



WORLD HEALTH ORGANIZATION IMMUNIZATIONS, VACCINES AND BIOLOGICALS

IMMUNIZATION PRACTICES ADVISORY COMMITTEE (IPAC) 11-12 June 2014

Final meeting report and recommendations

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Opening and Introduction

Mr Michel Zaffran, Coordinator of WHO's Expanded Programme on Immunization, officially opened the meeting. Dr Chris Morgan, the Chair, welcomed participants and acknowledged the regrets of Dr K.O. Antwi-Agyei, Dr Xavier Bosch-Capblanch, Dr Shelley Deeks, and Dr Folake Kio-Olayinka. He welcomed Mr Adama Sawadogo, representative of UNICEF replacing Dr Osman Mansoor, and expressed the regrets of Dr Majo Leroux-Lepage as the representative of the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA).

IPAC Members present:

Christopher Morgan (Chair)
Robin Biellik
Jonathan Colton
Francois Gasse
Najwa Khuri-Bulos
Jean Marc Olivé
Robert Steinglass
Carla Vizzotti

Session I. Home-based vaccination records

Ms Marta Gacic Dobo summarized the available information on format and utilization of home-based records, a useful but neglected tool. She underscored the upcoming opportunity to revitalize home-based vaccination records around the introduction of inactivated poliovirus vaccine (IPV) in many countries. Ms Skye Gilbert provided an overview of the Bill and Melinda Gates Foundation supported design contest, "Record for Life", including the process of selecting the finalists and a variety of innovative ideas from finalists.

Discussion:

The presentations were well received and followed with rich discussion. IPAC was requested to comment on presented activities and identify any additional ways to revitalize the role of home-based records within the service delivery bundle.

Integrated versus vertical approaches to home-based vaccination records were brought up by several IPAC members and participants. It was recognised that completeness of sections not related to immunization within home-based records is not well understood and poorly documented and that there is a need for additional operational research in this area. It was

also well recognized that an integrated approach can present challenges to immunization programmes in terms of coordinating with other programmes when confronted with the need to update in case of new vaccine introduction compared to a simple vaccination-only record. Furthermore, it was emphasised that home-based records should be synchronised with other monitoring tools such as facility-based records.

The current proxy measure of home-based record prevalence derived from survey results can be misleading, as it does not capture if the card was provided to a caregiver. In addition, in some areas this measure can overestimate the prevalence, as cards are based at health facilities and not with caregivers in many European countries. These instances should not detract from nor overshadow the global problem of low home-based record prevalence, particularly in low-income settings.

Improvements in home-based record prevalence may benefit more from improving community demand as much as from approaches focused on a technology push.

The issue and challenges around recording within a life course approach to immunization was also raised, including the need to document good practices. In many settings, it will take creative efforts to shift from current retention behaviours to expected retention beyond the first year of life.

Forecasting and proper stock management of home-based vaccination records is considered critical. Unnecessary extra stock of cards should be avoided, especially in case of frequent updates of immunization cards. There is a need for integration into stock management and inclusion in existing tools such as the district vaccine data management tool (DVD-MT).

The issue of whether or not to record doses received during SIAs on the home-based record was acknowledged by the presenters.

The main suggestions raised by IPAC included:

1. The need to identify the “value proposition” of the records, which may or may not be in the form of requiring caregivers to have a financial vested interest in the document. Ensuring that the records are valued by caregivers will, in many instances, address some of the household level retention issues. Encouraging school entry screening of immunization history may also assist with increasing home-based record retention and may also lead to vaccination in the case of missed doses.
2. The increasing need for greater commitment from government, and less reliance on external partners and donors for printing and financing immunization cards.
3. The essential role of adequate training of health workers on making the home-based record available and being able to communicate its contents to caregivers.
4. The importance of testing innovation and utilization of new technological solutions to home-based records within the local setting. While the ideal recording and monitoring situation is a comprehensive community-based electronic immunization registry with automatic caregiver reminders, the reality is that many countries remain far from implementing such an approach. Home-based vaccination records therefore have an important role in many settings. Solutions that introduce incremental transitions to tomorrow’s needs must be sought.

5. The value of conducting additional cost effectiveness analyses to document the marginal impact of small interventions vis-à-vis improvements in coverage, reductions in drop-out, overall improved satisfaction with the record which may lead to improved community demand/availability/utilization/retention.

IPAC members offered to review a draft guide document being developed to assist with the design and use of home-based records and provide further input.

Session II. Immunization Management Group (IMG) for IPV

Introduction

Three presentations were given during this session in order to provide an overview of Objective 2 of the End Game Strategic Plan and the work of the IMG in strengthening routine immunization, IPV introduction and the switch from trivalent OPV (tOPV) to bivalent OPV (bOPV).

A. Update on IMG and IPV introduction plans (*Michel Zaffran, WHO/IVB/EPI*)

Mr Michel Zaffran presented the work of IMG to coordinate efforts toward the implementation of objective 2 of the polio endgame strategic plan and provided the latest country update on implementation of the IPV introduction. As of June 2014, 72 countries globally are using IPV. Out of the 126 countries targeted to introduce IPV before the end of 2015, four have introduced already, seven are planning to do so in 2014, while 73 countries have expressed their commitment to introduce the vaccine during 2015. This will represent a programmatic challenge of unprecedented magnitude. There are currently 42 countries for which there is no plan or no information on intent.

To maintain this momentum, financing options for low and middle-income countries not GAVI-eligible are being explored as these countries might be at risk of non-implementation. There are clear risks if these countries do not meet the deadlines, particularly when some of these countries fall in the Tier 2 and Tier 3 group of countries, which are at high-risk of outbreak or importation in case of the reintroduction of type 2 vaccine derived polio virus. A decision (by the Polio Oversight Board) on this financial support is expected by the end of June 2014.

Other streams of work in cold chain improvement, communications and licensing of IPV were also briefly presented.

B. Routine Immunization activities in priority countries (*Rudi Eggers, WHO/IVB/EPI*)

Dr Rudi Eggers presented on the work of the routine immunization (RI) subgroup of the IMG, which promotes synergies between the Global Polio Eradication and RI strengthening. Under this plan, Global Polio Eradication initiative assets in 10 focus countries are to be utilized for RI strengthening. One of the main objectives of the IMG RI subgroup is to ensure that annual comprehensive EPI action plans clearly identify how the polio assets will be used to strengthen routine immunization. This objective is also an indicator of the polio endgame strategic plan. Currently eight out of the ten focus countries have such an annual plan which has been formally endorsed at national level (target all 10 countries by 2014).

The Bill and Melinda Gates Foundation (BMGF) grant to Chad, DR Congo and Nigeria to strengthen RI through polio was outlined. This project has shown good results in the three countries with an increase of coverage of the 3rd dose of pentavalent vaccine in the majority of

districts supported. As an example, in Nigeria, where the project was implemented in 39 polio high-risk LGAs of 10 northern states, there has been a substantial increase in the number of fixed and outreach sessions conducted during the first quarter of 2014 compared with the same period in 2013.

Other RI funding proposals from priority countries (Pakistan, Somalia, South Sudan, DR Congo, Ethiopia, India and Nigeria) were also presented in detail.

C. Draft framework for in-country operational protocol for switch from tri-valent to bi-valent OPV (*Alejandro Ramirez Gonzalez, WHO/IVB/EPI*)

Mr Alejandro Ramirez Gonzalez presented the draft protocol that is being developed for guiding regions and countries through the planning and implementation of the switch from tOPV to bOPV that should take place in April 2016. The protocol has 3 main areas: management and supervision, logistics and disposal, and communication. The protocol presents the major switch timelines from a global perspective but also translates the timelines into a country specific timeline, providing the main task and activities at each step.

It is envisaged that the existing national certification committees will play an important role in the switch process, both in the planning and supervision parts. At the service delivery level, there will be a need to have a cadre of switch monitors that will supervise and certify the successful switch within the given deadlines.

The importance of having a solid and well-prepared communication strategy was highlighted in several occasions throughout the discussion. Another area of critical importance that needs to be very carefully planned is the logistics involved in the removal of the tOPV from the supply chain and its safe and proper disposal.

Discussion:

Regarding the IMG work, IPV introduction plans and Routine Immunization activities, the following issues were discussed.

<p>Number of doses, preferred schedules and rationale for IPV</p>	<p>IPV has to be introduced in the remaining 122 countries that still do not use IPV. The IPV dose will not replace OPV, it will be provided in addition to OPV. SAGE has recommended that this dose be administered at 14 weeks or at the 1st immunization subsequent contact, together with the other scheduled vaccinations. The IPV dose is not recommended to be given in an SIA mode. (Indeed, the introduction of IPV is a risk mitigation strategy for when Type 2 OPV is withdrawn; it should therefore be given as part of the routine immunization programme. In exceptional circumstances, i.e. areas of difficult access in Nigeria and Pakistan and in the context of eradication efforts, IPV may be exceptionally given in campaigns). Alternative schedules can be considered in countries with specific epidemiologic characteristics or particular calendars in place. For instance, in countries where vaccine associated paralytic polio (VAPP) is the main concern, rather than circulating vaccine-derived polio</p>
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	virus (cVDPVs), the schedule can be adjusted and the IPV dose administered earlier (South American countries as an example).
Routine Immunization coverage thresholds required for the switch	No minimum coverage is required as a pre-requisite for the switch to bOPV to take place. There is a well-defined set of criteria to assess country readiness for type 2 OPV withdrawal, however this does not include coverage thresholds. As a matter of principle however, it is important that countries reach high coverage levels with all their vaccines, including IPV, and therefore the work on strengthening routine immunization is a strong component of Objective 2 of the Polio Eradication and Endgame Strategic Plan.
Routine Immunization systems in the post-eradication era	In the remaining polio endemic countries and areas, polio program health workers have been predominantly exposed to SIAs and eradication work, with less emphasis on routine immunization systems in the broader sense. This entire cadre of health and immunization workers should be trained in sustaining routine efforts after polio is eradicated.
Bio-containment	Bio-containment and stockpiles are critical for any unforeseen events in the future. This is part of objective 3 of the endgame plan. Objective 2 is focused on the safe and successful removal of Type 2 OPV.

Regarding the draft framework for the in-country operational protocol for switching from tri-valent to bi-valent OPV, the following issues were raised and discussed:

OPV supply	If the switch has to be delayed, enough production capacity and stock of tOPV will need to be secured to continue vaccination at least for another year. The industry has been consulted and the protocol is being discussed with UNICEF Supply Division on a regular basis. Different possible scenarios around the switch have been studied and forecasts of vaccine needs were developed accordingly. bOPV will be supplied through the same mechanisms as OPV, meaning countries procuring through UNICEF will continue to do so.
Existing national committees in the management and supervision	The proliferation of new committees should be avoided and, when possible, the expertise and experience of expert groups already established in-country should be tapped (e.g., the National Polio Certification Committees [NCCs]).

Type 2 cVDPVs and the withdrawal of Type 2 OPV	Most of the cVDPVs are caused by the Type 2 virus and withdrawing the Type 2 from the vaccine will have a direct impact on the number of cVDPVs. With the introduction of IPV and the administration of bOPV there will also be better protection against the risk of cVDPV types 1 and 3.
Environmental sampling for polio viruses	Environmental surveillance will continue to expand and to strengthen its capacity to detect polio viruses, not only for wild viruses but also for circulating vaccine viruses.
Timing of the switch	The switch has a global timeline set for the low transmission season. However this might not be the most appropriate timeframe in all parts of the globe. IPAC questioned whether there is any flexibility on this timeline. Currently, the switch is conceived as global and synchronized. The timing of the switch is based on the transmission patterns of the polio virus, coinciding with the lowest transmission time in the currently endemic areas.
Communization	A communication strategy is a crucial part of the switch. A comprehensive strategy will be developed to take into account the many aspects of the switch and to clearly communicate the complexities of the process.
Monitoring	If not all health facilities are monitored, the sense of importance and urgency may be lost. In the case that this is not feasible, a "0 case reporting" mechanism could be put into place so that all the facilities have the responsibility to at least report on their stocks.
Waste Disposal	Waste disposal is a very crucial part of the protocol. The end goal of the protocol is to safely dispose the remaining tOPV after the switch.

Recommendations and Decisions by IPAC

1. The target audience/s of the switch protocol and communication documents should be clearly defined.
2. The drafting committee is encouraged to consider allowing flexibility on the timeline and dates for the global switch.
3. IPAC suggests to structure the document into two parts: firstly, the rationale and the scientific background, and secondly the operational issues: the what, how, when and who (the actual guidelines).
4. The drafting committee is encouraged to strengthen the section on waste disposal
 - a. Provide concrete guidance on the hierarchy of disposal methods (rather than simply list them).

- b. Provide references to the key global guidelines.
- c. Gather data on current methods of disposal in countries.

Session III. Global Updates

A. Update on Vaccine Delivery Technologies Meeting (*Carsten Mantel, WHO/IVB/EPI*)

Dr Carsten Mantel summarized the diverse discussions and conclusions of this meeting held in Geneva, Switzerland in February 2014, attended by a broad representation of public health global stakeholders, including academia and industry. The main focus was lessons learned from prior technology development experiences as well as the landscape of new vaccine delivery, formulation, and packaging technologies.

It was agreed that among the key benefits of moving the new vaccine delivery technology agenda forward are increasing immunization coverage and safety, reduction of health care worker time spent on delivering vaccines, reduction of contamination risks and of programmatic errors. However, significant challenges were noted, including establishing consensus on public health needs, quantifying potential impact, influencing purchasers' decision-making processes, and meeting shifting and uncertain regulatory requirements. Recommendations were made on short-term and long-term goals for vaccine delivery technologies, as well as proposed steps towards coordinating and guiding the development and introduction of new technologies.

B. Vaccine Presentation and Packaging Advisory Group/VPPAG (*Debbie Kristensen, IPAC observer*)

Ms Debra Kristensen confirmed that the VPPAG serves as a valuable mechanism for dialogue across immunization stakeholders, including public and private sectors, addressing the programmatic suitability of the presentation and packaging of vaccine products. It was clarified that the group seeks consensus and provides guidance to vaccine manufacturers around presentation and packaging issues for future vaccine products, but its recommendations are not binding. Among the constraints faced by the VPPAG are the difficulty in engaging developing country manufacturers and the lack of dedicated funding. It was emphasized that anyone is welcome to listen in on the monthly teleconferences that take place on the second Tuesday of each month. The VPPAG's major areas of work for 2014 consist of guidance on barcodes, vaccine container dimensions, and insulated shipping containers. In addition, the group is in the process of updating the generic preferred product profile for vaccines.

Session IV. Programmatic Suitability of Vaccine Candidates for WHO Prequalification (PSPQ)

A. Update from the Standing Committee on PSPQ, (*Robin Biellik, IPAC Member*)

Dr Robin Biellik provided an update on the Standing Committee's operations which consist of reviewing the operational characteristics of vaccines submitted to WHO for pre-qualification (PQ) that do not comply with the "Programmatic Suitability for Pre-Qualification" (PSPQ) mandatory and/or critical characteristics in order to make a recommendation to the WHO PQ Secretariat on whether pre-qualification should proceed or not.

Two assessments have taken place since the IPAC meeting in October 2013. The first was in response to a new request for an advance opinion on a candidate malaria vaccine (not yet

formally submitted for PQ). The vaccine failed a critical requirement because it is a non-live unpreserved lyophilized product presented in a multi-dose vial. In view of the public health benefits of this vaccine, the Committee recommended that the product be accepted for PQ review, provided that specific field precautions are implemented. The issue of public health necessity triggered much discussion and it was agreed that the WHO Secretariat should provide guidance on a standardized approach to balancing the risks of potential programmatic errors against public health benefits of new vaccines. The IPAC was also reminded that advance opinions from the PSPQ Standing Committee are not binding on the PQ process, and reflect only the current situation.

The second review concerned a recommendation requested for a candidate rotavirus vaccine (formally submitted for PQ). The vaccine failed two critical characteristics: (a) thermostability data are non-compliant with the use of VVM2 and (b) the product is not ready-to-use (it requires the prior administration of an antacid buffer dose). The Committee recommended that this product be rejected for PQ review on the basis that the vaccine posed a high risk of programmatic errors, no shortage in rotavirus vaccine supply is foreseen over the next two years, and in 2016 the manufacturer plans to submit a ready-to-use, thermostable version of the same product that will be in compliance with PSPQ critical criteria.

The IPAC expressed concurrence with both of these Standing Committee decisions.

B. Progress of the review of the PSPQ process (*Rudi Eggers, WHO*)

Dr Rudi Eggers presented the process and findings emerging from the thorough review of the PSPQ process held over the last few months with stakeholder input from industry and the public sector. The new PSPQ requirements will come into effect on 1 January 2015.

The main issues which emerged during the review concentrated on: (1) Antimicrobial preservatives and the definition of “inadequately preserved” vaccines; (2) antigenic stability for 28 days; (3) the management of vaccines that were pre-qualified prior to the PSPQ implementation (grandfathering); and (4) new mandatory and preferred characteristics and the transition to critical characteristics.

An opportunity to make editing inputs will remain available through 10 July 2014. It was also suggested that the language associated with preferred characteristics should be strengthened.

Recommendations and Decisions by IPAC

1. IPAC members unanimously endorsed the PSPQ revisions as presented.

Session V. Field studies with Uniject

Mr Philippe Jaillard, Agence de Médecine Préventive, presented on two field studies conducted in Senegal and Vietnam with the use of a compact pre-filled auto-disable device (cPAD) for pentavalent vaccine. He highlighted how population and health workers concerns on immunization safety and immunization delivery could be addressed, and the potential to enhance immunization performance and trust by building on cPAD advantages.

The main advantages of cPADs perceived by parents and health workers in Senegal and Vietnam, related to immunization safety and efficacy, were the device's ease of use, its capacity to limit vaccine and needle exposure to dust and germs, and the assurance of delivering the

accurate vaccine dose. The main perceived constraints were related to the risk of confusion with other pharmaceutical products presented in the same device (ie: contraceptive) and that “low cost” technology may imply an inferior quality of device and product.

In the programmatic and logistics area, cPADs for pentavalent vaccines reduce both the weight and volume of waste generated and reduce dry storage capacity needs due to its integrated design, as compared to existing monodose and multidose vial presentations. Furthermore, cPADs reduce overall cold chain store requirements, depending on the presentation and formulation of the DTP-HepB-Hib vaccine in use in the country.

In addition, some vaccinators and program managers noted that cPADs may reduce missed opportunities for immunization by integrating vaccine, syringe, and needle and thereby reducing stock-outs; ease outreach or catch-up campaign efforts by reducing logistics requirements; reduce wastage in comparison with multi dose vial presentation; and reduce the time per injection and the workload to vaccinators.

Most of the challenges reported by the vaccinators regarding device handling and delivery technique may be addressed by proper training and communication.

The potential of cPADs may be further increased by using them in a controlled temperature chain; permitting trained lay health workers to immunize; and including it as an alternative presentation to existing vaccine presentations so that countries can adapt vaccine delivery methods.

Discussion

IPAC discussion noted the value of considering packaging innovation and investment as a topic of programmatic research. IPAC members also noted a number of advantages presented by cPADs for vaccine injection and the benefits of this single dose presentation. Meeting participants emphasized the importance of clearly differentiating the appearance of cPAD for pentavalent or other vaccines from cPAD for contraceptive injection, and encouraged the development of appropriate training and communication materials. They also recommended the generation of more data on economic evaluation, including the cost-savings by increasing immunization coverage and limiting vaccine wastage.

It was noted that cPADs have the potential to increase immunization coverage when used in hard-to-reach areas, during outreach sessions, or when targeting specific populations. A combination of vaccine presentations (for example monodose cPADs alongside multi-dose vials) could be used. WHO and UNICEF would be critical to advising and supporting countries.

Meeting participants noted that the potential for cPAD to reduce needle stick injuries in comparison with a single dose vial presentation is limited since most injuries occur when recapping the needle.

In summary IPAC,

- Recognized the benefits of cPADs for pentavalent vaccine delivery and its potential to overcome some reasons for non-vaccination and increase vaccine coverage;
- Strongly encouraged the increased use of cPADs for vaccine delivery with an increased diversity of vaccine presentations to enable countries to adapt their immunization delivery strategy according to their local characteristics.

- Recommended that further health economic and post-implementation programmatic research be implemented to document the added value of incremental cost versus efficiency and safety, and help identify the best conditions for cPAD use by countries.
- Noted that since cPADs are a preferred characteristic in WHO PSPQ, it is hoped this sends a strong signal to vaccine manufacturers to consider expansion of cPAD use for vaccination; and
- Advocated that GAVI look favorably upon the use of cPADs, particularly for Hepatitis B birth dose.

Session VI. Immunization Supply Chain and Logistics

A. Report-back from SAGE meeting April 2014, (*Chris Morgan, IPAC Chair*)

Dr Chris Morgan summarized the conclusions of the April SAGE meeting, where a second session on immunization supply chains was held in April 2014, as a follow-up to the November 2013 session. Attention was drawn to the key messages from the April meeting that: (i) SAGE re-affirmed its concern about the alarming state of immunization supply chain systems in developing countries, including vaccine availability, cold chain quality, and supply chain efficiency; (ii) SAGE endorsed the IPAC "*Call-to-Action*" and affirmed the importance of the WHO-UNICEF Joint Statement on the comprehensive EVM approach; and (iii) SAGE stressed the importance of thoroughly considering immunization supply chain impact in future recommendations on the introduction of new vaccines.

B. GAVI Alliance Immunization Supply Strategy, (*Daniel Thornton, GAVI*)

Mr Daniel Thornton presented an overview of the GAVI Alliance Immunization Supply Chain strategy that will be reviewed during the June GAVI Board. The strategy made the case for additional focus on and resources for immunization supply chains and outlined initiatives around: (1) supply chain network design and optimization; (2) cold chain equipment; (3) distribution systems for immunization; (4) data for management ; and (5) strengthening human resources for supply chains. Within the five pillars, four initiatives are prioritized in the short term:

- **Supply Chain Managers:** To ensure that EPI is staffed with qualified supply chain managers with appropriate capabilities and authority to oversee the entire national immunization supply chain.
- **Supply Chain Improvement Plans:** To support the development and implementation of comprehensive EVM improvement plans.
- **Supply Chain Dashboard:** To establish country data dashboards that strengthen the visibility of supply chain performance and use the information for improvement management.
- **Supply Chain Design:** To support countries in implementing supply chain network re-design and optimization approaches known to raise the performance of immunization supply chains.

During this part of the session, the IPAC was requested to provide high-level feedback on the proposed ideas that will support the implementation of the strategy. Overall, the IPAC welcomed the GAVI Strategy and felt that it was an early tangible response to the need for increased attention to this issue, as articulated in the IPAC "*Call to Action*". There were discussions on the following issues:

1. How the process to develop the strategy ensured that root-cause analyses had been thoroughly conducted. What game-changing interventions were prioritized and how.
2. How non-GAVI countries could benefit from the knowledge, tools, approach used to support GAVI countries through the strategy.
3. The perceived gaps remaining in the strategy, namely on Vaccine Arrival Reporting (VAR), and the importance of addressing such a big area.
4. Private sector engagement and cautioning about putting too much emphasis on the private sector to provide all the answers.
5. Cautioning about putting too much expectation on having a national level supply chain manager without strong support from country level partners like WHO and UNICEF and a mechanism in-country for change management.

In closing this session, the IPAC made a plea that WHO and partners continue the effort to landscape and gather all available evidence on immunization supply chain challenges and promising solutions and to continue to update the work done as part of the IPAC *“Call to Action”*.

Closing

Dr Morgan thanked all in attendance and summarised the proceedings. He noted that the following individuals have reached the end of their service term as members and acknowledged their service: Robin Biellik, Jonathan Colton, Francois Gasse, and Folake Kio-Olayinka. All members were thanked for their important contributions and dedication of service.

In closing, Mr Zaffran presented Dr Najwa Khuri-Bulos and Dr Xavier Bosch-Capblanch (*in absentia*), with a certificate of appreciation to acknowledge the end of their second term of service since April 2010. WHO, and specifically the Department of Immunization, Vaccines and Biologicals, greatly benefitted from the insights and contributions of Drs Khuri-Bulos and Bosch-Capblanch.

The timing of the next IPAC meeting will be determined at a later date.