



WORLD HEALTH ORGANIZATION IMMUNIZATIONS, VACCINES AND BIOLOGICALS

IMMUNIZATION PRACTICES ADVISORY COMMITTEE (IPAC)

4-5 April 2013

Final meeting report and recommendations

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Opening and Introduction

The Chair, Dr Shelley Deeks, welcomed two new members to the committee at their first meeting, Dr. K.O. Antwi-Agyei, EPI Manager of Ghana and Dr Carla Vizzotti, EPI Manager of Argentina. In addition, Shelley Deeks welcomed Dr. Majo Leroux-Lepage, who replaces Thierry Gastineau as the IFPMA representative in the observer seat on IPAC.

IPAC Members present:

Shelley Deeks (Chair)
K.O Antwi-Agyei
Robin Biellik
Xavier Bosch-Capblanch
Jonathan S. Colton
Francois Gasse
Folake Kio-Olayinka
Christopher Morgan
Jean Marc Olivé
Robert Steinglass
Carla Vizzotti

Session I. Framework of the Unvaccinated

Dr Eggers presented on the components of the Tools for Identifying Root Causes of Children Remaining Unvaccinated (UnVacc Toolkit) to brief the IPAC members who were unable to participate in the detailed discussion during a workshop on the preceding day.

This work originated from a request by SAGE for WHO to develop a methodology to reach persistently unreached children. This was also in line with the Global Vaccine Action Plan Objective 3: Benefits of immunization are equitably extended to all people, which includes the activities of developing and implementing new strategies to tackle low coverage and inequities, and recasting “Reaching Every District” to “Reaching Every Community” in order to deal with inequities within districts. This toolkit is meant to complement the existing strategies such as “Reaching Every District” (RED), and focus on those districts and areas with pockets or individuals that remained unvaccinated. Conceptually, this toolkit was designed to be focused on districts that are reasonably well performing and have already overcome major impediments in immunization systems, including weak programme management and systematic barriers.

The toolkit consists of a screening methodology to identify the broad core problem area(s), which is then followed by an in-depth analysis at the local level to diagnose the core problem in some depth and identify strategies to address the problem. A

summary of the presentations made in the 3 April 2013 workshop and the subsequent discussion was presented.

IPAC Discussion

The title of this project was discussed and IPAC suggested a re-branding to better describe its placement as a tool to reach the last 20% of unreached children.

It was well recognized that the core problem areas were overlapping, making it difficult to set a firm boundary around each one. The screening tool was considered a critical component of this process and required more specificity. In addition some members observed that specific screening questions may point to more than one core problem area.

Specific types of missed opportunities were discussed, including false contraindications, or lack of habitual practice to give missed doses. Several IPAC members indicated that missed opportunities were not an individual core problem, but rather a cross-cutting theme across core problem areas and therefore it should be considered to be part of the screening methodology. In addition, the screening methodology may be tailored using existing data acquired from the DHS/MICs surveys using “national predictors” to identify broad directions, and disease surveillance reports may provide further input into the screening process.

Several observations were made in relation to the fact that persons that were completely outside all health systems (e.g. “invisible children”) would not be adequately detected by these methods. Also, the methodology was inadequate in differentiating between unvaccinated children (those never vaccinated) and under-vaccinated children (those that were partially vaccinated).

Dr Chris Morgan was identified as the IPAC focal point for this project. Several other IPAC members have strong interest in this work, and communications on this will be placed on the common SharePoint site for all to access. A follow up-workshop for this project is planned for the day before the next IPAC meeting in October, and IPAC members were welcomed to participate.

Recommendations and Decisions by IPAC

1. IPAC expressed support for and acknowledged the importance of this work. Members encouraged that the items outlined in the discussion be incorporated in the next iteration of the toolkit.
2. IPAC recommended that the name of the project be modified and emphasised the importance of clearly articulating the objective of the tool.

Session II. Immunization Session Checklist

Three presentations were given during this session in order to provide an overview of experiences in the Patient Safety Program, its relevance to EPI and the progress to date.

A. Introduction to Patient Safety checklists (*Edward Kelley, WHO/Patient Safety Program*)

Dr Kelley explained the patient safety approach and shared the experience with the Surgical Safety checklist, which has improved compliance with standards and decreased complications from surgery in eight pilot hospitals where it has been evaluated (<http://www.who.int/patientsafety/implementation/checklists/en/>).

B. Applicability of checklist approach to immunization (*Carsten Mantel, WHO/EPI*)

Dr Mantel highlighted the main goal of the immunization checklist, which is to improve the quality of immunization sessions, to increase completion of vaccine schedules, to increase vaccine effectiveness, to reduce AEFI risk and to increase client confidence. The checklist is to be used at pause points to remind health workers of the critical tasks to conduct before, during, and after an immunization session. The intent is to emphasize items that, if not done, may lead to adverse outcomes.

C. Update on developments and next steps (*Jhilmil Bahl, WHO/EPI*)

Progress to date on developing the current draft checklist, which contains 18 items, was shared. EPI managers from AFRO and EMRO provided feedback on the checklist; out of 65 respondents, 97% perceived the checklist useful, 75% preferred a laminated poster format, and 80% stated willingness to pilot it in their country.

IPAC members were asked to:

- 1) Recommend how the checklist approach for EPI could be best utilized to help improve quality and safety; and
- 2) Provide overall guidance on how its utility could be evaluated.

IPAC Discussion

Overall, IPAC members received the checklist with enthusiasm and regarded its development as a worthy initiative.

Specific suggestions were made to add actions that were considered important such as hand-washing, availability of an AEFI kit, information on side effects. Regarding its optimal utilization, several members stated that the checklist needs to be perceived as useful by staff rather than viewed as a mandatory activity. Members emphasized the importance of considering implementation factors that differ from the operating room context, particularly since there may not be a team of staff at the immunization session but a single staff person, making a 'call-out' approach (when one person reads out the checklist and others verify the steps have been completed) -- as used in the surgical setting -- impossible.

Several members noted that the checklist includes three sections which reflect natural pause points, with the 'before' and 'after' sections having tasks that occur only once per clinic session, while the 'during' section including tasks that must be repeated for each vaccination encounter. Therefore the 'during' section of the checklist requires careful planning. Some mentioned the option of making the 'during' section a separate checklist, others stated that it is difficult to conceive use of the list for each child, expressing concerns that if staff do not use the middle 'during' section, they will stop using the 'before' and 'after' as well.

Several IPAC members underlined that the checklist needs to be adaptable at the country level, and may even need to allow integration of other services (i.e., a child health services checklist). A suggestion was made to include definitions on the back side of the checklist itself.

IPAC members also mentioned that the positive effects of the checklist may not be related only or primarily to the checklist itself, but as a result of the accompanying interventions that accompany the checklist implementation (e.g. changes in the location of drugs, peer-control, etc.).

Members believed that rigorous evaluation such as the one conducted by WHO/Patient Safety may not be needed; major outcome changes may be unlikely but reinforcement of Standard Operating Procedures and structure in immunization sessions may be an acceptable goal. Members acknowledged that during evaluation of checklist implementation, the subjects may modify their behavior because they know they are being studied ('Hawthorne effect'), although the phenomena may be difficult to address.

Dr Francois Gasse will be the IPAC focal point for checklist work and serve as bridge between IPAC and the Secretariat as needed.

Recommendations and Decisions by IPAC

1. IPAC received the checklist approach with interest and praised the structure, simplicity and clarity of the current draft.
2. IPAC observed that the 'middle' pause point is complex and challenging to express appropriately and encouraged further thinking in this area.
3. IPAC supported the idea of conducting an impact evaluation (before and after introduction), but cautioned the evaluators to pay attention to the potential 'Hawthorne effect'.

Session III. Global Updates

A. Update on Immunization in Practice (*Jhilmil Bahl, WHO/EPI*)

As a follow up to the IPAC session in April 2012, Jhilmil Bahl (WHO/EPI) provided an update on progress with the development of Immunization in Practice (IIP). IIP is a practical information guide targeted at district/health facility aiming to improve immunization services. The updated version will have seven modules and the main changes include: combining of Disease and Vaccines modules into one module and expansion of the Monitoring module to include surveillance (both disease and AEFI).

Different modules are at different stages of development however draft 2 for most modules would be shared for review in the coming weeks. Primary reviewers include IPAC members, WHO HQ/Regional/Country staff, Partners (UNICEF, CDC, MCHIP, AMP, NESI), MoH staff working at national and sub national level.

Final draft version is anticipated to be available by June 2013; a book version is planned along with web version that can be updated more frequently.

A sign-up sheet was circulated and several IPAC members agreed to review relevant modules when requested.

B. Update from the Global Advisory Committee on Vaccine Safety (GACVS) (*Madhava Balakrishnan, WHO/Quality, Safety and Standards*)

Dr Balakrishnan reported on the topics reviewed during the Global Advisory Committee on Vaccine Safety (GACVS) meeting conducted in December 2012. The conclusions are reported in the Weekly Epidemiological Record (WER) No 6, 2013, 88, 65-72. The topics included safety profile of varicella vaccines; risk of narcolepsy and Guillain-Barré syndrome with pandemic influenza vaccines; safety aspects of live attenuated dengue vaccines; and update on progress of the Global Vaccine Safety Blueprint through the Global Vaccine Safety Initiative.

C. Update from IPAC presentation to SAGE (*Shelley Deeks, IPAC Chair*)

Dr Deeks reported on the topics reviewed during the SAGE meeting conducted in November 2012. The conclusions are reported in the WER No 1, 2013, 88, 1-16. The topics included the routine report-back from the Director of Immunization, Vaccines and Biologicals; report-back from GAVI alliance; report-back from IVB advisory committees including IPAC; Decade of Vaccines Global Action Plan; optimization of *Haemophilus influenzae* type b (Hib) conjugate vaccine schedules; measles and rubella vaccination; vaccination in humanitarian emergencies; and new vaccine introduction in middle income countries. Areas of intersection with IPAC were discussed.

Session IV. Immunization Supply Chain and Logistics**A. Working group update and IPAC discussion points** (*Robin Biellik, IPAC member*)

Dr Biellik presented a status update on the work of the Immunization Supply Chain and Logistics Working Group (iSCL WG) to communicate timelines and progress; gain agreement from IPAC on the key messages and objectives for the SAGE session; secure consensus that the IPAC committee's iSCL WG recommendations should be endorsed by SAGE.

This will be the first time SAGE holds a session dedicated to iSCL issues. In addition, this provides an opportunity to better link the IPAC process with SAGE policy-making. The key objectives for the SAGE session, as proposed by the iSCL WG are:

1. Prime SAGE with a description of the iSCL progress and challenges from a global and country perspective.
2. Present SAGE with an IPAC recommendation that couples evidence-based supply chain knowledge with appropriate endorsements. There should be a clearly defined 'target audience' for the recommendation so that it can move to implementation.
3. Propose an on-going process for future IPAC iSCL recommendations to SAGE.

The WG is continuing to discuss and modify the recommendation to SAGE. The iSCL WG will meet in June to fine-tune the recommendation and outline concrete examples that support the recommendation. The Secretariat will lead the data-gathering activities as well as incorporate stylistic modifications to the existing presentation.

Proposed structure of the upcoming SAGE session (*Ryan McWhorter, WHO consultant*)

Mr McWhorter outlined the linkages between SAGE vaccine management recommendations and impacts on the downstream supply chain operations. This included the current state of the iSCL in countries and challenges faced by practitioners.

The session concluded with a presentation of iSCL WG's next steps, which are to fine-tune the recommendation, analyze literature for supply chain successes, and update and improve the presentation.

IPAC Discussion

Members reiterated that the objective is for SAGE to endorse an IPAC recommendation instead of making a specific recommendation of their own. It was agreed upon by the group that the IPAC recommendations will need to strike the right balance between having a detail-oriented statement (e.g., a specific supply chain process or technology), or an overarching statement to the point that there is little value to Member States (e.g., “supply chains should be flexible”).

Recommendations and Decisions by IPAC

1. IPAC concurred that the end objective is to have SAGE endorse IPAC recommendations rather than simply providing a technical update.
2. IPAC thanked the working group for the efforts to date and recommended further clarifications in the SAGE presentation by:
 - a. Updating key message slides by adding references, including more fixed/variable cost examples, etc.
 - b. Leading with referenced quotes instead of ending with referenced quotes, so that rationale for recommendations is clear.

Session V. Controlled Temperature Chain for Meningococcal A vaccine (MenAfrivac®)

A. Report back to IPAC on results and lessons learned from the CTC MenA pilot in Banikoara, Benin (*Simona Zipursky, WHO*)

As discussed and recommended by IPAC at the October meeting, WHO and PATH conducted a field test of the Controlled Temperature Chain (CTC) guidance document and its associated training materials during the November 2012 MenA campaign in Benin. The feedback received allowed WHO to revise and strengthen the guidance and training materials, which were circulated to IPAC members in advance for comment, along with a document summarizing key changes.

Ms Zipursky showed a video from the CTC pilot, which demonstrated how CTC was implemented and included perspectives from the MoH staff in Banikoara as well as WHO regional staff and consultants. The video, which was produced jointly with AMP, highlighted the active AEFI surveillance study that AMP conducted to confirm that, as expected, no additional AEFIs occurred—in total or in severity—due to the use of MenAfriVac in a CTC.

A summary of the survey conducted with health care workers (n=77) and supervisors and district staff (n=21) after the campaign illustrated that when given a choice, 100% of supervisors and 98.7% of vaccinators would prefer to conduct their next campaign using CTC. In a Polio NID, conducted 10 days after the end of the MenA campaign in the same district, no confusion regarding cold chain use was observed or reported.

IPAC was then asked to respond to the following questions:

1. Does the revised guidance adequately address key points previously raised by members?
2. Based on what you have been told of the pilot, what you saw in the video, and your review of the training materials, is there a need to add additional information/clarifications to the guidance and if so what?

3. Does IPAC endorse the guidance, clearing the path for its use in other countries?
4. What additional studies to support 'implementation assessment' does IPAC recommend WHO conduct in the future?

IPAC Discussion

IPAC commended WHO on the high quality of the document and the summary sheet prepared outlining key changes. The Committee felt their previous comments had been taken into account and the result was a stronger document. IPAC noted the importance of this groundbreaking work, which it felt had the ability to bring significant benefits to country immunization practices.

Key comments and suggestions included:

- **Review the tone.** While countries should be prudent in adopting this approach, the current tone of the document is overly conservative given the pilot results. In addition, clarify that certain elements like AEFIs are not specific to CTC use, but to the use of the vaccine in all situations.
- **Streamline the document** by making it MenAfriVac specific—i.e. in the section on AEFIs, delete all information not specific to MenAfriVac.
- **Clarify wording** around key issues: peak threshold indicator vs. threshold indicator (both are used), 'when to start' campaign in reference to time or location in the supply chain
- **Incorporate more learning from Benin.** Highlight key risk points (i.e. transport) more prominently, update benefits/risks table.
- **Develop new scenario diagrams.** Current version is hard to read when printed in black and white and can be complicated to understand. Look at ways to simplify.
- **Peak threshold indicator.** Update information about options and how and where interested countries can obtain the cards.
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IPAC concluded that document had adequately addressed their comments and that, with the proposed supporting documents, no additional guidance was needed. It was also noted that the subgroup could be suspended.

Recommendations and Decisions by IPAC

1. IPAC unanimously endorsed the proposed guidance, pending the revisions suggested above, and encouraged the finalization and publication of the document in English and French without further review or delay.
2. IPAC recommended that WHO initiate the development of specifications for the pre-qualification of peak threshold indicators as soon as possible.
3. IPAC recommended that WHO conduct additional research into the economic value of CTC and its impact on coverage.

Session VI. Visual cue and the Multi-dose Vial Policy

This session included an overview of the work-to-date and the intersections between the two streams of work, as well as an update from both the visual cue and multi-dose vial policy working groups and from the WHO secretariat.

A. Background and overview (*Simona Zipursky, WHO*)

The current Multi-dose Vial Policy (MDVP) is outdated and provides incomplete guidance to health workers as direction on how to handle many current EPI vaccines is not specified, and there is a more diverse range of vaccine presentations now available. The current MDVP relies on formulation as a 'trigger' for how long a vial can be kept once opened: liquid (keep for 28 days after opening) and lyophilized (discard after 6 hours).

However the number of vaccine presentations that are no longer compatible with the current MDVP are increasing. These include:

- Two dose unpreserved liquid vaccines (i.e., certain pneumococcal and human papillomavirus vaccines);
- Lyophilized vaccines containing thiomersal (i.e., DTP-HepB+Hib);
- Unpreserved single-dose vaccines that can be used as fractional multi-dose vials (i.e., Rabies); and
- Vaccines using alternative preservatives that may allow for a lesser time period than 28 days after-opening, such as 7 days (i.e., IPV).

The design, development and field evaluation of the visual cue icon-- an easy to read symbol that could be added to multi-dose vaccine vials in order to inform vaccinators how long opened vials could be kept for -- has been deliberated at multiple IPAC meetings (June 2010, Nov 2010, April 2011, September 2011). The refinement of the visual cue icon, as well as the Request for Proposals '*Process evaluation of visual cue vaccine vials introduction*', was presented at the April 2012 consultation.

In parallel, as noted, there is a need to revise and update the MDVP to reflect these new presentations, which are in some cases already being used in the field. Revisions to the Multi-Dose Vial Policy (MDVP) have been discussed at multiple IPAC meetings (June 2010, September 2011, and April 2012). At the September 2011 meeting, IPAC 'strongly recommended that the current MDVP be revised in a timely manner.' It is WHO's intent to finalize this policy revision by the end of 2013.

At the same time, as recommended by IPAC in the April 2011 meeting, work is on-going to do an overhaul of vaccine labels to improve their readability and reduce risk of programmatic errors. This work has highlighted a lack of space of the smallest vials used (which are used to reduce cold chain impact of single dose vials).

All three work streams are clearly interlinked, and WHO will need to weigh the impacts and linkages before proceeding.

WHO requested IPAC members to keep the discussion focused on the upcoming MDVP revision and that out of scope areas during this discussion included revisiting previous decisions on the visual cue and regulatory issues, such as the multi-challenge test or preservative efficacy protocols and validation.

B. Working group update on the visual cue (*Xavier Bosch-Capblanch, IPAC member*)

Dr Bosch-Capblanch reviewed the process and timeline followed by the working group in its attempts to find a suitable organization/company to conduct the visual cue pilot. As per the guidance from IPAC, WHO issued a request-for-proposals (RFP) for field testing and evaluation of the visual cue. The RFP was published in May, with a closing date of June 13 2012. One agency submitted a proposal. The initial proposal received was considered unsatisfactory, and the IPAC visual cue working group worked with the company to improve the proposal. Despite undergoing three

revisions, the proposal was still viewed as unsatisfactory and the working group decided in January 2013 to decline the proposal. The working group is now working to develop a list of possible collaborators to target and revising the Terms of Reference for the work.

C. Working group update on multi-dose vial policy (*Robert Steinglass, IPAC member*)

Dr Steinglass presented an overview of the working group's input into the MDVP. Key areas of input from the subgroup included: clarifying the main audience, enhancing readability by improving the structure and layout of the document to highlight key messages, ensuring relevance to country audience, and identifying contradictions and errors in the text. In addition the working group provided guidance on how to reference the visual/discard cue vs. the VVM in the document, ultimately recommending that the roles of both be clarified (including the dual role for the VVM) and that any reference to 'primary' or 'secondary' cue be removed. Finally, the working group discussed how to apply the MDVP in outreach situations, and decided to bring the topic to the full group for discussion.

D. Questions, Answers and Next Steps on the MDVP (*Diana Chang-Blanc, WHO*)

Ms Chang Blanc presented issues in response to questions received during the review process, which reflect the joint decisions of WHO QSS and EPI. These included the rationale and science behind the 6 hour and 28 day limit, along with the challenges inherent in changing them. The presentation also addressed the issue of how countries that do not use the VVM are impacted by the revisions to the MDVP. In addition, work already on-going in response to IPAC's guidance was presented, notably that WHO is in the midst of updating the individual vaccine product pages of the Quality Safety Standards (QSS) web catalogue to identify MDVP status. A timeline for next steps in revising the document was presented, outlining a plan by which the final draft of the MDVP revision will be available by July, enabling its publication and dissemination before the end of the year.

IPAC Discussion

Main points on the MDVP revision from the discussion are as follows:

- **Clarify terminology.** IPAC recommended that the term 'discard icon' be adopted rather than 'visual cue' to describe the pair of icons developed.
- **Reformat the document.** Currently the policy and tools for implementing it are mixed together. IPAC suggested the document be reformatted to first address the policy and then to describe the tools that can be used to implement it. It will be important to link to documents and/or include guidance on safe injection practices, without which the MDVP cannot safely be implemented.
- **Emphasize conditions of good practice.** In the interests of 'doing no harm', bring greater emphasis to the criteria needed to keep an open vial for 28 days; emphasize the need to avoid both heat and freezing temperature exposure.
- **Concerns about reliance on VVM.** PAHO re-iterated their concern about using the VVM as a visual trigger in the absence of a visual cue. It was noted that these countries have been implementing the original MDVP without a visual cue, however with the growing variation amongst presentation formats, there is greater risk for confusion.
- **Clarify wording.** At times, the implementation of the MDVP is used to refer to keeping vials open for 28 days, when in fact that is one of two options for handling vials when implementing the MDVP. It should be clear that the MDVP encompasses both time branches.

- **Country modification and adaptation.** IPAC noted that countries have and should continue to, adapt the MDVP to their own unique situation and conditions.
- **Guidance on outreach.** IPAC underlined that the conditions for keeping a vial open for 28 days should be applicable to outreach, mobile and campaign settings, provided the best practice conditions for keeping a vial open can be maintained. This is due to the lack of any data showing a significant safety risk and the potential to minimise wastage where these strategies are predominant.
- **Impact on wastage rates.** IPAC encouraged WHO to collect more data on vaccine wastage rates and analyse the impact of the MDVP on wastage rates.

Recommendations and Decisions by IPAC

1. IPAC recommended that the finalization of the MDVP is completed by the end of 2013, and is not delayed due to the visual 'discard cue' process.
2. IPAC recommended that the current MDVP revision make reference to the visual 'discard icon' in the main body of the document, and provide further details on its specifics and future options in the Annex. Furthermore, IPAC recommended that a visual 'discard icon' implementation assessment/ process evaluation occur in parallel with the MDVP revision.

Closing

Dr Deeks thanked all in attendance and closed the proceedings. The next IPAC meeting will be held 16-17 October 2013.