

**WORLD HEALTH ORGANIZATION
IMMUNIZATION VACCINES & BIOLOGICALS**

**IMMUNIZATION PRACTICES ADVISORY COMMITTEE (IPAC) 13TH MEETING
11-13 JUNE 2019**

FINAL MEETING REPORT & RECOMMENDATIONS

Agenda:

Session I: Opening
Session II: Innovation
Session III: Supply Chain
Session IV: Vision & Strategy for Immunization 2021-2030
Session V: Working Group Updates
Conclusions & Closing Remarks

IPAC Members Present

Kelly Moore (Chair)
Craig Burgess
Michael Free
Ian Gemmill
Masahiko Hachiya
Yang Baoping

EXECUTIVE SUMMARY

SESSION I: OPENING

The Immunization Practices Advisory Committee (IPAC) convened again for its annual meeting on 11-12 June 2019 in Geneva, Switzerland to provide external immunization programme expertise, support and advice to the WHO Department for Immunization, Vaccines and Biologicals (IVB), as per the Committee's Terms of Reference, last revised in 2017.

The WHO IVB Director opened this 13th IPAC meeting, pointing out what a dynamic time this is for global health, and for vaccines and immunization especially. She explained that IVB is seeking new direction in the context of the WHO Director General's Transformation Agenda and other new strategies such as the Gavi 2021-2025 Strategy, IVB's 2021-2030 Vision & Strategy for Immunization, and the new Polio Endgame Strategy 2019-2023. She highlighted the opportunity for the immunization community to work differently in driving the agenda for the next decade, stressing that the role of the IPAC is to see how to improve immunization practices at the country level and to articulate what countries and programmes need to drive success in coverage and equity and performance.

The new WHO/IVB/EPI Coordinator urged the meeting participants to focus on what new strategies and efforts are needed to reach coverage and equity in all countries. She stressed that IPAC is the heart and eyes and ears of immunization programmes, and the WHO/IVB/EPI welcomes such external input to confirm that the interventions that are being recommended are appropriate.

SESSION II: INNOVATION

IPAC was updated on the **Total System Effectiveness (TSE)** project which addresses the pronounced need at country level for support to immunization programmes with vaccine product evaluation and selection in the context of their specific programme needs, and to ensure vaccine products are designed and developed according to country preferences. TSE has the potential to help countries to achieve their coverage and equity targets for

existing vaccines, and to assist vaccine and technology developers in linking product attributes to market demand for pipeline vaccine candidates. With respect to novel vaccine delivery strategies, TSE aims to accelerate the availability and uptake of game-changing product innovations such as CTC, compact prefilled auto disable devices (CPADs) and microarray patches (MAP)s.

The TSE country framework is used for vaccine product evaluation and selection, relying on well-articulated barriers to immunization as the starting point for using the TSE decision support tool. These barriers are expected to be identified through the cMYP planning process, a methodology for which is currently under preparation. The TSE decision-support tool was piloted in Mali earlier this year with the objective of assisting key national stakeholders evaluate which WHO prequalified HPV vaccine was best suited for Mali's immunization programme, relying on evidence-based Multi-criteria decision analysis (MCDA) to consider the trade-offs between the products' respective attributes. Initial feedback has shown that TSE is useful at country level to make the product selection process more structured, rigorous and transparent. The aim is that this kind of evaluation process can be documented in such a manner that it also allows for data to be recorded on country preferences and the drivers underpinning certain product selections. When enough data can be collected from a broad set of countries, insightful analysis can be conducted to inform research and development for vaccine products, thereby ensuring product innovation reflects true programme needs. Consequently, the TSE decision-support tool could be used for real life situations in countries in the Africa Region facing product selection decisions.

IPAC urged the TSE Secretariat to consider reducing the burden on immunization programme personnel by streamlining the product evaluation process as much as feasible and guiding users to existing data and tools that are already being used and are owned by countries where possible. The TSE Secretariat is also encouraged to clarify the added value for countries to adopt a TSE approach and how this balances with the value offered to global and regional entities seeking insights on preferred product attributes for the purpose of research and development.

IPAC members appreciated the future potential of the **Vaccine Coverage Estimator (VCE)**, a tool being developed by the William Davidson Institute (WDI) at the University of Michigan to predict how new vaccine introductions and novel delivery technologies can affect vaccine coverage rates. The Committee recognized the value in modelling potential gains for those working in the immunization programme and how this also provides incentives to move forward with programmatic improvements especially for modelling coverage as this has been challenging with other tools available. However, it cautioned about the need to continue to use real life data and high-quality coverage surveys as data sources to improve immunization programme performance.

Microarray Patches (MAPs) have the potential to increase coverage, reduce logistics complexities, remove the need for reconstitution and vaccine handling, increase user satisfaction and overcome sharps disposal requirements. They are potentially a particularly powerful tool in reaching the 95% coverage target needed to achieve measles elimination.

But more work is needed to reassure manufacturers of the potential use case for MAP technology, the market, the route and timeframe to licensure, and the eventual public need. A Target Product Profile (TPP) has been developed by WHO, and endorsed by UNICEF, that articulates the minimal and preferable product attributes of MR-MAP, from the perspective of programmatic use and delivery. This TPP will be informative for MAP developers and other stakeholders who are contemplating WHO prequalification and UNICEF procurement. Acceptability of MAPs will be assessed through the development of a TSE-oriented country consultation process, starting with a country workshop to be held in Q4 2019 to introduce the technology and seek answers to some of the unknowns. MAPs are also under consideration for support under the VIPS process.

IPAC learnt that PATH has established a **MAP Centre of Excellence** that will develop a short list of high-potential MAP applications, including MR vaccines, and the Centre will fill information gaps to catalyze more rapid advancement.

IPAC was reminded that the upsurge in measles cases is now a global health crisis, and the increase in vaccine hesitancy and the misinformation being spread by antivaccination groups a serious threat to controlling vaccine-preventable diseases. So serious is this threat that WHO recently listed **vaccine hesitancy** among its top 10 threats to global health.

Although it is known that the poorest populations in a country are the least immunized, data on the reasons for vaccine hesitancy and the level of vaccine hesitancy at country level is scarce. A number of efforts are underway to gather more data on vaccine hesitancy and to provide guidance and solutions to countries to understand the reasons for, and level of, vaccine hesitancy in their country and take actions to solve the issues.

The **Global Partner Demand Hub** has been launched that is intended to be both a Center of Excellence and a Coordinator of Technical Assistance to countries in the area of vaccine hesitancy and demand. The Hub will provide technical tools and guidance, policy and normative guidance, technical assistance, and a community of practitioners to countries ready to tackle this issue.

IPAC was informed that **The Global Partner Planning Framework for Demand** is another tool to estimate and tackle vaccine hesitancy at country level. Also the **Measuring Behavioural and Social Drivers of Vaccination (BeSD) Working Group** has been launched to provide a set of standardized and adaptable tools and guidance for programmes and partners to boost the availability, quality, and use of local and global data, generate evidence to guide interventions, assess trends over time, and inform regional and global reporting processes. The BeSD Tool will be pilot tested, finalized and rolled out to many countries in the first half of 2020.

The goal of the **Vaccine Innovation Prioritization Strategy (VIPS)** – a collaboration between all Gavi Alliance Partners - is to prioritize innovations in vaccine-related product attributes to provide greater clarity to manufacturers and partners to make investment decisions. Twenty-four innovations have been assessed in Phase I, and in Phase II, the prioritized innovations from Phase I will be paired with priority antigens for further detailed analyses and prioritization.

IPAC was informed that country consultations will be held in September/October 2019 to seek inputs on countries' willingness to adopt innovations prioritized under Phase 1 paired with key vaccines/antigens, based on the anticipated benefits and trade-offs. The results will inform the final prioritization of innovations.

SESSION III: SUPPLY CHAIN

Effective Vaccine Management (EVM) assessments¹ are typically conducted every 3-5 years in countries, and to date, 163 EVMA have been conducted globally in 90 countries. The evolution of countries' scores over time is tracked at the global level, and although there is definite progress, there remains room for improvement.

A revised version of the EVM Tool – EVM2 - has been produced to streamline the assessment process, make it more useful to programme managers by making it more adaptable to the country context and encourage countries to move towards a continuous improvement process that is linked to the comprehensive multi-year plan (cMYP) and/or national processes for review and continuous improvement. EVM2 is available as a free downloadable Application available on android, Apple and PC. The new version generates reports according to criteria that can

¹ https://www.who.int/immunization/programmes_systems/supply_chain/evm/en/

be customized at country level by the immunization programme and has a dashboard and heat map showing key areas of weakness that can be of direct use to the programme.

The **Vaccine Management Handbook**², a component of the EVM Initiative, has been written for decision-makers at national and subnational levels to provide technical advice on key topics related to immunization logistics and to help countries develop and refine national policies.

To date, four VMH modules have been published and are available in English, French and Spanish. Three more will be produced in 2019-2021. Additionally, An EVM Requirements Mapping will be conducted to steer immunization programme managers to the resources available to support them to help strengthen their system. Where no relevant guidance exists, new EVM Good Practice guidance will be commissioned.

The **vaccine wastage factor** of an immunization programme's vaccine consumption is an important component for forecasting vaccine needs. Current guidance advises countries to use national wastage figures, and in the absence of these, to use WHO indicative figures per vaccine. However, the WHO indicative vaccine wastage figures are outdated, based on estimates, too generic, and not adapted to current vial presentations.

WHO has developed a **new Vaccine Wastage Calculator** that refines the ability to forecast and monitor wastage. At country level this will provide more accurate annual vaccine needs, reduce vaccine stock outs and over stocking, allow the adaptation of session frequency and size, and result in an increase in vaccine coverage. At the global level this will improve predictable global demand and reduce shortages. The tool is currently being tested and is available upon request for testing and feedback.

IPAC members acknowledged the huge effort that is has taken to get the EVM2 tool to this stage and urged the developers of EVM2 to link the results of the EVM assessment to improved programmatic results and to facilitate the linking of the improvement plan to the annual immunization plan to facilitate implementation of the suggested improvements. They also cautioned the team to ensure that any improvements in reducing vaccine wastage not be at the expense of increasing immunization coverage and equity.

SESSION IV: VISION & STRATEGY FOR IMMUNIZATION 2021-2030

With the Global Vaccine Action plan (GVAP) coming to an end in 2020 a new vision and strategy for vaccines and immunization is needed to set the new direction in immunization for the coming decade.

IPAC was informed that the **Immunization Agenda 2030 (IA2030)** has been co-created by key stakeholders and is intended to be a worldwide immunization agenda outlining where the immunization community needs to go next in immunization to achieve the results required. The document will be made up of two parts: The Immunization Agenda 2030 Vision & Strategic Framework; and The IA2030 Online Resources.

A broad consultative process has been initiated and is ongoing, and a robust draft of the document will be presented to SAGE in October 2019. Subsequent iterations will be presented to the WHO Executive Board in January 2020 and to the World Health Assembly (WHA) in May 2020.

The World Health Assembly (WHA) has requested that detailed monitoring and evaluation indicators be presented to the WHA in May 2021 at the same time as the final reporting on the GVAP indicators and achievements.

² https://www.who.int/immunization/programmes_systems/supply_chain/evm/en/index5.html

The meeting was updated on the **Working Together Guide**, a recently published WHO resource guide for immunization services throughout the life course that brings together relevant resources, summarizes current knowledge and provides guidance on the integration of immunization with other health interventions.

As high immunization coverage rates have increased interest in integration from other health services, the need to reach new target populations is highlighting the need for immunization to integrate with other health programmes. Such integration may result in increased coverage, improved efficiencies, user satisfaction and increased demand, but can also bring risks to overall coverage, reduced quality of care, and reduced client satisfaction.

The Working Together Guide aims to provide guidance to plan for and monitor integrated services to understand the change in services and provide a feedback mechanism to improve the programme. IPAC was informed that the Resource Guide is available on the WHO website, has been distributed to Partners and other teams in WHO and hard copies have been sent to the WHO Regional Offices.

SESSION V: WORKING GROUP UPDATES

While the **Controlled Temperature Chain Working Group (CTC-WG)** has not had to meet in almost a year, there has nevertheless been momentum within the CTC workstream, which will soon require additional input and guidance from the CTC-WG, especially as the current strategic roadmap for CTC nears its end and new priorities must be set for post-2020. IPAC was provided a brief update on the various activities and recent progress enjoyed by the CTC agenda, managed jointly by WHO and PATH.

A Desk Review was conducted in March 2019 to identify constraints to effective Human Papillomavirus (HPV) Vaccine delivery that are of particular relevance to **use of HPV in a Controlled Temperature Chain (CTC)**, and to provide evidence in support of the **use case for CTC with HPV**. The Desk Review included data from the CTC-HPV pilot project that took place in Uganda in October 2017, HPV Post-introduction Evaluations (PIEs) conducted in 11 countries, 31 other sources and consultations with relevant people from WHO/EPI and PATH.

The main findings of the Desk Review showed insufficient compelling evidence to favour CTC application to HPV delivery, despite the 2017 pilot CTC-HPV project in two provinces of Uganda which demonstrated that use of CTC facilitates the work of EPI staff and overcomes poor cold chain capacity problems. It was noted that even in the face of this positive finding, the Uganda immunization programme decided to revert to using traditional cold chain for HPV delivery, rather than roll out CTC to the rest of the country. Among the shortcomings of the case for adopting CTC is the lack of clarity around the economic trade-offs associated with its implementation and the ongoing shortage of global supply for HPV vaccine.

Besides the HPV vaccine manufactured by Merck, Gardasil®, there is one other vaccine product currently licensed and WHO-prequalified for use in CTC. This is the Oral Cholera vaccine (OCV) manufactured by Shantha, Shanchol™, which was approved in February 2018 for CTC use and for which CTC pilot preparations have been under way.

The **OCV-CTC pilot implementation** is intended to generate data in support of an OCV-CTC use case and to document lessons learned to inform the development of operational guidance on OCV-CTC implementation. Unfortunately, piloting this in the initial country identified has been delayed due to several challenges. Nevertheless, Bangladesh has documented their recent experience with CTC-like delivery in OCV campaigns, and Zambia has expressed interest to use CTC for their cholera pre-emptive campaign in September-October 2019 and has agreed to act as a pilot site for OCV-CTC.

IPAC were informed that, in addition to the downstream focus of the CTC agenda to scale up country-level experience and boost demand, there is also an **upstream effort in the form of regular dialogue with manufacturers and regulators** to promote awareness, understanding and interest in CTC. Despite ongoing efforts, a reluctance on the part of manufacturers to prioritize and pursue thermostability testing and CTC labelling persists.

While the use of more vaccines in a CTC is a global level priority endorsed by major global health stakeholders, there have been roadblocks on the road to licensure. It has become apparent that without better economic incentives, manufacturers will continue to resist investing in the necessary testing and other licensure requirements.

The CTC Working Group will convene in Q3 2019 to begin work on the *next Strategic Roadmap (2020+) for CTC*. One item for consideration will be the revision of the definition of CTC to prioritize duration over temperature, which may allow more flexibility and for more products to be submitted for licensure. IPAC suggested that it may be beneficial to solicit and include the position of countries' National Regulatory Authorities (NRAs) on CTC in the prioritization of vaccines. Given the supply constraints anticipated with HPV vaccine, IPAC members urged the CTC Working Group to explore another vaccine to advance the CTC agenda.

IPAC was reminded that the objectives of the **Programmatic Suitability of Vaccine Candidates for WHO Prequalification (PSPQ) Committee** are to define the characteristics that determine the programmatic suitability of vaccine products, define the process for assessing compliance with these characteristics, and indicate programmatic characteristic preferences to industry and other vaccine development stakeholders in order to shape the vaccine pipeline.

IPAC learnt that since July 2018 the PSPQ Standing Committee (SC) has reviewed two products: (1) Inactivated Influenza Vaccine (IIV) in a 0.5mL vial, unpreserved, which the SC recommended for acceptance, provided it met certain conditions. (2) Hepatitis B subunit vaccine, in a 1.0mL vial, unpreserved. The SC declined prequalification of the unpreserved adult 1.0mL single-dose vial but recommended that WHO should proceed to prequalify the unpreserved child 0.5mL single-dose vial.

Delivery Technologies Working Group (DTWG)

The goals of the DTWG are to provide a platform to enable industry and the public sector to engage in constructive dialogue to optimize innovation and maximize the appropriateness of immunization products for public-sector use.

Since 2016, the DTWG has been instrumental in reporting on the indicator in the GVAP related to licensure and launch of at least one platform delivery technology by 2020, reviewing nine vaccine technologies, establishing an early target product profile for the MR MAP and conducting two usability studies, engaging with developers and manufacturer through conferences and workshops, and reviewing the Vaccine Technology Impact Assessment (VTIA) economic analysis tool, the Total Systems Effectiveness (TSE) project, and the Vaccine Innovation Prioritisation Strategy (VIPS). The main progress in technology facilitated through consultations with the DTWG are the MAPs and the blow-fill-seal compact prefilled auto disable devices (CPADs).

Since mid-2018, the work of the DTWG has been paused to focus on supporting the launching of the VIPS but is being re-launched in July 2019 in tandem with the VIPS prioritization process.

IPAC members welcomed the work of the PSPQ and DTWG and agreed that IPAC members should continue to be part of these two committees to foster cross-fertilization of technologies.

FULL MEETING REPORT

SESSION I: OPENING

The Immunization Practices Advisory Committee (IPAC) convened again for its annual meeting on 11-12 June 2019 in Geneva, Switzerland to provide external immunization programme expertise, support and advice to the WHO Department for Immunization, Vaccines and Biologicals (IVB), as per the Committee's Terms of Reference, last revised in 2017.

The meeting was structured as two days of technical sessions, open to all invited participants, followed by a closed session for IPAC members only, which was held on the third day. The closed session served to further deliberate the key points of the agenda items, with a view to reaching consensus on main conclusions and recommendations, and to discuss the implications on IPAC of the current WHO transformation process and the outcomes of the recent independent evaluation of WHO's Strategic Advisory Group of Experts (SAGE) on Immunization.

The new IPAC Chair, Dr Kelly Moore, was welcomed and thanked for her work in ensuring continuity following the departure of the previous Chair, Dr Chris Morgan, in November 2018, and all IPAC members were thanked for the valuable and generous contribution of their time.

The meeting was formally opened by Dr Kate O'Brien who joined IVB in January 2019 as the Department's new Director. Dr O'Brien pointed out what a dynamic time this is in global health, and in vaccines and immunization especially. Not only is IVB working with the rest of the Organization to move forward with the Director General's Transformation Agenda, but it is also looking to position itself in the context of several new strategies such as the Gavi 2021-2025 Strategy, IVB's 2021-2030 Vision & Strategy for Immunization, and the new Polio Endgame Strategy 2019-2023. She highlighted that this is an exciting time and an opportunity to see what the immunization community can do differently to drive the immunization agenda for next decade. It was stressed that the role of the IPAC Committee is to think through how to improve immunization practices and to articulate what countries and programmes need to drive success in coverage and equity and performance. It is clear that polio eradication cannot succeed without focusing on routine immunization and this highlights the need to focus on global goals and on what new approaches are needed to achieve the impact that has been elusive to date. Dr O'Brien reiterated to IPAC members that the Department is grateful for the advice IPAC provides which feeds into policy norms and guidance.

A new IPAC Member, Dr Yang Baoping, was welcomed. Dr Baoping was formerly the EPI Manager in China, prior to joining WHO. Among the positions he held within the Organization before his recent retirement were Regional Adviser for Immunization in the Western Pacific Region and WHO Representative in Samoa, American Samoa and Cook Island. It was acknowledged that two other additional members have joined IPAC, Dr Pape Faye from Senegal and Dr Paba Palihawadana from Sri Lanka. Regrettably, neither was able to participate in this meeting.

The new WHO/IVB/EPI Coordinator, Dr Ann Lindstrand, was also welcomed to the meeting and invited to make introductory remarks. Dr Lindstrand is the previous EPI Manager, NITAG Chair and Head of Vaccination Programme Unit at the Public Health Agency of Sweden. She has worked for many years abroad in French Guyana, Mozambique, Angola and Guinea Conakry with Médecins Sans Frontières. She has been a lecturer in maternal and child health, humanitarian aid and vaccinology for over 25 years and has written a textbook on Global Health.

Dr Lindstrand urged the meeting participants to spend the next few days focusing on what new strategies and new efforts are needed to reach coverage and equity in all countries. She stated that WHO is looking for advice on the importance of the Total System Effectiveness (TSE) approach and of its utility to countries, and for whether

the agenda items on other technology innovations and supply chain improvements, will help countries to achieve their goals. She stressed that IPAC is the heart and eyes and ears of immunization programmes, and the WHO/IVB/EPI welcomes such external input to confirm that the interventions that are being recommended are appropriate.

SESSION II: INNOVATION

1) TOTAL SYSTEM EFFECTIVENESS (TSE) – Evaluating all trade-offs to inform choice

(a) Project Overview/Progress Update.

(Birgitte Giersing, WHO/IVR - presented for programme-oriented feedback and endorsement)

Total Systems Effectiveness (TSE) is a holistic approach to evaluate and prioritize between vaccine products, based on country specific criteria, taking into consideration coverage, equity, programmatic and systems implications. It is intended to enable decision-makers to evaluate the trade-offs in selecting one product over another within their specific country context and can be applied to both existing and hypothetical products. TSE is also intended to inform donors and vaccine procurement stakeholders on prioritization of future products that may help to achieve immunization targets, and to assist vaccine and technology developers in linking product attributes to potential demand.

IPAC was reminded that although several potentially game-changing innovations, such as Uniject™ and jet injectors, have been WHO pre-qualified, and innovative approaches to vaccine management such as the “controlled temperature chain” (CTC) have been evaluated and endorsed by WHO, there is very slow uptake of these at the country level and their impact remains sub-optimal. A possible reason for this is that the assumptions used in research and product development do not necessarily reflect country preferences due to limited, *ad hoc* country engagement in R&D and in the supply priority setting.

TSE aims to ensure vaccine products are designed and developed according to country needs by providing countries with a platform to communicate their needs and preferences in the context of their specific barriers, and hopefully accelerate the availability and uptake of key innovations needed to increase coverage and equity in immunization. Over the last 12 months, the TSE project team has been dedicated to proof of concept and field testing the TSE country framework to help countries evaluate existing products. The focus now is to determine if and how TSE can be used as a mechanism to engage country immunization programme stakeholders in global research and development (R&D) agenda setting, and to consider how to increase partner involvement in TSE at the regional level in readiness to transition the resources and management of TSE from global to regional level.

(b) Assessment of Barriers to Immunization for Total System Effectiveness (TSE) - Update. *(Margie Watkins, WHO/EPI – presented for programme-oriented feedback and endorsement)*

With a continuous aim of facilitating tasks and minimizing burden on immunization programme managers, WHO Guidance on Immunization Barriers Assessment is under development to incorporate a comprehensive review of barriers to immunization into the situation analysis component of the comprehensive multi-year (cMYP) planning process. This should leverage existing data, be less time-consuming than a standalone barriers analysis, and enrich the level of information available for the cMYP planning process.

The TSE pilot in Mali earlier this year confirmed how such an assessment would have value specifically to the TSE Country Framework. This pilot’s primary objective was to support decision-making around the selection of the most appropriate HPV product to include in Mali’s GAVI application for support to introduce HPV in 2020.

However, there were challenges in articulating the immunization programme's primary barriers, thereby undermining the capacity to link these to product attributes that could address the programme constraints which undermine effective immunization and high coverage and equity in Mali.

The next steps in this workstream are to complete the proposed structure and methodology for synthesizing data on barriers in the context of cMYP planning, provide suggestions on the steps to follow when considering immunization barriers within the TSE vaccine product evaluation process, and field test the guidance in August/September 2019. It is expected that this work will be mostly completed by October 2019, though not fully finalized and integrated into the cMYP planning process until December 2019.

Discussion

IPAC members pointed out that for the uptake of TSE as a country framework to be successful it should result in reducing the burden on national immunization programme personnel at all levels of the health system. To achieve this, programme incentives need to be a key driver in how the TSE country framework is designed at the macrolevel. At the microlevel, TSE needs to include the input of health care workers and caregivers in countries on the critical attributes of a product and to focus on facilitating increases in immunization coverage and equity in countries.

IPAC members noted the critical role of the WHO Regional Offices in the successful uptake of the TSE country framework and confirmed that they should serve as the bridge between WHO/HQ and the countries in demonstrating the utility of this tool.

Although a schedule of field testing in August/September 2019 and finalizing the WHO Guidance on Immunization Barriers Assessment document in October 2019 appeared short to the IPAC participants, as existing reports from bottleneck analyses will be used for data, it was agreed that this should be achievable.

IPAC members suggested that using focus groups in country to work on the analyses could help streamline the process. It was also suggested, to the extent possible, to take advantage of scheduled in-country assessments such as EPI programme reviews, the cMYP planning process, and EVM assessments and use these as alternative strategies for obtaining the information required by inserting additional questions to these established review mechanisms. Additionally, they noted that data from logistics management systems in countries could be good sources of detailed information as well as utilizing reports from in-country NGOs who may have also spent time focusing on barriers in immunization systems.

Additional points from the closed session of the IPAC members

IPAC members summarized the three main benefits of the TSE country framework as follows: (1) Articulating the value of a product to a country; (2) Demonstrating the trade-offs between products and their uses for different populations and settings; and (3) Offering countries a voice to create demand for products and specific product attributes to be fed into market shaping. However, they advised the TSE Secretariat to communicate a clear and transparent vision for TSE and its intended use. They also suggested renaming the framework, as "Total System Effectiveness" was felt to be too general, inadequately representing the central tools promoted for country use and their intent. No specific suggestion for a new name was made at the time.

While IPAC members recognized that using TSE tools to support countries in barrier analysis and optimal product selection of existing products has potential, they were less optimistic about the interest of countries to participate in workshops on pipeline products with a less tangible immediate benefit. They suggested the TSE project focus on using the Regional R&D workshops to obtain the market shaping insight required. It was also proposed that

TSE look beyond Gavi to entities such as the PAHO Revolving fund, UNITAID and the Coalition for Epidemic Preparedness Innovations (CEPI) to see what tools they are using in the area of barrier analysis and whether any lessons can be learned from their experience and efforts.

Recognizing the value of the TSE, IPAC members recommended an intensified focus on its sustainability and on building the capacity of key stakeholders at country level, e.g. EPI Managers or other who work with NITAGs, in its use, and on investigating possibilities to adapt existing tools at country level to provide the data for TSE to reduce the proliferation of tools and dependence on international consultants. They also highlighted the need to ensure that this exercise remain linked to the planning and budgeting of the immunization programme and suggested that improved data visualization of the potential impact on lagging areas in the programme could facilitate this.

As TSE has the potential to improve equity by suggesting how a vaccine can be delivered in new ways that address the needs of marginalized, vulnerable and mobile populations, including through the private sector and NGOs, IPAC members encouraged the TSE Secretariat to accentuate the equity point of view in TSE. It was suggested that the TSE Secretariat follow up with the WHO/EPI Equity Reference Group who are looking at ways to increase access by analyzing barriers, and to ensure that the findings of this group continue to be reflected in TSE thinking going forward.

(c) Demonstration of the Draft TSE Decision-Support Tool

(Siobhan Botwright, WHO/IVR – presented for programme-oriented feedback and endorsement)

IPAC was presented the Excel-based TSE decision-support tool, which has been developed iteratively with country consultations and experts and is designed to guide group discussions at country level to come to an evidence-based, context specific recommendation on what product is best suited to the national immunization programme. The tool relies on multi-criteria decision analysis (MCDA) to make explicit the valued underlying decisions and brings together different types of evidence. It also focusses on the social aspects of the evaluation and recommendation process.

Implementation of the tool is structured around five phases: preparation; a criteria workshop; evidence assembly; a recommendation workshop; and conclusions and is estimated to take between 3-5 months. The tool was piloted in a workshop in Mali in Q2 2019, allowing for key feedback on revisions to be incorporated into the next version which will be further piloted in Q3/Q4 2019.

Also under development is a TSE tool kit which will provide users with a manual, templates for slides, agendas, and reports, and a resource catalogue on where to find the evidence to input into the tool.

Future priorities for the tool are to ensure its sustainable roll out for use at country level. This will be done through additional piloting during ‘real’ product selection decision-making processes at country level, coordination at the regional level for developing and testing training materials and facilitating a mechanism for continued feedback, and through the update and determining decision point and process for ‘validation’ and regional implementation.

(d) TSE Pilot Implementation in AFRO: Experience and Way Forward

(Jason Mwenda, WHO/AFRO – presented for technical input and programmatic guidance)

In order to determine whether the concept of TSE is useful for immunization programmes to assess tradeoffs between products and make better informed decisions, in February 2018 WHO/AFRO solicited and received interest from several countries, including Malawi, Mali, Rwanda, Uganda, Zambia and Zimbabwe, for piloting TSE.

IPAC were informed that Mali was selected as a pilot country, and an introductory workshop was held in Mali in August 2018 for participants from the Ministry of Health (MoH), the Center for Vaccine Development (CVD) Mali, the Paediatric Association, University of Bamako, UNICEF and WHO. Following the workshop, these key national stakeholders indicated TSE could be a useful tool to add structure and accountability to product selection in Mali and it was decided to fully pilot TSE in March-April 2019 to support the newly formed NITAG in choosing between HPV products for the new vaccine application to Gavi.

Other activities in the Africa Region to date include a TSE orientation for 8 countries in West and Central Africa conducted through the two sub-regional annual Joint Reporting Form (JRF) meetings.

The WHO Africa Regional Office have indicated interest by countries in the Africa Region to pilot TSE due to the flexibility and discussion aspects of the tool as well as the ability to document a logical and rational evidence-based process. However, it is recognized that engagement from the Ministries of Health in the countries is essential for TSE to be truly beneficial.

Next steps for WHO/AFRO are to identify countries facing new vaccine introduction or product switch decisions in 2020 and disseminate TSE lessons learned and the experience with the tool in the Africa Region to encourage the use of TSE during the upcoming decision-making processes in these countries. WHO/AFRO will also evaluate how to pilot an R&D framework for TSE and how to implement the tool in such a way as to reduce burden on countries.

Regarding the sustainability of TSE, there are plans to transition TSE from the global level to regional ownership by providing additional resources at the regional level to support training, supervision of country pilots, and continued collation of best practices at country level. Training materials and a plan for sustainable roll-out with continued technical assistance and quality assurance from the WHO Regional Office will also be developed.

Discussion

IPAC members suggested that given the time constraints on EPI Managers, dedicated focal points in countries may be needed to champion the roll out of the TSE approach. However, in order to secure buy-in at country level for this, it will be necessary to demonstrate to countries the benefits of the final outcome of the TSE process.

(e) Proof of Concept: Vaccine Coverage Estimator (VCE).

(Pascale Leroueil, The William Davidson Institution (WDI) at the University of Michigan – presented for technical input and programmatic guidance)

In view of the lack of tools and methodologies to predict how new vaccine introductions may affect vaccination coverage rates, the William Davidson Institution has been collaborating with the WHO TSE Secretariat to develop a vaccine coverage estimator (VCE). This tool is designed for use at central level, relying on **potential** attributes of a vaccine and its target population to estimate an expected coverage level and quantify the barriers to immunization that could be affected by vaccine product choice. Preliminary findings from applying the tool to a Measles-Rubella Microarray Patch (MR-MAP) with data from Indonesia, Peru and Zambia have confirmed the proof of concept. The resulting information could inform vaccine investment and portfolio-building decisions, planning for new vaccines introductions at country level, and strategies to improve coverage and equity among sub-populations within a country.

However, it should be noted that not all immunization barriers can be addressed, and the study focuses on six barriers that can be overcome by technological solutions, i.e. schedules, temperature storage, administration, acceptability, dose, dose per container.

Next steps are to establish a working group with both programming and modeling expertise to provide input on the methodology and present the model to IVIR-AC in September 2019.

Discussion

Although currently the VCE is not combined with TSE, the VCE is a model to assess the immunization barriers that can be addressed by technology and may give a sense of potential market and demand. The VCE could provide a global picture of potential coverage and equity gains from a novel delivery technology which complements the VIPS and TSE processes, with VIPS being a process of prioritization to identify novel delivery technologies that will give the greatest coverage and equity gains and TSE being a landing platform to inform VIPS and WHO of countries' needs and preferences, allowing countries to evaluate the potential impact of these novel products if and when they come to market. It is hoped that these three pieces will be brought closer together next year.

Additional points from the closed session of the IPAC members

IPAC members expressed concern that the VCE was currently focusing more on global level upstream objectives related to market and demand rather than exploring its utility at country level to see how to impact coverage and equity issues by modelling different products at different levels.

IPAC members expressed caution over the fact that modelling is not a substitute for real life data, and that high-quality coverage surveys and using data for action in the field remain key strategies for making programmatic adjustments.

2) MICRO ARRAY PATCHES (MAPs)

(a) Measles Rubella Microarray Patch Target Product Profile.

(Mateusz Hasso-Agopsowicz, WHO/IVR – presented for validation and guidance)

Developing a target product profile (TPP) for Microarray patches for measles-rubella vaccines (MR-MAPs) can help address issues early in the product development process and prevent late-stage development failures. Through a widespread consultative process between vaccine developers, regulatory agencies, programmatic experts and independent experts a TPP has been developed and endorsed and is expected to be published jointly with UNICEF in July 2019. Table 1 shows a summary of current challenges with delivering and administering Measles containing vaccines (MCVs) and how MAPs can address these challenges.

Table 1: Current challenges with the delivery and administration of Measles Containing Vaccines (MCVs) and how Microarray Patches (MAPs) can address these challenges

Current challenges with the delivery and administration of Measles Containing Vaccines	How Microarray Patches can address these challenges
<ul style="list-style-type: none"> ▪ Safety of reconstitution and administration ▪ Stringent cold chain requirements ▪ Complex handling, time for administration and availability of trained health care workers ▪ Vaccine hesitancy and wastage ▪ Medical waste disposal. 	<ul style="list-style-type: none"> ✓ No reconstitution and easy to deliver ✓ Thermostability and easier administration reduces logistics complexity ✓ Integrated device may allow community health volunteers to administer ✓ Hesitancy and wastage reduced as a single dose presentation ✓ Can be disposed of as biohazardous waste

IPAC learnt that a number of contentious areas surfaced during the consultative process for the TPP, most notably in the areas of target population, stability and wear time. For all these areas, balance is being sought between minimum targets driven by available data and aspirational optimum targets for which data are not yet available. In a survey of IPAC and Technet21 members, both dissolvable and solid patches were considered biohazard waste and as such do not need to be disposed of as sharps waste – an additional advantage for using this technology.

(b) Proposed Approach for TSE MR-MAP Product Development Workshop.

(Birgitte Giersing, WHO/IVR – presented for validation and guidance)

As population density decreases, the logistical complexity of delivering measles vaccine increases, and with global coverage of measles currently at 85% and the need to reach 95% plus to achieve elimination, Micro-Array Patches could be a key tool to achieve these targets.

A MAP acceptability study recently conducted in Benin, Nepal and Vietnam met with much interest and enthusiasm. However, assumptions about how these products will be used and adopted in countries cannot be made and socializing the new technology in countries as early as possible to build advocacy and awareness is pivotal for the pull mechanism.

A MR-MAP Working Group was formed in 2018, and as part of this, CDC and UNICEF are conducting an assessment about potential market size for MR-MAPs based on the five scenarios of how MR vaccines are currently used, i.e. in supplementary immunization activities (SIAs), in outbreak response, in routine immunization and in hard to reach populations.

Additionally, using TSE to assess context specific barriers and country specific preferences for products is a good basis for country engagement to provide information on use cases, TPP, attributes and potential demand.

An initial brainstorming meeting was scheduled on 13 June to review these different elements and to seek country partners interested in supporting a country workshop in Q4 2019. This workshop represents an opportunity to introduce MAP technology to programmatic staff and it is hoped that it will provide some answers to the many questions that remain, as the first MR-MAPs enter Phase I trials in 2020.

Discussion

IPAC expressed concern that from the presentations on TSE, the impression is that TSE is about more rapid introduction of new products and less about evaluating the value of different products in a primary health care context. IPAC would like to see a focus on the trade-offs between programmes and products and on where new products fit into an essential health package at country level. IPAC suggested that if the intention is that TSE be used to make choices on which presentation countries adopt today, as well as to inform research and development priorities, it may be worth considering two different names or another strategy to differentiate and clarify the two different intentions.

Furthermore, when using TSE as a framework to analyse barriers, IPAC highlighted the need to focus on the barriers to coverage and equity, on the constraints to reaching hard to reach populations, on the needs of health care workers and how they respond to new products, and on the benefits of linking with the private sector and NGOs as potential partners in delivering products in hard to reach areas.

Regarding other potential sources of information, IPAC suggested that the TSE Secretariat look at the 38 Core Indicators of the Primary Health Care Performance Initiative (PHCPI3) that provide a snapshot of primary health care performance based on existing, globally comparable data. These, and a review of previous barrier assessments conducted for Gavi Health Systems Strengthening (HSS) in 2004-2006, could serve as potential inputs to the analysis of barriers to immunization.

(c) PATH's Microarray Patch Center of Excellence - Overview.

(Courtney Jarrahan, PATH – presented for validation and guidance)

Micro-array patches provide opportunities to enable alternative delivery scenarios to increase coverage, to enhance immunogenicity of novel vaccines, to improve adherence to drug regimens, and to reduce the burden on health systems.

IPAC heard that some of the challenges of advancing MAPs for use in LMICs have been the limited opportunity for platform-wide efficiencies given the product-specific focus, siloed information, unclear pathway to manufacturing scale-up and regulatory approval, and uncertain market potential in LMICs. With support from UK-DFID, PATH has established a MAP Center of Excellence to advance MAPs as a technology platform for high-priority needs in LMICs.

Work in this area includes the development of a short list of high-potential MAP applications based on potential health impact, probability of technical and regulatory success, and potential commercial viability. The short list will be prioritized for the Center of Excellence portfolio based on in-depth analysis of high-potential MAP applications through literature research, SAG, DFID & expert review and portfolio strategy analysis that will generate information and resources that will broadly support the MAP technology field.

For priority MAP products that are already the focus of coordinated product development efforts, e.g. for MR vaccine and hormonal contraceptive, PATH will fill information gaps to catalyze more rapid advancement. For high-priority candidates at an early stage of development, e.g. HPV and rabies vaccines, and HIV treatment and prevention, PATH will generate data to determine feasibility and demonstrate value to potential development partners and global health stakeholders. PATH will provide platform-wide support to other areas such as use of MAPs in outbreak response, the Regulatory Working Group, manufacturing and dissemination issues, and product-specific support where appropriate.

Discussion

IPAC was informed that, regarding the target product profile for the MR MAP, while pre-clinical data show comparable immunogenicity to that of the standard vaccine, this comparability still needs to be confirmed in the target population through clinical studies. Furthermore, thermostability still needs to be tested for each antigen and cannot be assumed to be the same for all antigens.

To increase uptake of MAPs in LMICs, the cost of the delivery device needs to be within acceptable limits. As MAPs as a delivery device may also be advantageous in high income countries, it was suggested to encourage the use of MAPs to deliver HPV vaccine (for which thermostability has been established) in high income countries to demonstrate that this technology works well, where people will be willing to pay the additional cost for an easier, less painful administration, and use this uptake to cover some of the early research and development (R&D) investments and eventually bring the cost down for everyone.

³ <https://improvingphc.org/about-phcpi>

Although there is substantial interest in MAPs over other new technologies, vaccine manufacturers have yet to see data pointing to a viable market that would warrant the R&D investment on their part. The interaction between the MAP Working Group and manufacturers is important in accelerating the development of MAPs, and it is crucial that the right people, i.e. those involved in engineering production, be involved in the ongoing discussions.

Additional points from the closed session of the IPAC members

Given the substantial programmatic potential, IPAC members confirmed their support for the MR MAPs. However, they suggested that the project could benefit from improved communication and advocacy on the benefits of using MR MAPs. IPAC members were clear that responsibility for providing oversight and advice on issues of production will be with WHO's Product Development for Vaccines Advisory Committee (PDVAC), and that the role of IPAC has been to provide advice on the programmatic perspective of this new technology.

Given some of the discussions, IPAC members felt that further studies are needed to confirm that vaccination with MAPs does not provide an inferior response as this will be a key issue when advocating for uptake. Also, attention should be given to other technologies (e.g. Double chamber auto-reconstitution devices) that could address most of the barriers to MR delivery and are likely to face lower regulatory and scale-up hurdles.

3) MEASURING BEHAVIOURAL AND SOCIAL DRIVERS OF VACCINATION.

(Lisa Menning, WHO/EPI – presented for technical input)

While programmatic improvements and introductions of new strategies and new technologies to reach the hitherto unreached will go a long way towards increasing coverage and equity, it was suggested to IPAC that it is time to focus on helping countries to measure behavioural and social drivers of low immunization rates. The efforts to generate these data and address these questions is often confused with the initiative presented earlier in the meeting agenda to assess immunization barriers. This presentation therefore aimed to clarify that this workstream is more focused on generating data, which the cMYP-based barriers assessments can leverage to capture and characterize a particular dimension of immunization barriers.

Vaccine hesitancy is defined as a delay in acceptance or refusal of vaccines, despite available services, that is complex and context specific, varying across time, place, and vaccine.

Currently, WHO and UNICEF collect data through the annual Joint Reporting Form (JRF) on hesitancy through two specific questions: (1) Name the top three reasons for vaccine hesitancy; and (2) % of countries that have assessed the level of hesitancy at national or subnational level. But while 83% of countries provided at least one reason for vaccine hesitancy, only a third of countries based this response on an assessment, i.e. the majority response was based on an assumption, making the utility of these statistics very limited.

It has become evident that the poorest populations in a country are most often the least immunized as vaccination is not always their biggest priority.

To start systematically addressing this issue, the Global Partner Demand Hub, intended to be both a Center of Excellence and a Coordinator of Technical Assistance to countries, has been launched. The Hub will provide technical tools and guidance, policy and normative guidance, technical assistance, and a community of practitioners.

Another tool that is being used in this area is the Global Partner Planning Framework for Demand which focuses on addressing five main areas (service quality and accountability, community engagement, risk and resilience, social and political will, and social data), to increase demand and reduce vaccine hesitancy.

The Measuring Behavioural and Social Drivers of Vaccination (BeSD) Working Group aims to provide a set of standardised and adaptable tools and guidance for programmes and partners to understand the reasons for under-vaccination, which is a highly context-specific issue. This will increase the availability, quality, and use of local and global data, generate evidence to guide interventions, assess trends over time, and inform regional and global reporting processes (e.g. WHO/UNICEF JRF). It has been recognized that these data will also have value for the cMYP-based Barriers Assessments. The initial development of these tools and associated field testing will take place in a range of countries during the course of 2019, and in Q1-Q2 2020, with the eventual goal of a roll out to many countries.

Discussion

IPAC expressed concern that the use of such structured data collection tools for issues that countries currently assess based on their assumptions may not have rapid uptake. It is expected that while end users will vary between countries, the key will be to ensure that the tools are developed at the right level of brevity and clarity to foster their uptake. IPAC was informed that Partners are attempting to align tools at national level with key questions on vaccine hesitancy and demand that can be reported up to global level and remove the need for a separate process. The BeSD Working Group is employing different global and regional mechanisms to generate awareness of the importance of gathering this kind of data.

IPAC confirmed that this work is not about ranking issues or prioritizing solutions and strategies, but rather on enhancing and sustaining demand. The outputs, therefore, will be tailored to the results of the assessments conducted in countries and will consist of a variety of different strategies or interventions. Community engagement, for example, may be one recommendation, working with high profile individuals as champions of vaccinations, e.g. local pop or sports stars.

Additional points from the closed session of the IPAC members

IPAC members expressed interest in the vaccine hesitancy and demand work and the importance of making sure countries are guided on how to collect data on demand and vaccine hesitancy to inform programmatic changes to increase immunization coverage and equity.

Furthermore, they emphasized the need for the data collected to be one of the sources that the cMYP and TSE draw from via the barriers assessment.

4) VIPS - VACCINE INNOVATION PRIORITIZATION STRATEGY (Focusing on vaccine product attributes)

(a) Overview and Update from VIPS Working Group.

(Marion Menozzi-Arnaud, GAVI – presented for technical input)

GAVI, the Vaccine Alliance, aims to pursue a common agenda of driving vaccine product innovation to better meet country needs and support Alliance goals on immunization coverage and equity. The goal of the Vaccine Innovation Prioritization Strategy (VIPS) – an Alliance wide collaboration - is to prioritize innovations in vaccine products and product attributes to provide greater clarity to manufacturers and partners as they make investment decisions.

VIPS includes two phases:

- Phase I: innovations will be analysed in terms of their characteristics and potential public health value, and in terms of their breadth of applicability to several antigens.
- Phase II: the prioritized innovations from Phase I will be paired with priority antigens that are in scope for VIPS, based on technical feasibility and further detailed analyses.

Under Phase I, 24 innovations have been assessed and work is currently ongoing to prioritize 10. These 10 will then be analyzed to prioritize 3-4 innovations as platforms in their own right, and where relevant, to indicate for which individual antigens the innovation is seen to be most valuable. This will send signals to innovation developers and vaccine manufacturers and partners on the most valuable innovations, rationales and recommendations for next steps.

During Q3 of 2018, the VIPS Alliance Working Group conducted country consultations with the following objectives: (1) To guide the evaluation framework and support the prioritization of innovations that meet country needs; (2) To review the preliminary prioritization and discuss feasibility and interest in product uptake based on benefits and known trade-offs of innovations; and (3) To review the final prioritization of vaccine-specific innovations to gain more insights into potential product adoption.

The VIPS Alliance Working Group, together with PATH and CHAI (Clinton Health Access Initiative), is planning additional, more in-depth country consultations with the EPI Technical Working Group and the Logistics and Supply Coordination Technical Working Groups, to seek inputs on countries' willingness to adopt innovations prioritized under Phase 1, paired with key vaccines/antigens, based on the anticipated benefits and trade-offs. These consultations are planned in the Democratic Republic of Congo, Kenya, Nigeria and Uganda (and possibly, Lao, Nepal, Pakistan, Senegal and Zambia) in September/October 2019. The outcomes will inform the final prioritization of innovations.

(b) Antigen Prioritization for VIPS.

(Birgitte Giersing, WHO/IVR – presented for technical input)

Phase II of the VIPS will further analyze the ~10 prioritized innovations with priority antigens to ensure that the innovations in Phase II are applicable to relevant immunization challenges.

The VIPS Steering Committee, which met for the first time in November 2018, proposed the following criteria to prioritize antigens from the preliminary long list of 48 antigens: Global coverage targets are not met; Clear public health need as defined by vaccine preventable disease burden; Pathogens likely to cause an outbreak; Target atypical population; Benefit from dose sparing; and Standard multi-dose vial with preservative not feasible.

Additional considerations and criteria were identified and applied to the long list, resulting in the selection of 10 licensed vaccines and 7 pipeline candidates. For the licensed vaccines, the list of antigens prioritized those that are Gavi-financed vaccines or that have other signals, such as an elimination or eradication agenda.

Barriers to vaccine delivery of each priority licensed antigen that could be alleviated by innovative products were prioritized to assist with the coverage and equity agenda. Table 2 summarizes the barriers to vaccine delivery and the innovations that could overcome the barriers.

Table 2: Delivery issues and technology innovations that would solve the delivery issues

Delivery Issue	Technology Innovations that Would Solve Delivery Issue
Acceptability (pain)	Reduce pain and result in a greater vaccine acceptability by the user
Timeliness	Increase the chances for a vaccine to be delivered within the recommended timeline
Delivery outside health facility/routine schedule	Facilitate vaccine delivery outside of a healthcare facility or through a complicated or unusual immunization schedule
Freezing leads to wastage	Decrease chances of vaccine freezing or indicate that freezing took place
Thermostability	Enhance the thermostability of a vaccine
Reluctance to open a multi dose vial	Address the reluctance to open multi dose vials by increasing the open vial time or other means
Vaccine handling	Facilitate vaccine handling through reduced risk of contamination or needle-stick injury
Route of administration	Facilitate vaccine delivery through a specific route of administration
Need for dose sparing	Increase the availability of a vaccine through dose sparing

The ranking of these delivery issues for each priority antigen was carried out by IVB vaccine focal points and surveying IPAC meeting participants, with thermostability highlighted as the most frequent need across prioritized vaccines. With more data, this analysis could be used to identify the priority technology and delivery barriers that need to be addressed by innovations.

The VIPS Steering Committee was scheduled to meet on 24-25 June 2019 to review the list of 24 innovations and select up to 10 for further assessment in combination with the priority antigens. This Steering Committee's composition has intentionally been made up, by over 50%, of a cross section of PDVAC and IPAC members, to provide formal input on behalf of WHO

During the weeks just prior to the IPAC meeting, all participants and a relevant selection of EPI staff were urged to complete a survey for VIPS through which they could confirm their agreement with the process for identifying the priority antigens, react to the antigen list and the problem statements proposed, and provide additional input on the ranking of problem statements. It should be noted however, that most of the respondents to this survey found the instructions and survey design confusing, which undermined the quality and number of responses.

Discussion

IPAC understood that VIPS is a robust process intended to identify three or four innovations that are technically feasible and considered important for public health by the VIPS Steering Committee. The TSE Framework will then be used to evaluate these innovations through a country workshop. This will be an opportunity to “socialize” the innovations and highlight how they can be transformative at country level. This will also give an indication of what the demand might look like from the country perspective.

Additional points from the closed session of the IPAC members

IPAC members stressed the importance of having IPAC representation on the VIPS Steering Committee to ensure continuity and programmatic input to the decision-making processes of the VIPS.

SESSION III: SUPPLY CHAIN

1) EFFECTIVE VACCINE MANAGEMENT 2 AND VACCINE MANAGEMENT HANDBOOK STATUS UPDATE.

(Daniel Brigden, WHO/EPI – presented for information)

Effective Vaccine Management version 2 (EVM2)⁴

IPAC learnt that there are now nine criteria that are key to effective vaccine management and the safe and effective delivery of vaccines to where they are required. The latest version (EVM2) of the Effective Vaccine Management (EVM) assessment evaluates these nine criteria, at the four administrative levels of the immunization programme. The objective is to measure strengths and areas for improvement in immunization supply chains, and guide development and implementation of improvement plans. For each category, minimum standards (requirements) are established that set the standard for immunization supply chains. There are currently 346 EVM2 requirements.

EVM assessments (EVMAs) are usually conducted every 3-5 years, and to date, 163 EVMAs have been conducted globally in 90 countries. The evolution of countries' scores over time is tracked at the global level, and although there are definite improvements, there remains room for improvement, especially in some countries. It was decided to produce a revised version of the EVM to move countries away from conducting assessments at 3-5 year intervals and towards a continuous improvement process that is linked to the cMYP and/or national processes for review and continuous improvement. In addition to assessing the facilities, EVM2 also assesses the management of both the facility and the immunization programme itself.

The original EVM assessment tool was available as an Excel tool. EVM2 is now available as a free downloadable mobile application on Android, Apple and Windows devices. The new version can be used to create assessments that are customized according to the needs of the immunization programme. It also has a dashboard and heat map showing strengths and weakness. While no internet connection is needed for the data collection using the EVM Assessor app, the initial assessment creation and subsequent results analysis will need an internet connection.

EVM2 was tested in 2018 in Uganda, Jordan, Bhutan and Iraq, and in 2019 in Burkina Faso, Côte d'Ivoire and the Democratic Republic of Congo. Later in 2019, those countries scheduled to conduct EVM assessments will use the EVM2 framework, i.e. Iraq, Maldives, Vietnam and Iran.

EVM2 is currently available in English and Arabic. Once the tool is finalized it will be translated into French, Spanish, Russian and Vietnamese in 2019, and other languages, as required.

Vaccine Management Handbook (VMH)⁵

The Vaccine Management Handbook, a component of the EVM Initiative, has been written for decision-makers at national and subnational levels to provide technical advice on key topics related to immunization logistics and to help countries develop and refine national policies.

To date, four VMH modules have been published and are available in English, French and Spanish.

⁴ https://www.who.int/immunization/programmes_systems/supply_chain/evm/en/index3.html

⁵ https://www.who.int/immunization/programmes_systems/supply_chain/evm/en/index5.html

Next steps:

- In 2019 two of the VMH modules published in 2015 (“How to use passive containers and coolant-packs for vaccine transport and outreach operations” and “How to monitor temperatures in the vaccine supply chain”) will be revised and updated, and a new VMH module “How to maintain adequate levels of immunization stock throughout the supply chain” will be published. A new VMH Glossary will be published, and ongoing VMH dissemination activities are planned.
- An EVM requirements mapping will be conducted to steer immunization programme managers to the resources available to support them to help strengthen their system. This will be done by mapping every EVM requirement to the most relevant WHO-UNICEF guidance material (for example, VMH modules or how-to videos). Where no relevant guidance exists, new EVM Good Practice guidance will be commissioned, as the VMH becomes discontinued. EVM2 enables supportive supervision, self-learning, even training and eLearning delivery.
- In 2020, one new VMH module “Creating a CCE inventory and rehabilitation plan” will be published and the “EVM Good Practice” based on the requirements mapping will be created, repackaging existing guidance where possible.
- In 2021, one new VMH module on Vaccine Distribution will be published, and work will continue on the creation of the EVM Good Practice modules.

2) WHO VACCINE WASTAGE CALCULATOR- LAUNCH AND UPDATE

(Souleymane Kone, WHO/EPI – presented for strategic guidance)

The wastage factor of an immunization programme’s vaccine consumption is an important component for forecasting vaccine needs. There is a direct link between vaccine wastage and immunization coverage whereby even a slight increase in wastage impacts vaccine needs.

Currently, vaccine wastage can be monitored at country level in three different ways: through randomly selected sentinel sites; through systematic routine monitoring at all facilities at all levels; and through retrospective wastage studies of a selected sample of storage and service facilities. However, the quality of the data collected is sometimes poor and highly variable. There is low incentive for programme staff to monitor wastage and there is a lack of clear guidance to conduct the monitoring and take corrective action afterwards.

UNICEF guidance presently advises countries to first use national wastage figures, and in the absence of these, to rely on WHO indicative figures per vaccine. However, the WHO indicative vaccine wastage figures are outdated, based on estimates, too generic, and not adapted to current vial presentations.

In 2015, IPAC endorsed the WHO demonstration that routine immunization session size distributions are governed by Binomial statistics and proposed the use of this methodology for new estimation of indicative national vaccine wastage rates.

WHO has subsequently developed a new vaccine wastage calculator that refines the ability to forecast and monitor wastage. At country level, this provides more accurate annual vaccine needs, reduces vaccine stock outs and over stocking, allows the adaptation of session frequency and size, and results in an increase in vaccine coverage. At global level, this could improve predictable global demand and reduce shortages. In country testing, refinement and development of the new web-based vaccine wastage calculator tool started in Q2 2019 and the tool is currently available upon request for testing and feedback.

Next steps in this area are to revise global indicative wastage rates to achieve more accurate wastage rates based on binomial distribution. This work is expected to be completed by Q2 of 2019. Subsequently, work will commence

on refining country wastage rates to provide more accurate wastage rates based on local circumstances as well as developing tailored country wastage rates at each service point for each country.

Discussion

IPAC recognized the extreme utility of these tools and resources – EVM2, VMH and the vaccine wastage calculator, highlighting the importance of making WHO and UNICEF Regional and Country Offices aware of them. Historically, EVM1 assessments were run by international consultants, which resulted in little country ownership. The expectation for EVM2 is that by making the tool available on an application, it will be more flexible and dynamic and able to be used independently by countries, thus fostering more country ownership of the assessment and improvement process. However, IPAC recognized that marketing and advocacy of these new tools will be critical to their widespread uptake, and that linking their use to the work of National Immunization Technical Advisory Groups (NITAGs) and National Regulatory Agencies (NRAs), will contribute to ensuring that.

For the time being, WHO/EPI maintains responsibility for developing and implementing the EVM2 and the Vaccine Wastage Calculator tool. IPAC suggested that sustainable use of these tools could be strengthened by engaging with regional and in-country institutions. UNICEF will be leading this part of the work and has already started engaging with relevant institutions at different levels.

Additional points from the closed session of the IPAC members

IPAC members congratulated the team on the work conducted to date in the areas of EVM2, the Vaccine Management Handbook and the vaccine wastage calculator, as well as the collective focus on ownership at country level. They suggested that to ensure sustainability, in addition to focusing on identifying institutions in country or regionally to hand this work over to, WHO and UNICEF look beyond the immunization programme at shared supply chain initiatives such as the Global Fund to fight AIDS, Tuberculosis and Malaria (GFATM⁶) and UNITAID⁷. Linking with these could pave the way for health systems improvements.

IPAC members cautioned the team to ensure that any improvements in vaccine wastage not be at the expense of coverage and equity. They stated that one of the strengths of improved vaccine wastage rates and information in this area is the ability for a country to forecast its vaccine needs more accurately, and to give health care workers permission to incur wastage by opening a multi-dose vial for one child, noting that this is a key theme in the Missed Opportunities for Vaccination (MOV⁸) area.

IPAC members also urged the developers to make sure to link the EVM2 assessment with programmatic results, e.g. improvements in coverage, reduction in dropouts and reduction in vaccine wastage. The EVM team was also urged to facilitate the linking of the improvement plan to the annual immunization plan to facilitate implementation of the suggested improvements.

IPAC members noted the high number of questions in the EVM2 and suggested that to reduce the burden on the assessors at country level, the EVM2 team could examine whether there are questions that could be removed.

⁶ <https://www.theglobalfund.org/en/>

⁷ <https://unitaid.org/#en>

⁸ https://www.who.int/immunization/programmes_systems/policies_strategies/MOV/en/

SESSION IV: VISION AND STRATEGY FOR IMMUNIZATION 2021-2030

1) “IMMUNIZATION AGENDA 2030” TOWARDS A VISION AND STRATEGY FOR VACCINES AND IMMUNIZATION FOR THE DECADE AHEAD

(Ann Lindstrand, WHO/EPI – presented for information)

With the Global Vaccine Action plan (GVAP) coming to an end in 2020, a new vision and strategy for vaccines and immunization is needed. This will set the new direction for the next decade that engages and aligns stakeholders at all levels, addresses emerging issues, harnesses new solutions for impact, and reiterates the importance of vaccinations in contributing to the broader health and development agendas.

The Immunization Agenda 2030 (IA2030) has been co-created by key stakeholders and is intended to be a worldwide immunization agenda. The new Strategy builds on recent other global health strategies, disease specific strategies, partnership strategies and different immunization roadmaps. WHO/IVB is working closely within this context to link and not duplicate efforts.

The appointment of the new IVB Director accelerated the process for developing the new Immunization Agenda with a three-day Forum in March 2019 bringing together representatives from 50 Organizations and 30 countries to brainstorm around the new Immunization Agenda.

Draft zero of the document was the result of the Forum and is being reviewed between now and August 2019 through a variety of means. There are dedicated events to provide regional and country consultation opportunities – the WHO Africa Regional Office will hold a 2-day meeting to discuss it with countries - and the document can be reviewed by anyone using offline/online methods⁹. Draft 2 will be presented to SAGE in October 2019, and subsequent iterations will be presented to the WHO Executive Board in January 2020 and to the World Health Assembly (WHA) in May 2020.

The Immunization Agenda 2030 which will be presented to the WHA in May 2020 will include two components:

1. The **Immunization Agenda 2030 Vision & Strategic Framework**, a document setting direction and highlighting priorities made up of:
 - a. **The Vision** – a 1-2 page document for everybody
 - b. **The Strategic Framework** – a 15-20 page document for the immunization community and wider stakeholders. This framework is driven by six interlinked Strategic Priorities that are tailored and flexible to the changing world ahead: Systems and Integration; Equity and Access; Fragility and Emergencies; Value and Ownership; Research and Innovation; and Sustainability and Accountability.
2. **IA2030 Online Resources** made up of technical guidance, examples of operational plans, and disease-specific technical guidance and best-practice documents.

Adaptive ways and means in four areas – country driven, broad partnerships, people-focused, data-driven – will guide implementation through actions at global, regional and country levels. Different responsibilities will be outlined at the three different levels.

The WHA has requested that detailed monitoring and evaluation indicators be presented to the WHA at the end of GVAP in 2021 at the same time as the final reporting on the GVAP.

⁹ Pulse survey: <https://www.surveymonkey.com/r/IA2030>

Written comments: immunizationagenda2030@who.int or <https://tinyurl.com/ia2030>

Discussion

IPAC congratulated WHO on the leadership and collaborative approach it has demonstrated during the process of developing the Immunization Agenda 2030. It was suggested that WHO continue to focus on asserting itself as the technical partner and play a key role in advocating for immunization as a public good. IPAC suggested that high visibility backing of the IA2030 by the WHO Director General would have enormous impact, especially with the Ministries of Health and Ministries of Finance of Member States.

IPAC learnt that care is being taken to continue building strong immunization systems and not undermine this flagship intervention. The focus is more on reorienting better on how to reach the remaining 20 million in a changing global environment, identifying new directions, working with other actors, and building new platforms with other interventions where parents understand the value of coming to health services. Throughout this, identifying and addressing social and cultural barriers and demand issues will be key.

IPAC suggested that a greater level of detail, including an operational plan that outlines the linkages between the global plan and the regional and country plans, will be very important in future iterations. Members noted the importance of the WHO Regional Offices continuing to be fully engaged in this process as that is who will be the face of the Immunization Agenda 2030 from the country perspective.

It was also cautioned that care needs to be taken to ensure that the financial and human resources to ensure implementation of IA2030 are made available at the different levels. However, as Overseas Development Aid (ODA) for health is decreasing and more and more countries are moving into the Middle-Income Country (MIC) category, IPAC recognized that the emphasis will need to be on countries' own domestic funding and concentrating the global focus on the weakest countries, making GAVI support key.

IPAC further commented that according to their initial review of the document, the following areas could be better emphasized: Vaccine hesitancy; Immunization throughout the life course; Innovation and research (new delivery strategies and technologies are going to be needed to do things differently); Integration and linkages to other areas of health (although care needs to be taken not to dilute the successes of the immunization programme that are due to its verticality); Fragile and emergency settings; and Operational research. IPAC members also encouraged WHO to pay more attention to regulatory aspects and push for regulatory harmonization, i.e. reducing the time lag between licensure of products in the US and licensure of products in Africa and Asia,

WHO informed the meeting that the umbrella framework may change to make the work in vaccine hesitancy and demand more visible, and there may be a second strategic priority on life course and integration. They also recognized that vaccine safety and AEFI monitoring may need to be better emphasized.

Given the breadth and scope of the document, IPAC felt that prioritization will be needed and suggested that as no new vaccines will be available for introduction during the first five years of the Strategy that the focus be on consolidating and delivering what vaccine portfolios there are to those who need them most, i.e. those countries and populations with the highest disease burden, the most unimmunized, and to fragile settings. IPAC noted that to reach these underserved populations, new collaborative partnerships will be needed that might involve the private sector, CSOs, other entities that have newer ways of working in immunization.

IPAC suggested that the involvement of communities will also be key to achieving success and as these are often populations that are marginalized and have no voice, countries and governments need to be encouraged to include communities in the planning, implementation and monitoring process by engaging with different groups such as youth groups, religious groups and women's groups.

IPAC further noted that as IA2030 is operationalized, the changes in ways of working required to increase immunization coverage and equity will have a disruptive effect on front-line personnel. To reduce this and foster buy-in, creative ways need to be found to make sure that the beneficial impact of the changes on the work of the programmatic people and their communities is demonstrated.

It was confirmed that the goals for IA2030 will be presented to SAGE in October 2019. Discussion is ongoing as to whether these should be vertical, disease-specific goals, or goals related to horizontal integrated ways of working. A suggestion from IPAC was to use disease burden modelling to start with the achievement of disease-specific goals and work backwards to see what programmatic steps would need to be taken to achieve this level of vaccine preventable disease (VPD) control across all diseases. As the WHA has requested a report on the feasibility of measles eradication for May 2020 and the modelling for that is underway, this could be a possibility.

IPAC welcomed the information that an accountability loop detailing who is responsible to make this ambitious agenda work will be finalized by 2021, when WHO will present the Monitoring and Evaluation (M&E) framework to the WHA while presenting the final report on the GVAP.

An IPAC member reflected on the value of strong monitoring and field vaccine effectiveness evaluations to ensure that WHO goals and action plans take into account field realities in the next decade.

Additional points from the closed session of the IPAC members

IPAC members noted the importance of accountability mechanisms for the IA2030 and urged CSO engagement in the setting of country level indicators. They also noted that the increasing networks of partnerships that will be required to deliver and provide support to achieve the aims of the IA2030 should not be underestimated, and that thought as to how this will be implemented at field level is important.

2) WORKING TOGETHER GUIDE: OVERVIEW, DISSEMINATION AND ACTION

(Emily Wootton, WHO/EPI – presented for strategic guidance)

IPAC was updated on the *Working Together Guide*¹⁰, a recently published WHO resource guide for immunization services throughout the life course. The aim of the document is to bring together relevant resources, summarize current knowledge and provide guidance on the integration of immunization with other health interventions, health policies and activities to strengthen health systems. The document is aimed at national managers from immunization, reproductive, maternal child and adolescent health, and other related programmes, as well as global, regional and country level policy-makers and partners.

The Appendix provides key information about integrated service delivery. For each service type, e.g. nutrition, malaria, deworming, etc., it provides the relevant WHO Recommendation, highlights opportunities to link with immunization, provides a summary of documented experiences and outlines considerations for integration and useful references.

Vaccine innovations have increased the number of vaccines included in immunization programmes, and while the publication is mainly about integration, it also looks at immunization along the life course. “Delivery platforms” provide a useful way to group populations for the delivery of vaccines (and other interventions). Countries can

¹⁰ https://www.who.int/immunization/documents/ISBN_9789241514736/en/

determine their own groupings for delivery platforms based on their needs and context, e.g. school health programme availability.

In recent years, high immunization coverage rates have increased interest in integration from other services. Conversely, integration of immunization with other health programmes is starting to be seen as beneficial as increasingly innovative approaches are needed to reach new target populations, e.g. delivery of HPV vaccine through adolescent health services and as part of a comprehensive cancer control strategy over the life course. Integrating immunization with other health services may result in increased coverage, improved system efficiency, improved user satisfaction and increased demand. But there are potential risks associated with integration, such as a negative impact on overall coverage or equity, reduced quality of care due to less healthcare worker time being available, unwillingness of healthcare workers to take on additional responsibilities and beneficiaries not accepting integrated services. In order to overcome these potential risks, careful planning for integrated service delivery is key. The Integrated Service Checklist included in the Integration Resource Guide will help to make sure that planning is sufficient to mitigate potential risks.

Monitoring and evaluation was also emphasized also important. Integrated services should be monitored and evaluated in order to understand the impact of the change in services, to provide a feedback mechanism to improve the programme and to build the local, regional and global evidence base on the benefits of integration. Guidance in this area is also provided in the Resource Guide.

The Resource Guide is available on the WHO website, has been distributed to Partners and other teams in WHO and hard copies have been sent to the WHO Regional Offices. The materials contained in the Guide have been used by others, e.g. in the Gavi guidelines, and the Guide has been added to the TechNet Library and Forum and included in WHO's online Scholar Course.

Discussion

IPAC welcomed the Resource Guide and were pleased to hear that the WHO Regional Office for Africa has already used the content to update their Reaching Every District (RED) guide, and that the document will be disseminated more at the annual Regional Technical Advisory Group (TAG) meetings.

IPAC noted that that some of the best examples of integration are cases where donor financing and the accompanying monitoring and evaluation programme design have been changed so funding and results are expected as an integrated package. IPAC suggested expanding the audience for the Resource Guide to a wider global community, including funding agencies who are supporting communities in countries, to provoke such a reorientation.

It was made clear, however, that documentation of the services being integrated at country level and on the impact of integration is lacking. Although this year's Joint Reporting Form asked countries to provide information on these aspects, many countries did not answer these questions.

IPAC noted that impetus for change will need to come from an economic point of view and suggested that additional consideration be given to documenting the savings in societal costs of a mother coming to a clinic for all health services and not having to return for each individual intervention, using this to make a stronger case for integration. As there are very few cases in literature showing savings by integrating interventions, it was suggested that WHO turn more to the Primary Health Care and Health Systems Strengthening groups in the Ministries of Health, as these, together with health care workers coalitions and Civil Society Organization, can help with gathering information and advocating for integration at country level.

Additional points from the closed session of the IPAC members

Regarding further dissemination of the Resource Guide, IPAC members suggested that IAIM Network¹¹ (International Association of Immunization Managers) could be helpful in disseminating the concepts and the document. The IAIM network is an international network of immunization managers and it may be possible to offer a Webinar on this topic through their network.

SESSION V: WORKING GROUP UPDATES

1) CONTROLLED TEMPERATURE CHAIN (CTC) WORKING GROUP.

While the **Controlled Temperature Chain Working Group (CTC-WG)** has not had to meet in almost a year, there has nevertheless been momentum within the CTC workstream, which will soon require additional input and guidance from the CTC-WG, especially as the current strategic roadmap for CTC nears its end and new priorities must be set for post-2020. IPAC was provided with a brief update on the various activities and recent progress enjoyed by the CTC agenda, managed jointly by WHO and PATH.

(a) Human Papilloma Virus (HPV) Vaccine use in a Controlled Temperature Chain (CTC) - Desk Review.

(Dijana Spaseniska, WHO/EPI, presented for strategic guidance)

The benefits of delivering a vaccine using a controlled temperature chain (CTC) include cost savings, programme efficiencies, improved coverage and equity and reduced risks associated with the mishandling of vaccines. The Human Papilloma Virus (HPV) vaccine is one of the four vaccines prioritized for CTC use and Gardasil® 4 is eligible for CTC delivery, with an upper limit of 42°C for up to three days.

However, there are challenges in advancing the uptake of HPV in CTC. A Desk Review was commissioned on behalf of WHO's EPI team to identify constraints to effective HPV delivery that are of particular relevance to the use of HPV in CTC, and to provide evidence in support of the case of CTC use for HPV. The Desk Review included data from the CTC-HPV pilot project in Uganda in October 2017, HPV Post-introduction evaluations (PIEs) conducted in 11 countries, 31 other sources and consultations with relevant people from WHO/EPI and PATH.

The main findings of the Desk Review showed insufficient compelling evidence to favour CTC application to HPV delivery, despite the 2017 pilot CTC-HPV project in two provinces of Uganda which demonstrated that use of CTC facilitates the work of EPI staff and overcomes poor cold chain capacity problems. However, effective implementation requires a well understood target population and appropriate microplanning efforts to estimate the needed vaccine. Among the shortcomings of the case for adopting CTC is the lack of clarity around the economic trade-offs associated with its implementation.

With regard to the logistics for outreach, transport was a challenge for healthcare workers making it difficult for them to reach distant schools. The fact that the healthcare worker was away from the health facility for an increased amount of time was disruptive to other activities in the health facility and required compensation through longer work hours, task shifting or use of staff from other areas.

From the rest of the literature, although it appears that financial costs were driven by allowances and transport costs for health workers and supervisors and by social mobilization, countries were not clear about the long term

¹¹ <https://www.iaimanagers.org/en/about-us>

financial needs to implement HPV-CTC, beyond the procurement of the vaccine. Cost-effectiveness studies did show higher delivery costs for rural schools due to costs for transport and additional personnel needed.

Regarding cold chain related problems, the 11 PIEs found issues of non-functional equipment, insufficient cold storage space and cold chain capacity, and absence of electrical power back up during power outages in a number of the countries. These are issues that are frequently part of national immunization programmes in many countries which if acknowledged, could be alleviated by using HPV in CTC.

It was confirmed to IPAC that the Desk Review had some limitations. As the literature mainly focusses on HPV demonstration projects and only one study was done using HPV in a CTC setting, there is limited ability to draw conclusions on the constraints to effective HPV delivery related to the use of HPV in CTC and to provide evidence in support of the case of CTC use for HPV. In the PIE reports, 6/11 countries reported difficulties in estimating accurate coverage, so drawing conclusions as to the increase in coverage is of minimal value. Furthermore, the costing studies conducted as part of the PIEs are either not published or published with methodological limitations; therefore the cost-effectiveness is estimated based on models with underlying assumptions. Tanzania and Senegal have started delivering HPV and more studies will be conducted with results expected in 2020.

(b) Progress on the Application of Controlled Temperature Chain to Oral Cholera Vaccine.

(Maricel de Quiroz Castro, WHO/EPI – presented for strategic guidance)

The CTC Strategic Roadmap (2017-2020) has as objectives, to facilitate vaccine delivery for better coverage and to achieve equity targets for CTC-qualified vaccines, and to support MICs and LICs with limited resources and infrastructure. It has two areas of strategic focus: Upstream development and licensure of more CTC-compatible vaccines (TTCV and HepB), and downstream scale-up of country-level experience (HPV/ Gardasil® and OCV/ Shanchol™ - both WHO CTC prequalified).

An original commitment was made through the current CTC Strategic Roadmap to pilot Oral Cholera Vaccine (OCV) with CTC in at least one country by 2018, support uptake by at least two new countries within 2019, and explore potential synergies in co-administration by 2020. However, the delays in obtaining prequalification for an OCV product have translated into implementation delays which the WHO Secretariat is now working on mitigating.

Although there are three WHO prequalified oral cholera vaccines, only Shanchol™ has been prequalified for use in CTC. The conditions attached to prequalification for effective CTC use are: One excursion just prior to administration of the vaccine; Specifically, limited duration - maximum of 14 days; Maximum ambient temperature up to 40°C; and use of vaccine vial monitors (VVMs) and Peak Threshold Temperature Indicators (PTTIs).

There are three programmatic settings for use of OCV in CTC, all of which are in rural, isolated areas or slums with limited infrastructure: Periodic mass vaccination campaigns; Pre-emptive vaccination campaigns; and Reactive vaccination campaigns.

The OCV-CTC pilot implementation is intended to generate data in support of an OCV-CTC use case in any of the above three scenarios and to document lessons learned to inform the development of operational guidance on OCV-CTC field implementation. However, there are several obstacles this project is working to overcome, including competing priorities in the country initially selected as pilot site, insufficient supply of Shanchol™ vaccine, as well as slow uptake of the CTC approach by other countries.

But other opportunities remain. Euvichol™, another OCV formulation, is expected to be submitted for WHO CTC prequalification during the first half of 2020. There are countries such as Bangladesh and Mozambique that have

already elected to take a CTC approach in their recent OCV campaigns. The protocol, tools, and a new study setting for the OCV CTC pilot are already available.

The protocol for the OCV CTC Pilot has as its general objective to demonstrate the superiority of the CTC strategy in terms of the average number of people vaccinated per day by a vaccination team compared with the standard cold chain strategy holding all other resources constant. Secondary objectives include comparison of vaccine wastage, cost per dose delivered and vaccination coverage in areas using CTC and standard cold chain, assessing the perceptions of the CTC strategy among vaccination teams, assessing the knowledge, attitudes and practices towards vaccination among vaccinators and vaccine supervisors, and comparing the average number of vaccines, cost and coverage between the door to door strategy and the fixed site strategy if both strategies are used. PATH is also committed to conducting cost effectiveness analysis as part of the pilot OCV-CTC effort to further contribute to the growing evidence base in support of CTC.

(c) Status Update on Advocacy with Vaccine Manufacturers

(Anna-Lea Kahn, WHO/EPI – presented for strategic guidance)

In 2015, an Evaluation of Manufacturers' Perceptions of CTC revealed a lack of general awareness of the advantages of CTC, insufficient clarity on the regulatory pathway and insufficient economic incentives. To date, a reluctance on the part of manufacturers to prioritize and pursue CTC testing and licensure persists.

The CTC Working Group was established in July 2016, as a subgroup to IPAC, and includes industry representation (DCVMN¹² & IFPMA¹³). One of its key outputs is the *CTC Strategic Roadmap for Priority Vaccines (2017-2020)*, mentioned above.

The CTC Strategic Roadmap includes four priority CTC vaccines that were selected based on their potential in terms of adequate heat stability, a delivery strategy that would benefit from CTC use, an expressed country need and the technical feasibility of CTC licensure. The first two, HPV and OCV, have a downstream, programme level focus. The other two, Hepatitis B birth dose (HepB-BD), and Tetanus toxoid containing vaccines (TTCV), have an upstream, industry level focus.

For the HepB-BD and the TTCV, manufacturers are required to submit to three levels of validation for CTC: their own scientific laboratory validation of stability testing, regulatory approval, and WHO prequalification approval. Support is provided for manufacturers through the CTC agenda in the form of Generic Preferred Product Profiles (gPPP)* as of 2015 – on heat stability, PSPQ, WHO Guidelines on Stability Evaluation of Vaccines under *Extended Controlled Temperature Conditions* (ECTC), and regular bilateral discussions, including with the WHO Prequalification Team.

For HPV, more country uptake is required, and an optimal use case determined that prioritizes duration of excursion over upper temperature limits.

As discussed above, Shanchol™, an oral cholera vaccine, is to be piloted for use in a controlled temperature chain most likely during Q3 2019, and an additional cholera vaccine, Euvichol™, is expected to be prequalified for CTC use in Q2 2020. Both have high public health impact and should bring much needed momentum to the CTC agenda.

¹² Developing Countries Vaccine Manufacturers Network - <https://www.dcvmn.org/>

¹³ International Federation of Pharmaceutical Manufacturers Associations - <https://www.ifpma.org/>

To encourage manufacturers to submit appropriate candidate vaccines for CTC licensure, GAVI and UNICEF Supply Division will need to support or consider preferential procurement incentives that are not solely based on price. There is also a need for stronger advocacy on the importance of the public health impact of vaccines using CTC and not just a focus on the relative cost of the vaccine.

The CTC Working Group will convene in Q3 2019 to begin work on the next Strategic Roadmap (2020+) for CTC. Having industry representation on the Working Group will be a major advantage. One item for consideration will be the revision of the definition of CTC to prioritize duration over temperature, which may allow more flexibility and maybe more products to be submitted for licensure. The CTC Working Group will also evaluate the potential recommendation for VVM+ - a vaccine vial monitor which integrates a peak-temperature indicator. And they will discuss new potential priority vaccines, e.g. typhoid, rabies, rotavirus.

Discussion

IPAC thanked WHO and PATH for the lead they have taken on this initiative and are confident that over time evidence of increased coverage and equity made possible by CTC will be generated. Although there may be price increases due to the higher amount of antigen required for vaccines to remain effective in CTC use, the meeting was reminded that Gavi and UNICEF do not award vaccine tenders based only on price, but also on public health impact and programmatic suitability.

WHO was also congratulated for the good relationship between the WHO/EPI programme and the WHO/Prequalification team and was urged to provide clarity to manufacturers on their priorities for vaccines usable in the CTC context so these preferences can be absorbed into investment decisions. Note was taken of the importance of not changing programmatic requirements, but to establish a target product profile and ensure that manufacturers have a good understanding of what programmes require.

WHO recognized potential advantages to relaxing temperature requirements as this could yield more vaccines being requested for CTC licensure, but needs to balance this with the programmatic advantages and the requirement for WHO to specify 40°C as an upper temperature limit given the breadth of countries for which it licenses products. IPAC was reminded that the original intent of CTC was to use the flexibility it afforded to store vaccine up to 40°C for the last mile before delivery. Initially, WHO requested a longer duration for CTC viability but no VVM was available that covered such an extended duration. Now that a 250-day VVM exists, discussions are needed with manufacturers to see when this VVM and the duration it covers can be implemented in a CTC setting.

Despite the complexity of the *in vivo* quantitative testing required for potency testing, this could be an area for manufacturers to focus on to increase uptake. Shanchol™ is licensed for 14 days' use in CTC which means that both the first and second dose can be removed from the cold chain potentially allowing the second dose to be left for the patient to self-administer, which would be a big step in achieving full immunization with this vaccine in difficult settings. The revised definition of CTC to be discussed by the CTC Working Group will take these issues into account.

IPAC suggested that it may be beneficial to solicit the position of countries' National Regulatory Authorities (NRAs) on CTC through the WHO Regional Offices as the regulatory positions of different countries and their willingness to approve CTC need to be included in the prioritization of vaccines.

Additional points from the closed session of the IPAC members

IPAC members expressed concern about the slow advancement of the CTC agenda for delivery of HPV vaccine, noting that it is hard to build a use case based on the available evidence. Equally concerning is that after piloting HPV in CTC use, the positive feedback from healthcare workers who welcomed the flexibility CTC provided did not translate into clear impact on coverage or cost, leading Uganda to revert to using the traditional cold chain rather than scale up the CTC approach nationwide. IPAC members suggested conducting a study in Uganda as to why the decision was made to abandon the use of CTC, as this may provide insights into the concerns behind the change in practices required by CTC, which can be used to advocate with decision-makers and explain this decision to other countries considering CTC.

Given the supply constraints anticipated with HPV vaccine, IPAC members felt it is risky to tie the advancement of the CTC agenda to this vaccine, and urged the CTC Working Group to explore another vaccine to spearhead this work, such as OCV. Although the Hepatitis B birth dose would also be a good candidate, licensure of a product for CTC use is not expected soon, and it will be hard to define a use case aligning an unpredictable event (birth) and licensure.

2) PROGRAMMATIC SUITABILITY OF VACCINE CANDIDATES FOR WHO PREQUALIFICATION (PSPQ): UPDATE ON PSPQ PROCESS AND ACTIVITIES

(Kelly Moore, PSPQ-SC Member & IPAC Chair – presented for strategic guidance)

The objectives of the PSPQ Standing Committee (SC) are to define the characteristics that determine the programmatic suitability of vaccine products and define the process for assessing compliance with these characteristics, and to indicate programmatic characteristic preferences to industry and other vaccine development stakeholders in order to shape the vaccine pipeline.

The SC is an independent advisory committee composed of two IPAC members (David Brown and Kelly Moore) and three independent experts, thus guaranteeing immunization programme and policy experience. Additional information from manufacturers and other sources is requested as needed. Final recommendations of the SC are sent to the WHO Prequalification Secretariat and the Director of the WHO Essential Medicines and Health Products (EMP) Department.

Since July 2018, the PSPQ Standing Committee has reviewed two products for review: Inactivated Influenza Vaccine (IIV) in a 0.5mL vial, unpreserved, and Hepatitis B subunit vaccine, in a 1.0mL vial, unpreserved. A common issue in both vaccines is the dosing for some children at half of volume in the vial and the potential for field use as an unpreserved two-dose vial.

For the candidate influenza vaccine, the Steering Committee recommended that the product be accepted, given the supply challenges often associated with annual seasonal influenza immunization, provided it meets the following conditions: (1) A clear statement be included in the package insert instructing user to discard the unused fraction immediately after administration of a 0.25mL dose to a child aged 6-35m; (2) WHO, UNICEF Supply Division and PAHO Revolving Fund websites be revised to state clearly that when a 0.25mL dose is used, the remainder should be immediately discarded. This statement should also be included in supervisory checklists issued by national immunization programmes where such products are used.

For the candidate hepatitis B vaccine, the Steering Committee declined prequalification of the unpreserved adult 1.0mL single-dose vial for three reasons: the risk of mishandling of 1.0mL unpreserved vials is unknown; the effectiveness of the Product Insert (PI) instruction to discard is unknown; and because no supply constraints or

other conditions were described to justify the need to accept the possibility that the unpreserved 1.0mL dose could be used contrary to the PI as unpreserved paediatric 2-dose vial. However, the Steering Committee recommended that WHO should proceed to prequalify the unpreserved child 0.5mL single-dose vial.

Discussion

IPAC noted that there are sometimes delays in reviewing candidate vaccines. The PSPQ Standing Committee has taken steps to streamline its review process and although there is a time limit of three months to review candidate vaccines, the Standing Committee is usually able to complete the process more swiftly. The Standing Committee also noted that as there are many novel vaccines on the horizon, thereby likely requiring that a face-to-face meeting be held this year to review the various issues.

3) DELIVERY TECHNOLOGIES WORKING GROUP: UPDATE FOR IPAC.

(Courtney Jarrahian, PATH – presented for information and coordination)

The goals of the DTWG are to provide a platform to enable industry and the public sector to engage in constructive dialogue on the presentation, packaging, and delivery aspects of vaccine products, and to optimize innovation and maximize the appropriateness of immunization products for public-sector use.

The DTWG is jointly led by PATH and WHO, is comprised of up to 15 members with diverse expertise in global public health, product development and manufacturing, vaccine policy and implementation, LMIC immunization programmes, new delivery technologies, and marketing, including representation from IPAC, PDVAC, VIPS, IFPMA, DCVMN, MSF, JSI, UNICEF, and the Bill and Melinda Gates Foundation.

Since 2015, the DTWG has been instrumental in reporting on the indicator in the GVAP related to licensure and launch of at least one platform delivery technology by 2020, reviewing nine vaccine technologies, establishing the target product profile for the MR MAP and conducting two usability studies, engaging with developers and manufacturer through conferences and workshops, and reviewing the Vaccine Technology Impact Assessment (VTIA) economic analysis tool, the Total Systems Effectiveness (TSE) project, and the Vaccine Innovation Prioritisation Strategy (VIPS). The main progress in technology facilitated through consultations with the DTWG are the MAPs and the blow-fill-seal compact prefilled auto disable devices (CPADs).

Since mid-2018, the work of the DTWG has been paused to focus on supporting the launching of the VIPS but is being re-launched in July 2019 in tandem with the VIPS prioritization process.

Discussion

IPAC noted that while the scope of the DTWG goes beyond technologies being evaluated by VIPS, the DTWG will be called upon in the next 6 months to evaluate the 10 specific innovations for VIPS from the perspective of technical feasibility, manufacturability, regulatory hurdles, alignment with manufacturer priorities, and incentives needed to encourage product development and uptake.

Meeting participants also noted that as the outcomes of the DTWG may feed into IPAC deliberations, participation of manufacturers in the DTWG may need to be revisited to make sure that the IFPMA and DCVMN nominees are individuals with the requisite expertise.

Additional points from the closed session of the IPAC members

IPAC members welcomed the work of the PSPQ and DTWG and agreed that IPAC members should continue to be part of these two committees to foster cross-fertilization of technologies.

CONCLUSIONS AND CLOSING REMARKS BY THE CHAIR

The IPAC Chair closed the meeting by expressing her thanks to all participants. On behalf of the Committee, she recognized the immense amount of work undertaken by WHO's IPAC Secretariat and the different Working Groups.

**WORLD HEALTH ORGANIZATION
IMMUNIZATION VACCINES & BIOLOGICALS
IMMUNIZATION PRACTICES ADVISORY COMMITTEE (IPAC)**

REPORT OF THE CLOSED MEETING - 13 JUNE 2019

Present:

- IPAC members: Kelly Moore (Chair), Craig Burgess, Ian Gemmill, Masahiko Hachiya, Yang Baoping.
- WHO Staff Members: Anna-Lea Kahn (Secretariat).

Agenda:

- I: Deliberations and recommendations
- II: Summary of SAGE evaluation outcomes and implications for IPAC

I: Deliberations and Recommendations

The additional points from the closed session of IPAC members on the meeting agenda items are included in the main body of the report.

II. Summary of SAGE evaluation outcomes and implications for IPAC

For information, in addition to the SAGE, the WHO Department for Immunization, Vaccines and Biologicals has three Advisory Committees¹⁴ that provide evidence-based guidance on immunization and vaccine-related policy and programming: The Immunization and Vaccines Related Implementation Research Advisory Committee (IVIR-AC); The Immunization Practices Advisory Committee (IPAC); and The Product Development Vaccine Advisory Committee (PDVAC).

An external evaluation of WHO's Strategic Advisory Group of Experts (SAGE) was held in 2018/2019 by an independent group. Although the general conclusions of the evaluation did not refer to IPAC specifically, several of the outcomes have implications for IPAC, a summary of which follows.

The importance of the IVB Advisory Committees was acknowledged, and there was a call for more clarity on roles, scope and linkages with the SAGE. It was felt that the agenda development process for the different Advisory Committees warranted further examination, and better decision-making on which issues should be discussed by which Advisory Committee, including what subject matter could be better suited for the Regional Immunization Technical Advisory Groups (RITAGs).

It was noted that the SAGE should maintain its scientific and advisory role while limiting its involvement in facilitating implementation to supporting the respective Regional Immunization Technical Advisory Groups (RITAGs) and National Immunization Technical Advisory Groups (NITAGs). There was no suggestion that this be taken up by IPAC.

There were questions on whether the Advisory Committees are having the desired level of impact and whether the SAGE could help facilitate optimization of this.

While SAGE makes recommendations to the Director General of the Organization, the Advisory Committees provide advice to the IVB Director. Given the difference in visibility, there is an increasing trend for issues to be

¹⁴ <https://www.who.int/immunization/policy/committees/en/>

directed to SAGE and bypass the respective Advisory Committee. This inconsistency will need to be considered by the incoming IVB Director as the restructuring of IVB proceeds.

The following topics were considered not appropriate for SAGE and it was suggested that they be transferred to IPAC: Behavioural science; Supply and cold chain; Immunization Workforce; Implementation evidence synthesis; Consideration of operational issues.

The General Recommendations emerging from the SAGE Evaluation included the need for improved coordination and harmonization across IVB Advisory Committees and clarity around roles, responsibilities and potential overlap.

Additional general recommendations with implications for IPAC are a call for less global and generalized meetings, more targeted and fit-for-purpose short-term technical working groups, and the possibility of transferring discussions on implementation and operational issues from Global to Regional level for discussion by RITAGs and NITAGs.

Discussion

IPAC members agreed that, although it makes sense to divert responsibility for issues of specific regional context to the regional advisory bodies, they emphasized that IPAC provides a necessary programmatic perspective that contributes to ensuring research and development agendas remain oriented towards the most significant challenges at the operational level.

Regarding the suggestion that the SAGE limit its focus to scientific, disease-specific or vaccine-specific issues, IPAC members urged caution that if the SAGE agenda is reoriented to focus solely on setting norms, standards and policies at the global level and all implementation issues are delegated to the regional level, there is a risk that the global level becomes too remote from programmatic realities.

Furthermore, it was noted that consideration of implementation science appears in the Terms of Reference of the SAGE yet is rarely reflected in its meeting agendas. IPAC members feared that delegating implementation issues entirely to IPAC will result in an imbalanced dialogue in the SAGE Meetings. The Committee proposed that the focus of the next 10 years be on increasing equity and coverage where the main gains in this area are going to come from changes in implementation strategies, not necessarily from new vaccines or technologies. Therefore, SAGE's continued involvement in implementation issues and its key role in advising on priority topics for implementation research is key to achieving the goals of the next decade.

IPAC members recognized that more regular communication between the Chairpersons and Secretariats of the respective Advisory Committees would help overcome possible confusion over the roles and scope of each Advisory Committee and facilitate the identification and prioritization of emerging issues and agreement on the appropriate Advisory Committee for their deliberation. IPAC's comparative advantage is to stimulate thinking in the other Committees to look beyond products and to factor in the programmatic, political and financial dimensions required to get vaccines delivered.

Some concern was expressed over the suggestion that more short-term technical working groups be used, as establishing such working groups in a credible and independent manner takes time, and the work frequently goes on longer than initially expected.

Lastly, IPAC members questioned whether the current IPAC Membership and meeting participation is providing the different expertise needed. In the past, the IPAC meetings had included official Observers from key partner

institutions but this was discontinued after the 2017 revision of the IPAC TORs. Currently there is *ad hoc* representation from UNICEF, PATH, CDC, DCVMN, IFPMA, NGOs, JSI, and MSF, although this is not consistent nor systematic. It was questioned whether such entities should have a standing invitation or whether they should be invited on a case by case basis according to the agenda.

A key conclusion of this discussion was the important role IPAC has played in informing global policy considerations, including upstream research and development priorities, with the perspective of programmatic realities. In this way, IPAC has helped to shield national immunization programmes from unrealistic burdens and expectations. IPAC has also offered a unique forum, in principle, for industry members to engage in dialogue with programme professionals on immunization practices and for partners to track IVB's priorities and most pressing implementation issues. Though impact at the country or programme level has not always been evident nor easy to measure, the opportunity to regularly convene relevant stakeholders from country to global level around programme concerns and immunization practices is viewed as extremely valuable for preserving open dialogue and partnerships, as well as ensuring that programme interests are foremost in the discussions.