whether IPV-only schedules should be implemented across the region, to prevent VDPV outbreaks.
- Previous SAGE recommended schedules are: post-OPV cessation schedule: 2-dose IPV schedules (14 weeks and 9 months); and SAGE early schedule: 3-4 dose IPV schedule administered at 6, 10, 14 weeks and ≥9 months, or 2, 4, 6 months.
- There was consensus that it is necessary to update the WHO polio vaccine position paper, including to provide guidance for a 2 dose IPV schedule prior to OPV cessation.
- Since there are no tailored IPV-only schedules, especially for the polio-free Regions (from now until all OPV cessation), the WG needs to review this need in the future meetings

Day 2
22 August 2019

nOPV2 and nOPVs 1&3
J. Modlin

The preliminary data from the two Phase II nOPV2 clinical trials were reviewed – a) study in adults conducted in Antwerp, Belgium and b) study in infants and toddlers in Panama. To date, there are no safety signals and both nOPV2 candidate strains appear immunogenic. Both candidates replicate in the human gut as expected. The planned regulatory pathway for nOPV2 includes pre-licensure via WHO Emergency Use Listing (EUL), and eventually licensure (Badam POM) and WHO pre-qualification.

Outline of clinical development of novel OPV 1 and 3 were presented.

- The WG welcomed the availability of preliminary data from the adult, toddler and infant trials of both nOPV2 candidate vaccines.
- The WG supported the clinical development of nOPV2 and recommended the accelerated assessment of nOPV2 under EUL.
- The WG acknowledged that there are risks associated with nOPV2 development, and contingency plans that include mOPV2 production must be put in place.
- The WG emphasised that nOPV will not replace IPV in routine immunisation and nOPV2 ultimately still not compatible with eradication of all polioviruses.
- There was discussion that there will be a time when nOPV2 and mOPV2 are both available for outbreak response in the global stockpile, and it will be necessary to decide where the available nOPV2 doses should be prioritised.

Update on Antiviral development
J. Modlin

An update on the development timeline was provided for the two antiviral drugs against poliovirus: Pocapavir and V-7407.

Discussion:

- WG agreed that development of polio antivirals is a priority in addressing chronic poliovirus infections among immunodeficient persons
- The highly active antiretroviral therapy (HAART) for treatment of human immunodeficiency virus (HIV), requires the combination of multiple antivirals to prevent resistance developing. Therefore, it shouldn't be assumed that combination of two poliovirus antivirals will be fully effective to prevent resistance.

Results from mOPV2 one-drop immunogenicity study
O. Mach

A randomised control trial was conducted to compare humoral immunogenicity for poliovirus 2 after one dose with either 1-drop or 2-drop administration of mOPV2. The study was carried out in 360, 9-22-month-old children residing in Mocuba, Mozambique, during the mOPV2 outbreak response campaign in 2019. The immune response was 53.6% (CI: 95%: 44.5–62.6) for 1 drop vs 60.3% (CI: 95%: 56.1–73.4) for 2 drops. Due to high drop-out rates, the final study size was underpowered to confirm or not whether 1 drop was non-inferior to 2 drops with a 10% margin.

Discussion:

- There are no plans for an additional study, due to the difficulty of conducting a study with mOPV2 under containment.
- It is important to consider the potency of the vaccine product when considering one or two drops. This study was conducted with a medium-potency vaccine from a single supplier.
- The WG recommended that the preference for mOPV2 vaccination is to use two-drops (the standard dose) of vaccine. However, in the event that mOPV2 supply deteriorates to levels inadequate to cover the required population, the off-label use of one drop mOPV2 could be considered as a measure to stretch mOPV2 supply.
- WG recommended that GPEI should establish a minimum level of mOPV2 stocks which would avoid the need for one-drop use.

Update on decisions regarding IPV/Hexa financing
GAVI, The Vaccine Alliance.

In June 2019, the Gavi determined the post-2020 IPV support modality and approved principles of IPV support and investment options. The scope consists of 70 currently IPV-supported countries, for 10 years of support following global bOPV cessation with different levels of financial contributions. Guidance from the SAGE is required on pre-cessation IPV 2 dose immunization schedule and wP Hexavalent vaccine schedules.

Discussion:

- The WG welcomed the continued support of IPV by GAVI.

VAPP analysis
G. Macklin

A refined analysis of VAPP (vaccine associated paralytic-poliomyelitis) burden was requested by the WG at the 17th WG meeting in February 2019. VAPP is a rare but serious consequence of the administration of OPV. The global VAPP burden in 2019 was estimated to be 168 cases per year, reduced from 400 prior to IPV introduction and OPV2 withdrawal. The introduction of IPV into RI has significantly reduced the incidence of VAPP from any serotype. The removal of OPV2 has reduced the incidence of VAPP2 to zero (in countries with no mOPV2), but is likely to have led to an increase in VAPP1 and VAPP3 because of the greater immunogenicity of these serotypes in bivalent versus trivalent OPV.

Discussion:

- The WG welcomed the refined analysis and the reduction in VAPP incidence with IPV introduction.
- It was requested that estimates of the reduction of VAPP cases since the introduction of IPV and removal of OPV2 from routine immunisation is shared for communication.
- There was discussion over the underlying reason for an increase in VAPP1 and VAPP3 after the switch from tOPV to bOPV, observed in the data.
- The definition used for VAPP in this analysis – an AFP case with residual paralysis at 60 days follow up, and excretion of Sabin-like virus – is not a confirmation of poliovirus-induced paralysis; therefore, there will be an underlying rate of AFP not caused by poliovirus vaccine.

SAGE Meeting, October 2019
Polio the last mile-Session 9

Presentation of clinical data from nOPV2 trials and plan for EUL
A. Bandyopadhyay
Bill & Melinda Gates Foundation

Synopsis

Background:

The epidemiology of type-2 vaccine-derived poliovirus (VDPV2) circulation in recent months was markedly different than anything seen since the switch, with continued circulation and spread of some outbreaks in Africa and numerous independent emergences of cVDPV2 in areas not included in an mOPV2 response area. The current strategy has not been successful in eliminating VDPV2 transmission and emergence. The uncontained emergence and on-going spread of VDPV2 viruses have led to an urgent need to accelerate development and maximize availability of novel OPV2 (nOPV2).

In the nOPV2 vaccine development program we are studying two live, attenuated poliovirus candidate vaccines derived from Sabin monovalent OPV2 (mOPV2). Both candidate vaccines are designed to stimulate the production of serum neutralizing antibodies and induce mucosal immunity to type 2 polioviruses. The goal of the project is product licensure and WHO prequalification of the final nOPV2 candidate in the context of control of outbreaks. The final candidate vaccine should be immunogenically non-inferior to mOPV2 and more genetically stable (less neurovirulent with fewer key mutations based upon deep sequencing), with an acceptable general safety profile. The clinical development plan provides data from adult populations with varying prior polio vaccine exposure and, based on the safety in adults, has now advanced to testing in young children and infants.

Given the cVDPV2 situation has been designated as a Public Health Emergency of International Concern, and the increasing risk of seeding new emergences with use of current mOPV2, enabling pre-licensure use of nOPV2 through early clinical data generation, at-risk manufacturing at scale, and submission for WHO Emergency Use Listing (EUL) is considered a high priority of the global eradication program.

Clinical Development and EUL pathway:

Prior to global cessation of Sabin OPV2 use in 2016 and prior to the availability of nOPV2 candidate vaccine for clinical trials, phase 4 clinical trials (Belgium, Panama) were conducted with mOPV2 to provide data for comparison with nOPV2 evaluated in later trials. To maximize comparability of safety, immunogenicity, and genetic stability data, the mOPV2 phase 4 trials were designed to parallel the expected design of the phase 1 and 2 nOPV2 studies with respect to overall design, endpoints, location and study populations and employed the same laboratory for the polio serologic and viral shedding assays. For studies aligning with the nOPV2 development plan (M1 and M2) serologic samples were reserved to be assayed alongside corresponding nOPV2 samples, in a blinded fashion.

A phase 1 study (M4a) in adults (15 adult participants each receiving either nOPV2 candidate 1 or nOPV2 candidate 2), conducted under biological containment in Belgium in 2017, provided an initial assessment of clinical safety, immunogenicity, and the genotypic and phenotypic stability of shed vaccine virus in exclusively IPV-vaccinated adults (*Van Damme, P., De Coster, I., Bandyopadhyay, A. S., et al. The safety and immunogenicity of two novel live attenuated monovalent (serotype 2) oral poliovirus vaccines in healthy adults: a double-blind, single-centre phase 1 study. The Lancet. 2019*). Since the primary intent of

this study was to gather information on safety and the profile of shed virus, a relatively high dose (10^6 $CCID_{50}$ [50% cell culture infectious dose]) was used for this study. In general, the safety data were reassuring, and there were no serious adverse events reported. In M4a, immune responses to both candidates were observed despite the high baseline titers in the previously IPV-vaccinated subjects. Median rise in neutralizing antibody titer was 8.0-fold for candidate 1 and 12.7-fold for candidate 2. In addition, fecal shedding of the candidate vaccine viruses was observed in most participants for both candidates. The median time to shedding cessation, defined as the first instance of three consecutive PCR-negative stool samples, was 23 (95% CI: 13, 35) days for candidate 1 and 12 (95% CI: 1, 14) days for candidate 2. In this study, virus shed in participants' stools was assessed for genetic stability by two methods: a mouse neurovirulence test and deep sequencing. The modified transgenic mouse neurovirulence test (mTgmNVT), was used to assess the potential neurovirulence of shed virus and the administered candidate vaccine. No meaningful increases in neurovirulence were detected in any samples compared to the administered candidate. Deep sequencing was conducted on the shed virus to provide supportive information for genetic stability of the candidates, primarily by demonstrating retention of key genetic modifications. Deep sequencing analyses generally support the neurovirulence observations. For both candidates, no variants known to be consistent with increased virulence were detected in domain V of the 5' untranslated region, the site of the primary determinant of attenuation for Sabin OPV2 (nucleotide 481).

In addition to the completed dataset from M4a, preliminary, partial results are available from the subsequent, larger study (M4) in adults in Belgium that was implemented without containment, and an on-going study (M5) in toddlers (1 – 5 year) and infants (18 – 22 weeks) in Panama. Consistent with the first-in-human study, review of safety data by an independent data safety monitoring board supported progression into young children and then infants. For humoral immunogenicity, both the adults in M4 and toddlers in M5 generally showed high seroconversion rates when administered a 10^6 $CCID_{50}$ dose. Immunogenicity data from infant cohorts receiving 10^5 or 10^6 $CCID_{50}$ doses will be available later this year. Shedding post-vaccination with nOPV2 in adults was also consistent with prior observations with mOPV2. Results on genetic stability and neurovirulence of the shed vaccine virus from M4 and toddlers in M5, alongside comparative data from the historical control trials, are expected to be available over the next few months.

Conclusions:

Overall, the pre-clinical and clinical data generated so far are supportive of further clinical development for both candidates and prioritization of one candidate for initial EUL submission and stockpile production at-risk with an aim to have maximum possible volume of one of the nOPV2 candidates in the shortest possible time-frame, the target being by Q2-Q3 2020. We anticipate that data available in early 2020 should be sufficient to conduct a relative benefit-risk assessment for the selected candidate against mOPV2. Provided the data are sufficient to support an EUL approval, this assessment, the current epidemiological context, and information on supply of nOPV2 and mOPV2 should help inform a policy position on use of these vaccines.

Summary of PRELIMINARY results ahead of print:
Immunogenicity of mOPV2 administered as 1-drop or 2-drops

Background

Africa has experienced several outbreaks of circulating vaccine-derived poliovirus type 2 (cVDPV2) since the switch from trivalent oral poliovirus vaccine (tOPV) to bivalent (bOPV) without the type 2 component [1]. The scope and number of these outbreaks have been higher than what had been predicted. Therefore, a stockpile of monovalent OPV type 2 (mOPV2) that was created to respond to these outbreaks is now running low. GPEI is at risk of exhausting all available mOPV2 stock in early 2020. While new mOPV2 manufacturing capacities are being explored; and while development of new genetically stable OPV2 vaccine (nOPV2) is accelerated, alternative strategies to stretch existing supplies of mOPV2 are being explored. One such strategy is use of one drop of the vaccine instead of two drops as an immunizing dose. Here we present preliminary results from a trial conducted in Mozambique between March and July 2019 on comparison of immunogenicity of mOPV2 administered as 1-drop or 2-drops.

Scientific Justification

The recommended titer of Sabin type 2 virus in one dose (2 drops) of tOPV or mOPV2 is 10^5 +/- 0.5 log TCID 50 (50% Tissue culture Infective Dose). But the testing results show that the antigenic content is exceeded in most batches by 2-4 times of this minimum cut off.

This “overdose” of virus content is built in intentionally in the final formulated mOPV2 batches to compensate for any loss of titre with heat exposure and as well as for variation in testing results. We believe that at least double the quantity of Sabin virus above the standard recommended content remains up to the point of administration.

We therefore hypothesized that half of the conventional dose of 2 drops of the vaccine (i.e. 1-drop) will provide sufficient immunogenicity while providing opportunity to successfully vaccinate double the amount of children with the same amount of vaccine.

Methods

We enrolled children between the ages of 9 and 22 months. These children were naive to live type 2 poliovirus. Some of them received one dose of IPV prior to this study.

The study design was a parallel, open label, two-arm, randomized controlled trial where one arm received one drop of mOPV2 and the other arm received 2 drops. This was a non-inferiority trial to demonstrate non-inferiority with delta=10%.

Blood samples were collected at visits 1 (prior to mOPV2 administration) and at visit 2 (one month post mOPV2 administration). The samples were transported in cold chain to CDC Atlanta, USA, tested using standard micro-neutralization assay to measure titers of antibodies against poliovirus types 1, 2 and 3.

The primary outcome was seroconversion which was defined as change from non-detectable to detectable antibodies in children with no detectable antibodies at visit 1 (baseline). If children had detectable antibodies at baseline, boosting was calculated which was a 4-fold rise in antibody titer from visit 1 to visit 2. Immune response was defined as either seroconversion or boosting [2].

The study coincided with the mOPV2 campaign in Mozambique in response to cVDPV2 outbreak in that country. This was done to satisfy containment requirements regarding use of mOPV2. This provided a limitation on the number of children we were able to enroll; which in the end limited the power of the study.

Results

Baseline characteristics of the study population are in Table 1.

Table 1: Baseline characteristics

Baseline characteristics	1-drop		2-drops	
Median Age in months, median, (IQR)	14, (11-18), n=184		14, (11-17), n=191	
Sex, (Male) (n/N %)	n/N 92/184	% 50.0	n/N 104/191	% 54.2
bOPV dose history (based on cards) 0 doses 1-3 doses >3 doses	 11/163 76/163 76/163	 6.8 46.6 46.6	 4/159 75/159 80/159	 2.5 47.2 50.3
IPV history (based on cards) Yes	 106/138	 76.8	 114/133	 85.7
Diarrhea in the 24 hours before visit 1	1/182	0.5	3/190	1.6
Median baseline titers Type 1* Type 2* Type 3*	 ≥10.5 (10.2-≥10.5) 3.3 (<3-3.5) 9.8 (9.2-10.2)		 10.2 (10.2-≥10.5) 3.2 (<3-3.5) 9.8 (9.5-10.2)	

*Note: Bootstrap confidence intervals

Table 2 provides the primary outcome findings. The seroconversion rates in 1-drop was (35/54) 65% (95% CI: 51 to 77) while 2-drops was (50/74) 68% (95% CI: 56 to 78). The difference between 1-drop and 2-drops seroconversion was -3% (-19 to 14). Boosting was 45% (33 to 57) in 1-drop; 52% (39-65) in 2-drops (Difference = -7% (-24 to 11)); Immune response: 54% (45 to 63) in 1-drop vs 60% (56 to 73) in 2-drops (difference = -7% (-19 to 5)).

There were no differences observed in the distribution of pre and post titers of type 2 antibodies between the one- and two-drop groups.

Table 2: Primary outcome

Results	1-drop			2-drops			Difference (95% CI)
	%	95%CI	n/N	%	95%CI	n/N	
Seroconversion	**64.8**	50.6 – 77.3	35/54	**67.6**	55.7 – 78.0	50/74	-2.8 (-19.4, 13.8)
Boosting	**45.1**	33.2 – 57.3	32/71	**51.6**	38.6 – 64.5	32/62	-6.5 (-23.5, 10.5)
Immune response	**53.6**	44.5 – 62.6	67/125	**60.3**	56.1 – 73.4	82/136	-6.7 (-18.7, 5.3)

Note: Only those samples that could further enhance protection (boost further) were considered for the above analyses (titers above 362 (or 8.5log2) were excluded for the above analyses).

mOPV2 is usually administered in 3 rounds of outbreak response vaccination campaigns. Table 3 shows what difference in immunogenicity could be assumed assuming the same rates of immune response and 100% coverage (Table 3). It was found that the projected immunogenicity loss after three rounds of mOPV2 vaccination was low (between 1% to 4%).

Table 3: Projected immune response after three rounds of vaccination

	Immune Response			Seroconversion only		
mOPV2 rounds	1-drop immune response	2-drops immune response	Diff (%)	1-drop immune response	2-drops immune response	Diff (%)
	%	%		%	%	
Round 1	53.6	60.3	-6.7	64.8	67.6	-2.8
Round 2	78.5	84.2	-5.7	87.6	89.5	-1.9
Round 3	90.0	93.7	-3.7	95.6	96.6	-1.0

There were no severe adverse events related to the study procedures observed.

Interpretation and program impact

Immune response was 53.6% (CI95%: 44.5 – 62.6) vs 60.3% (CI95%: 56.1 – 73.4) for 1 drop and 2 drops respectively. The 10% non-inferiority hypothesis could not be rejected. However, after 3 mOPV2 rounds the projected population immunity will be very similar regardless of 1 and 2 drops (difference in population immunity <2%).

As previously demonstrated, development of mucosal immunity is closely correlated with seroconversion after OPV therefore we assume same mucosal response after 1 or 2 drops of mOPV2.

This study suggested that by administering one instead of two drops of mOPV2, we may lose little in terms of immune response while preserving precious vaccine supplies.

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