Meeting report and recommendations

1 Opening and Introduction

The second bi-annual Immunization Practices Advisory Committee (IPAC) meeting was opened by the IPAC Chairperson, Dr Shelley Deeks, welcoming nine IPAC members (three members could not attend the meeting), five IPAC formal observers from representative partners (CDC, UNICEF, IFPMA, DCVMN), as well as other participants and presenters from WHO headquarters, WHO regional offices, and industry.

Dr Rudi Eggers, WHO/IVB Group Leader of Immunization Services Strengthening, introduced in absentia Professor Jon Colton as the new member of IPAC. He is a former Technical Advisory and Logistics Committee (TLAC) member, and could not attend this meeting. He will be replacing Mr Jules Millogo, who had resigned from IPAC membership.

Dr Eggers reiterated that for each IPAC meeting the declaration of interest forms were to be filled and duly signed by IPAC members (not observers). In the situation where there was no change since the last meeting, members could indicate “no change since June 2010” on the form. In the future meetings, WHO would require these forms to be signed prior to each IPAC meeting.

IPAC members and observers confirmed and adopted minutes of the June 2010 IPAC meeting, with a change in the initial terms of service in the meeting report. The corrected minutes have been posted on the website.

2 Visual Cue

2.1 Update on focus group research - outcome of Synovate study in Cambodia

Ms Moodley, from Synovate, presented completed results from the studies conducted in Uganda and Cambodia. She mentioned that the study currently under way in Peru would be completed in December 2010. Her presentation covered three main sections: research overview, findings, and points for consideration.
Within Uganda a total of 124 main-stage and 38 follow-up interviews were conducted; while in Cambodia 100 main-stage and 40 follow-up interviews were conducted. Of these 100 main-stage interviews, 47 were from rural areas, 23 from urban areas, and 30 from peri- or suburban areas. In order to evaluate the most preferred visual cues, spontaneous understanding of the cues, ease of communication, as well as long-term recall of the visual cues were assessed. Health workers were presented with five pairs of visual cues selected for testing, which were as follows:

![Visual Cues](image)

**Icon pairs**

<table>
<thead>
<tr>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
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These cues were presented to health workers on labels of actual vaccine vials (both with and without VVM) during main-stage interviews and on in equivalent size on A4 size paper during follow-up interviews.

According to Ms Moodley, analysis suggested that visual cues using familiar symbols (such as clock, watch, and calendar) were most likely to communicate the correct discard message intuitively, ie without further information being given. The key findings of the study were as follows:

- For the 6-hour message, in both Uganda and Cambodia, options B (watch with 6h) and C (man with bin) were most likely to be correctly identified.
- For the 28-day message, option A (calendar) was mostly likely to be correctly identified in both Uganda and Cambodia. Additionally, in Cambodia, option B (calendar with 28d) was accurately identified.

Although both countries had similar levels of spontaneous recognition, patterns for overall preference for visual cue differed. Uganda consistently preferred Pair A on all parameters. However, Cambodia did not show a strong preference for a particular pair. Pairs A, B and C were all feasible for Cambodia. It was noted that option E was the least intuitive and most likely to be misinterpreted in both countries. Results of the follow-up study were also consistent with the main-stage study results. Assessing overall suitability for both Uganda and Cambodia, Pair A could be seen as appropriate for both markets, because both the image and the message seemed very clear, intuitive, and concurrently easy to understand.

In the previous IPAC meeting, several IPAC members had considered feasibility of valid alternatives to the originally defined pairs. Ms Moodley proposed three other feasible options, for communicating the 6-hour discard message intuitively and correctly:

![Alternative Visual Cues](image)

Another point of concern raised in the previous meeting was adapting pairs for different expiry times, other than 6h/28d. Although only these two time periods were explored in the research study, Synovate’s observations and analyses of current data indicated that cues could be adapted for different time periods. Particularly with reference to Pair A, health workers clearly understood the story/message behind the cue. If the time period was changed on the cue, their understanding would be retained, and they would be able to apply the message for the new time period.
In the discussion, the following points were highlighted:

**Legibility of the visual cue:** Several IPAC members and observers were concerned about the legibility of the visual cue. In particular, observers representing manufacturers raised the concern that the calendar icon may not be legible as it would be quite small. However, study results showed that the calendar was one of the most preferred cues. Ms Moodley pointed out that health workers knew what the calendar represented; they may find it comprehensible, even though the message size was small. Thus, it was considered worthwhile to explore the presentation of the label on the vaccine vial in detail. Dr Thierry Gastineau, an observer representing IFPMA, proposed to provide members and observers with mock-up vials containing multi-lingual tables (business case examples).

**Reinforcing country policy:** Representatives from WHO regional offices mentioned that for several countries the discarding of vials and the length of time that a vial could be kept were based on their national policies. Countries were not obliged to follow WHO guidelines. However, by instituting such a global visual cue system, the acceptance of global guidelines would be supported. Dr Eggers also added that the process of implementation of the visual cue would be similar to that for VVM. Each vaccine would have a particular visual cue, which will depend on the discard-or-keep rule applicable to individual vaccines. Dr Wood added that country policies would be taken into account during the pre-qualification of vaccines.

**Use of letters in visual cues:** An IPAC member mentioned that in order to overcome language barriers, letters like ‘h’ and ‘d’ to indicate hour and day respectively, should be avoided in the final visual cue selected. Instead, visual symbols should be used. WHO secretariat asked Synovate whether identification of alphabets was a problem in a non-English speaking country like Cambodia. Mr Jeff Lucas from Synovate said that the interview process in Cambodia took a longer time than in Uganda, where people were more familiar with English. Whether this was because of language reasons only or because of health workers’ previous understanding and training about vaccines could not be determined.

**Implementation of the visual cue:** The issue of introduction of a new visual cue and the time required for its implementation in the field were discussed. Based on experiences with VVM, it could take a few years. IPAC acknowledged that training of health workers was also an issue to be considered. Dr Eggers estimated that the actual implementation of the cue in the field would take two or three years from now.

### 2.2 Opportunities for piloting visual cues

Dr Rudi Eggers presented issues regarding piloting visual cues in a country, assessing the training and behaviour change of health workers. Ideally, a country in which a new vaccine is to be introduced and a vaccine where the visual cue would denote a new approach to MDVP should be used for the pilot study. The pilot study would also have to be performed in a reasonably well functioning programme in a developing country, with the cooperation and agreement of the vaccine manufacturer.

WHO had initially considered Kenya as an option country, where PCV-10 is to be introduced in early 2011. However, several research programmes were already in place there to assess the programmatic consequences of the new vaccine presentation. The PCV10 introductions would have been ideal for the pilot, as the next introductions beyond PCV-10 would be with PCV-13, but this would be a single-dose vaccine. Rotavirus vaccine, which could be another option, was an oral vaccine. Finally, HPV vaccine was also considered, but this was administered in a different age group (adolescents) and setting (school programmes).

The alternative for piloting visual cue in a country would be to wait for the next PCV-10 introduction countries (which could be Ethiopia or Pakistan). This in turn, awaited the outcome of the Kenyan assessments. Also, using a vaccine introduction where there was no MDVP issue could be an option. Alternatively, an existing vaccine could be used instead of a new vaccine...
setting. Dr Eggers requested IPAC, vaccine manufacturers, and others present to give their ideas on possible solutions to the outlined problems.

Dr Najwa Khuri-Bulos, an IPAC member, proposed that Jordan might be a suitable candidate country, because several new vaccines were being introduced there. Furthermore, there were disparities between several areas in Jordan regarding performance, which would provide an ideal setting for testing the pilot visual cue. WHO took note of this suggestion.

2.3 IPAC recommendations on the visual cue

2.3.1 Flexibility of the visual cue

The VCSG proposed that should remain flexible and expandable; i.e., those visual cues that did not follow only the 6h/28d binary possibilities. The rationale behind this recommendation was that future vaccines might require to be discarded at times other than 6 hours and 28 days. Practically, this could be achieved by considering an adaptation of the text-labelled visual cues, and an adaptation of the highlighted day in the calendar.

IPAC endorsed the VCSG recommendation that visual cue would remain flexible and expandable, rather than being confined to 6h/28d binary system.

2.3.2 Application of a visual cue on all PQ vaccines

The VCSG proposed that all pre-qualified vials be marked with a visual cue, and not only those vials that could be discarded 28 days after opening. This would mean that, in the context of two possibilities, a visual cue pair should be chosen. The rationale behind this recommendation was to avoid the occurrence of programmatic errors due to reliance on training to ensure that all unmarked vials be discarded after 6 hours. Furthermore, it also presented a high safety risk in the context of a liquid, unpreserved, multi-dose vaccine vial.

IPAC endorsed the recommendation that the visual cue should be applicable to both vaccines that have to be discarded after 6 hours and those that have to be discarded within 28 days.

2.3.3 The 6h/28d binary system

Initially, existing vaccines should be marked with the visual cue according to 6h/28d categories. In reviewing new vaccine Pre-Qualification (PQ), the PQ team should note if the vaccines presented have stability data that fit them into one of these two categories or if a new category would be necessary. Dr Steinglass further mentioned that the 6h/28d thresholds were originally chosen to quantify the concept of "at the end of the session" and "when the health centre is restocked." The 6h/28d designation was agreed to be an acceptable limit, even though stable, opened vaccines could remain usable beyond 28 days. In future, manufacturers could present WHO with sufficient data for other thresholds to be accepted as new categories for their products. Hence, a category would be fixed for the time being, with the provision of having new categories in the future.

IPAC considered whether the existing 6h/28d category would be adequate for all vaccines, or whether new categories would be needed.

IPAC recommended that the pre-qualification team should review existing and new vaccines with different stability data, and to indicate their stability in pre-qualification documents. The final decision as to whether to allow a new category for the vaccine or to require it to comply with existing categories would rest with the pre-qualification team.

In conclusion, IPAC suggested that the VCSG modify this recommendation (in terms of wording) to allow for current and future vaccines to have flexibility regarding new categories for discard and keep, while keeping it logistically feasible.
2.4 **Unresolved issues on the visual cue**

**2.4.1 Decision on selection of visual cue**

It was anticipated that IPAC would select a visual cue pair for pilot testing at this meeting. However, due to delays in the visual cue focus group study in Peru, the final results from all three countries were not available at this meeting. IPAC members considered that it was important to wait for results from Peru, rather than making a decision based on only two-thirds of the data, especially since the results available thus far were not overwhelmingly in favour of one specific pair.

Dr Eggers indicated that the initial urgency was due to a vaccine product that would be launched in Kenya in 2011. However, an interim solution had been found, and the immediacy factor, therefore, had somewhat reduced. IPAC acknowledged that several countries were applying for new vaccines to be pre-qualified, hence, it was important to maintain the pace in the visual cue selection and implementation.

There was unanimous consensus among IPAC members that it was imperative to wait for focus group study results from Peru, in order to make a decision about selecting a visual cue. It was decided that the results of the Peru study would be discussed in a teleconference meeting in January 2011, and a decision on selecting a visual cue be made in the next April 2011 IPAC meeting, taking into consideration the results from the three countries tested as well as the concerns by manufacturers.

**2.4.2 Multi-dose vials only versus multi-dose and single-dose vials**

However, there were questions raised by members and observers about whether this recommendation was applicable only to multi-dose vials, or whether single-dose vials were also included. Many members felt that in order to maintain consistency, safety, and encourage good practices by health workers; the visual cue should be recommended for all vials. However, other members, observers, and WHO secretariat suggested that because the Multi-Dose Vial Policy (MDVP) would be applicable for “time after opening” of vials, single-dose vials would not have to face this situation. Hence, the visual cue should be recommended only for all multi-dose vials, and not for single-dose vials. Dr Eggers mentioned that this was also TLAC’s original recommendation.

Dr Deeks asked IPAC members to vote on the issue, which resulted in five members agreeing for the visual cue to be recommended only for multi-dose vials, and four members agreeing for the visual cue to be recommended for both single and multi-dose vials. Hence, at this meeting, IPAC did not reach a consensus on this issue, and it requires further discussions.

**2.4.3 Legibility of visual cue**

It was decided that legibility of the visual cue would be discussed by the full IPAC, after reviewing mock-up examples of empty vials containing multi-lingual labels and visual cues, as proposed by IFPMA. These examples would be sent to IPAC members prior to the teleconference in January 2011. It was also decided that icon pair A would be used as an example on the mock-up vial, as it was quite complex, and may present legibility issues.

**2.4.4 Pilot testing of the visual cue**

IPAC members did not come to agreement whether to choose to pilot the visual cue in a poor-performing or adequately performing country, or if pilot testing one visual cue pair in one country was sufficient. Also, no consensus was reached in determining if HPV vaccine was suitable for pilot testing.

IPAC said that it would need further information to decide several factors and components of the pilot, before making a recommendation. The VCSG would discuss design of the pilot along with aforementioned issues, in its next teleconference meeting.
3 Controlled Temperature Chain (CTC)

An introduction to the Controlled Temperature Chain (CTC) was provided at the June 2010 IPAC meeting, and background reading documents were provided to IPAC members. The main objectives of this session were to update IPAC on the CTC strategy and on work done by the CTC sub-group, and to obtain endorsement of the CTC strategy by IPAC.

3.1 Reasons for developing CTC strategy

Mr Michel Zaffran, Senior Advisor WHO and Director Project Optimize, presented issues surrounding use of vaccines in a CTC. Firstly, the working definition of CTC was presented:

The principle of CTC is to allow specific vaccines to be kept and used at ambient temperatures, i.e., up to 37°C, for a limited period of time (the length of time would vary by antigen and setting), immediately preceding administration.

It is meant to be used in circumstances where it impossible or difficult to maintain a 2°C to 8°C cold chain in the periphery of services, and only to those vaccines that met a number of pre-determined conditions. Several licensed and future vaccines that are heat stable, some of which are stable at 40°C for at least one to two months and longer. Thus, it was important to explore CTC in order to reach more people, deliver vaccines to the right groups at the right time, reduce or eliminate the risk of freezing, promote more integrated supply chains, and reduce reliance on costly specialized equipment.

To make progress in the CTC area, three inter-linked streams of work are being explored: (a) Vaccines (regulatory pathway), (b) Technologies (threshold indicators etc), and (c) Guidance to countries on how to operationalize CTC at the country level. IPAC was being consulted to make sure that no key area had been overlooked by CTC and IPAC sub-group. Moreover, IPAC will be asked to endorse the CTC strategy as an acceptable roadmap to explore the feasibility and conditions for the applicability of CTC.

Several IPAC members and observers supported the principle of CTC, because it would be very beneficial to administration of birth doses and bypass cold chain requirements, for example in the case of Hepatitis B birth dose programme in low income countries.

Mr Zaffran underscored the importance of addressing this complex issue. He mentioned that in countries like Vietnam, where there was no WHO recommendation about CTC, they were hesitant to build on the results of their pilot with Hepatitis B birth dose to move to a national policy and implement the strategy to the whole country. Furthermore, the recent influenza pandemic was an example of the same. Large quantities of vaccines needed to be deployed fast in the absence of sufficient cold chain storage capacity. Since recommendations about bypassing the cold chain do not exist, this has complicated vaccine deployment. These problems could have been alleviated with a suitable CTC recommendation.

3.2 Vaccine work stream- regulatory pathway that allows for vaccines to be licensed and reflect their true stability

Dr Christoph Conrad from WHO/FCH/IVB/QSS presented work done in defining a regulatory pathway for vaccines to be licensed for use at higher temperatures than the traditional 2°C to 8°C range. He talked about the regulatory considerations for Hepatitis B (HB) vaccine to be used in a CTC.

A WHO position paper (Weekly epidemiological record No. 40, 2009, 84) stated that recombinant HB vaccines showed no change in immunogenicity or reactogenicity, even though the vaccine had been exposed to temperatures up to 45 °C for 1 week, and temperatures up to 37 °C for 1 month. Dr Conrad said that although there was strong evidence for stability of recombinant HB vaccines, existing data were still limited.

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1 Traditionally, all vaccines are required to be stored at 2 to 8°C. However, the cold chain has certain limitations, which were discussed as follows: (i) the cold chain often freezes and damages some vaccines; (ii) it is costly, as it requires specialized equipment; (iii) it does not reach certain populations; and (iv) it limits the ability to administer birth doses, particularly in countries where deliveries largely occur outside of the health facilities.
A study\textsuperscript{2} financed by Project Optimize under the auspices of WHO/QSS was conducted on recombinant HepB vaccines in order to determine stability and change in potency of six different, pre-qualified, monovalent recombinant HB vaccines held at temperatures up to 45\textdegree C. A copy of the full study report is available for IPAC members and observers. For this purpose, vaccines were kept at 2 to 8\textdegree C, 37\textdegree C, and 45\textdegree C until VVMs changed at 45\textdegree C.

The conclusions drawn from this study suggested that the VVM can be used as a predictor of \textit{in vitro} potency up to 45\textdegree C, as long as the vaccine meets release specifications at 37\textdegree C for 30 days. The characteristics tested did not appear to be functions of shelf life. Dr Conrad further added that the potency assay was an unreliable indicator of immunogenicity and HepB vaccine integrity. Thus, a crucial question remains open: Is there a need for human immunogenicity data or would it be sufficient to perform further testing on vaccine integrity after high temperature exposure, to draw a correlation with clinical safety and efficacy. Examples of further quality parameters to be tested are listed in the respective WHO guidelines and other recent publications.

Ideally, regulatory decisions should be made on studies that predict clinical behaviour of the vaccine. In case of HepB vaccines where there is no direct quality parameter available that correlates with clinical safety and efficacy, quality, nonclinical and clinical data should be evaluated. Thus, would it be acceptable to support a label change for the CTC approach based on stability and shelf life considerations only (a “quality only” approach), or are the data required equivalent to a change in the manufacturing process potentially causing changes of the (clinical) product characteristics?

Consultation with HepB vaccine experts and manufacturers was needed in order to define stability and comparability criteria to evaluate the CTC approach, and define steps to be taken for its implementation. WHO would continue to explore view of regulators and manufacturers in different countries.

In the discussion, the methodology used in the Project Optimize study were questioned, and significance of the low temperatures used. Dr Christoph Conrad explained that there was one time point selected - when VVM changed on exposure at 45\textdegree C - at which potency was measured. A change in vaccine stability during shipment, handling, and transportation was reflected by a change in VVM. Moreover, if the vaccine was not stable at 37\textdegree C, then it would not be stable at 45\textdegree C.

IPAC members discussed that variability in characteristics of the same vaccine from different manufacturers should be considered while proposing guidelines and recommendations. It would present a huge regulatory burden considering revision of pre-qualification, changes in packaging and package insert, labels, as well as storage conditions. WHO secretariat said that manufacturers should be encouraged to produce vaccines that countries would prefer to have. Conversely, if it was possible to produce a vaccine with some license variation, it was important for countries to know this, and state their preferences.

Several IPAC members expressed concern that, in order to change labelling on vials, the approval of regulatory bodies would be important. Manufacturers could agree to undertake this issue.

\textbf{3.3 Technologies work stream-proven technologies for implementation of CTC}

Mr John Lloyd from PATH presented work done in the technologies work stream for the implementation of CTC. Mr Lloyd explained that the technology work stream was aiming at: (i) monitoring the time/temperature exposure and warn of possible extreme exposures of the vaccine up to the point of administration; and (ii) monitoring the cold chain system for high temperature excursions as well as for freezing, to assure the maximum residual life of the vaccine at the periphery.

\textsuperscript{2} Include reference to full study report
Monitoring the vaccine: Currently, VVMs are the only proxy to warn of excessive time/temperature exposure. However, only 30% of approximately 250 million doses of vaccine used in developing countries globally carry a VVM. Work is under way to develop high temperature (e.g. “flash heating”) threshold indicators needed to supplement VVMs, determine the potential of e-indicators as an alternative to chemical indicators, determine requirements for developing a PQS specification, and consideration of launching a possible ‘challenge’ to industry to develop combined time/temperature threshold indicators.

Monitoring the cold chain: It is critical that the temperatures are closely monitored at all levels of the cold chain, as successful implementation of CTC requires a solid cold chain up until the periphery. Work under way in this area includes use of ‘SmartConnect’ device which combines temperature recording, transmission of alarms, and stock information data from vaccine stores to managerial hubs. Also, a ‘Libero based-SMS Alarm’ and the ‘FoneAstra’ systems are being pilot tested in Albania. Finally, the remote control of the temperatures of store-buildings and equipment to store drugs regulated for Controlled Room Temperature (CRT) is a project undertaken in Tunisia, at regional and district drug stores.

Mr Lloyd asked whether (i) IPAC supported the notion of a new industry ‘challenge’ to develop combined time-temperature and threshold-temperature vial monitors, and (ii) IPAC endorsed the general direction of the work on CTC technologies.

In the discussion, few IPAC members also suggested that freeze indicators would be needed for cold countries. The extreme threshold indicator should, thus, be able to monitor both hot and cold temperatures. Mr Lloyd agreed that, ideally, the indicator should detect both thresholds. However, there currently is a significant problem with the development and use of freeze indicators. The lack of quantification of the temperature exposure problem was also discussed. Thus, alternative indicators should be developed. IPAC agreed that it was important to encourage industry to develop better tools, indicators, and VVMs.

IPAC unanimously supported the notion of a new industry ‘challenge’, and endorsed the direction of the technologies workstream.

3.4 Country-implementation: Guidelines to operationalize CTC at country level

Ms Simona Zipursky from PATH presented examples of operationalization of CTC at country level. The country implementation work stream aims at developing operational guidelines for Hepatitis B and other vaccines in a CTC. The country-level guidelines would support both the decision making process, by highlighting necessary pre-conditions for success, as well as methods to assess the suitability in specific settings, as well as guidelines for field operations, to ensure safe handling of vaccines in a CTC environment.

From existing literature, data on Hepatitis B and meningococcal C showed no significant serological differences between vaccines used in the cold chain and those used in the CTC. Ms Zipursky also mentioned a document published by WHO, which supported the use of Oral Polio Vaccine in a CTC during campaigns, when equipped with a VVM. She recounted documented practices in the field, citing studies conducted by Optimize in Mali and Chad as examples.

(i) Mali, June 2009 The first systematic documentation of using OPV in a CTC, during National Immunization days. The objective of the study was to determine if transporting OPV without icepacks during a vaccination campaign was feasible and advantageous. Temperature monitoring was done; vaccines were used until VVMs reached their discard/end point; and VVM status was recorded at different time points. Out of the 15,000 children vaccinated, 53% were

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administered OPV kept in CTC (between 25 to 40°C, during an average seven hour day). No VVM on any OPV vial had reached its endpoint before administration of the last dose after seven hours in CTC. CTC practice was easy to use, time and cost effective, achieved higher coverage, and reduced wastage and was preferred by both health care workers and supervisory. However, a limitation of this study is that no potency data was collected, and VVM status was used as a surrogate. Nonetheless, this study showed that CTC is a feasible and useful approach, provided vaccines had a VVM, and proper training and guidelines were in place.

(ii) Chad, April 2010 The first field-level validation of vaccine potency and VVM correlation was done in Chad. The objectives of the study were to demonstrate that the potency of OPV, used in a CTC, was still within acceptable range. Test vials were exposed to ambient temperatures during all campaign activities but remained closed at all times. Post-campaign, all test vials were transported to the Belgian National Control Laboratory for quality lot release control and VVM reading via densitometer. Records showed that test vials were exposed to ambient temperatures of up to 47.1°C, with a vial being exposed to temperatures above 8°C and 37°C for a maximum of 86.9 hours and 9.7 hours respectively. VVMs behaved as expected, and all vials were above the potency threshold (given a CI of +/- 0.3) specified by WHO for release. Although the study had its limitations, it provided evidence that some types of mOPV3 could be safely kept, for limited periods of time, outside of a 2 to 8°C cold chain, in alignment with the WHO Flexible Cold Chain management guidelines, without a significant decrease in potency levels, provided a VVM was used.

(iii) Other CTC country examples were given, including the Western Pacific Regional Office of WHO, which has developed guidelines for HB vaccine\(^5\), allowing use of HB vaccine in CTC for one month, but only those vaccines with VVMs, only for ‘birth dose’, only at the point of use, and only after adequate training of health workers. In Papa New Guinea, monovalent HB vaccine has been used in CTC, along with Uniject and better tracking methods, resulting in increase in coverage from less than 10% to 30-98%.

In 2011, an outline for guidelines will be developed and reviewed by the IPAC sub-group on CTC, with input from countries and regions with relevant experience (Q2). After field-testing, subsequent revision, and endorsement of the revision by CTC sub-group (Q3/Q4), guidelines will be presented to IPAC for endorsement (Q4/2011 or Q1/2012).

Questions were raised on whether CTC guidelines were for specific vaccines and settings or general. Dr Eggers suggested that separate guidelines be outlined for campaign settings, for birth dose administrations, etc.

It would be useful to engage the regulatory bodies in the discussions while setting guidelines, taking into consideration operational training, monitoring, costing, operational costs, and other factors. Better coverage data with other antigens were also needed as well as addressing operational issues such as data recording for coverage.

The importance of maintaining the right balance between optimal use of vaccines and CTC was emphasized. There were concerns regarding health workers resisting use of CTC. Concerns were raised regarding influence of WHO guidelines on regulatory decisions, making it imperative that the guidelines be evidence-based. Ms Zipursky mentioned that it was not possible for all existing vaccines to undergo a label change, due to regulatory and other complications. However, several countries were implementing CTC regardless of the information on the label. These countries required guidelines and support from WHO, in order to implement CTC as safely as possible, and when considering a national policy. It was also noted that, in the first stream of work on vaccines, an active dialogue with regulatory bodies was already ongoing.

Dr Deeks asked IPAC members to provide further input and suggestions on this topic via personal communications to Mr Michel Zaffran and Ms Simona Zipursky.

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\(^5\) Preventing mother-to-child transmission of Hepatitis B: Operational field guidelines for delivery of the Birth Dose of Hepatitis B vaccine. WHO Geneva
3.5 Update on CTC sub-group work done so far, and next steps

Dr Francois Gasse, IPAC member and Chair of the CTC sub-group, presented work done by the sub-group thus far. The sub-group comprised IPAC member, Dr Jane Soepardi, two IPAC observers (Dr Gastineau and Ms Kristensen), consultants, academicians, UNICEF staff members, and representatives from WHO regional offices. One more member a national logistician, was yet to be recruited.

Dr Gasse said that the sub-group was required to review, provide input, and get a subgroup consensus on the CTC strategy. Its role in the future would be to advise on the development of country guidelines, determine how to assess suitability of CTC in specific countries, participate in its testing, assess areas where more evidence was necessary, and review and support the development of guidelines.

The main sub-group discussion points on the CTC strategy were presented, including temperature and time limits for using vaccines in a CTC, antigens to which CTC would be applicable, strengthening the background and rationale for CTC, the role and engagement of NRAs, and CTC during transport to avoid freezing. Future areas of discussion of the sub-group included assessing MDVP introduction as a case study, examining issues of liability of guidelines, gathering data to the country decision-making process, and quantifying the benefits of CTC. IPAC was requested to discuss critical elements missing from this strategy, and information needed before guideline development could begin.

IPAC members asked for further clinical data on vaccine efficacy in CTC, and stability data on individual vaccines from different manufacturers - the report will be made available to IPAC. It was also suggested that the cold chain problem needed to be quantified.

Moreover, members also advised that the CTC strategy should consider implications to manufacturers. Observers representing manufacturing bodies raised concerns over changing labels on vials, which would lead to a huge regulatory burden. Alternatively, it might be better to emphasize using vaccines off-label but following WHO-endorsed CTC guidelines. WHO secretariat said that changes in label, without getting into complications such as relicensing, were desirable and that promoting off-label use would be less desirable but potential option.

3.6 Endorsement of the CTC strategy

Overall, CTC was considered as beneficial to countries where cold storage was a big challenge, and to reduce volume in the cold storage. However, it would reduce the burden of transportation only if a large proportion of vaccines could be taken out of the cold chain.

In conclusion, IPAC unanimously endorsed the CTC draft strategy as a roadmap to move forward in this direction. However, IPAC requested that the gaps and issues raised at this meeting be incorporated and addressed in the CTC strategy.

4 Programmatic Suitability of vaccines for Pre-Qualification (PSPQ)

4.1 Consultation with vaccine industry on PSPQ content and revision of the PQ procedure

Dr David Wood from WHO/QSS presented the consultations of WHO with the vaccine industry regarding PSPQ content and the resulting revisions of the PQ procedure after considerations of comments from industry. Dr Wood stressed that this would provide transparency to the PQ process. The revised draft was published on the WHO website for comments by the public and by industry partners and incorporated, after careful consideration, into a third draft for internal circulation. The revised draft presented was at this meeting for IPAC’s endorsement,
agreement, and input. The final document will be published and available on the website following IPAC's recommendations.

Dr Wood mentioned that whereas several concerns expressed by industry and other reviewers were addressed, not all comments from industry were accepted. Chief reviewers were from the VPPAG, DCVMN, IFPMA, and other organizations. This presentation covered the key comments and their adoption by the Secretariat in development of the final draft.

In conclusion, Dr Wood said reviewers’ concerns had been considered and/or addressed throughout development of the successive drafts. The document was intended to provide clear guidance for future vaccine development, so that populations in need would have access to vaccines of public health importance meeting their programmatic needs. The official record of PSPQ committee would serve as reference for future discussion and practice of policy. In the end, he said that the relevance and importance of this document would grow as it is applied over time.

4.2 Summary of final draft of the PSPQ paper, outline of terms of reference, and modus operandi for the PSPQ Standing Committee

Dr Rudi Eggers presented the summary of the revised draft of the PSPQ paper. He mentioned that the PSPQ document was beneficial to all due to its clear procedure, its clear direction to vaccine industry, and its shorter decision track for complicated presentations.

Dr Eggers stated that the PSPQ process would apply to future screenings of pre-qualification applications. It would currently not apply to previously WHO pre-qualified vaccines or their renewal, or to vaccines that were under review for pre-qualification at the time of publication of this document. In addition, WHO expected that regional variations in programmatic suitability characteristics would be expressed in the procurement and tendering process.

Vaccine characteristics that would affect pre-qualification were explained. Compliance to mandatory characteristics was compulsory; failure to meet this characteristic would prevent the vaccine to be further considered for pre-qualification. Although compliance to critical characteristics was also compulsory, the PSPQ Standing Committee (SC) would review deviations in vaccine characteristics. Under special circumstances, exceptions could be granted to vaccines that deviated from the critical characteristics. Furthermore, the PSPQ SC would also review unique characteristics. With the help of flowcharts, Dr Eggers explained the process of compliance or non-compliance with certain mandatory and critical vaccine characteristics. These flowcharts are included in Annex 2 on page 22. Lastly, preferred characteristics were characteristics that were preferred in a vaccine, but compliance to these characteristics did not affect pre-qualification. A preferred characteristic may in future revisions be deemed to become critical or mandatory.

The decision taken by the PQ Secretariat would include consideration of recommendations from the PSPQ SC, and public health need. The final decision to pre-qualify a vaccine lay entirely with the PQ team and the Director IVB.

Dr Eggers explained that the PSPQ SC was an independent advisory committee to the WHO PQ Secretariat, was made up of experts with immunization program and policy experience, and was one of IPAC’s Standing Committees. The PSPQ SC may engage in confidential discussions with manufacturers and additional technical experts. It may also recommend validation by research of the acceptability of non-compliant characteristics. The maximum allowed time for review by the PSPQ Standing Committee was three months.

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4.3  IPAC discussions on PSPQ

In the discussion it was re-iterated that the PSPQ process would apply to new applications and that PQ renewals would - for now - not be subjected to the PSPQ process. WHO secretariat said that the revised procedure would come into force for new PQ by the end of 2011.

The renewal time for the review of pre-qualified vaccines varied between two to five years. However, the date by which the process would apply for pre-qualified vaccines was not specified in the document. The document would continue to be revised when needed, with input from IPAC. However, the time interval of revision was not yet specified, and IPAC was invited for its input on the issue.

The process for revising the document had not been formalized yet, but WHO would comply with IPAC’s agreement on defining a time point for the transition period. He added that during the review of the document, if certain characteristics would be moved from critical to mandatory, this change would apply to future vaccines, but not to vaccines undergoing the PQ process.

It was suggested that the minutes for discussion meetings with manufacturers and PSPQ committee members, be officially drafted. WHO accepted this suggestion.

Several inputs were made in relation to the rewording of or additions to the current document:

- The lack of dose volume specification for oral vaccines.
- The scheduling for only five vaccines was presented. It was not clear whether it applied to other vaccines as well.
- The application of the visual cue to multi-dose or single-dose vials.
- Specify quantity of diluents corresponding to the vaccines. Dr Eggers mentioned that packing of the diluent was not presently required as a criterion, although this point could be considered in the future.
- Preservatives would be unable to "prevent" contamination, but rather to "control" or "modify" contamination.
- Several members and observers suggested re-wording of VVM characteristics, and to specify a demand for better VVM standards. Dr Eggers answered that the emphasis was on vaccine characteristics, and that vaccines should be able to be assigned VVM, rather than emphasis on VVM per se. Hence, components in the vaccines should be able to match one of the VVMs currently being used and approved by WHO. Dr Wood added that WHO secretariat would consider re-wording of this characteristic.

There were concerns about inflexibility of the procedure regarding inadequately preserved multi-dose vials. Specifically, if a ten-dose vial contained a reduced amount of preservative and could be kept for only 7 days and not 28 days, then it would get automatically rejected according to currently specified criteria. This would mean that vaccines that did not fit into rigid criteria would not be allowed to be pre-qualified. Dr Eggers addressed this issue by stating that if a multi-dose vaccine could not comply with current MDVP in terms of period for which it could be kept and in terms of amount of preservative it had, then it presented safety risks. In that case, WHO would recommend a two-dose vial instead of a multi-dose vial for that vaccine.

Conversely, concern was raised by some members that two-dose preservative free vaccine was included as acceptable within the mandatory criteria. It was noted that this situation would be referred to the PSPQ SC. Dr Eggers explained that WHO was looking forward to results from the performance of newly introduced PCV10 vaccine in Kenya, which would give WHO a better idea about safety and practicality of using two-dose vials without preservatives. WHO would change this criterion, depending on results. Regarding questions on the use of
single-dose vaccines as multi-dose vaccines, WHO secretariat said that this issue was not yet addressed in the document, and took note of this point.

Several observers asked about the role of countries in formulation of the document. Dr Eggers replied that the working group comprised of two regional members, one country representative, and two procuring-agency members (UNICEF and PAHO). However, in the later draft revisions, countries did not provide their input.

Regarding questions about an intention to de-centralize the PQ procedure from WHO, Dr Wood replied that although PAHO dealt with pre-qualification of medicines, pre-qualification of vaccines would remain a central issue. Overall, IPAC appreciated the efforts undertaken by WHO to formulate the presented document.

4.4 Establishment of the PSPQ Standing Committee and appointment of IPAC members to the same

Dr Rudi Eggers explained the role of the PSPQ Standing Committee (SC), and also proposed names of IPAC members to be part of the PSPQ SC. The recommendation being sought from the PSPQ SC was either acceptance or rejection of the application. In rejecting an application, the PSPQ SC could include a recommendation for re-submission, after validation by research of the acceptability of specific characteristics.

According to Dr Eggers, the PSPQ SC’s official records were confidential; they could only be shared with the PQ Secretariat and the Director IVB and could be published only with the explicit approval of the manufacturer submitting the PQ application, the PSPQ Chair, the PQ secretariat, and Director IVB. Accordingly, the PSPQ document would be updated, and vaccine community would be informed about policy revisions.

All five members of the PSPQ SC would serve in their personal capacity. Of the five members, one member should have expertise in the management of developing country immunization programs, while another member should have regulatory expertise in that area. The other three members would be designated from the WHO IPAC, and appointed by Director IVB. Dr Eggers invited IPAC members Drs Robin Biellik, Jane Soepardi, and Robert Steinglass, to be members of the PSPQ SC. Whereas Drs Robin Biellik and Jane Soepardi accepted the proposal, Dr Robert Steinglass declined due to prior commitments. Dr Eggers invited IPAC to provide their input and give their suggestions for the determination of a third member.

4.4 Recommendations from IPAC

4.5.1 Appointment of IPAC members to the PSPQ SC

IPAC endorsed the memberships of Drs Robin Biellik and Jane Soepardi, and agreed to await further suggestions from WHO regarding appointment of a third member. There were suggestions to include secretarial support from regional office representatives for the PSPQ SC, to help with issues relating to programmatic regulations. WHO secretariat accepted this suggestion.

4.5.2 Endorsement of the PSPQ document by IPAC

IPAC Chair Dr Shelley Deeks mentioned that IPAC members had had time to review and think through concepts between June 2010 and the present meeting. She put forth the following issues for discussion, recommendation, and endorsement by IPAC

Implementation date: WHO proposed the end of 2011 as the implementation date for the PSPQ document, and that once implemented, would be applied fully for all new products with no further transition period. IPAC endorsed the proposed timeframe.
There were concerns about manufacturers being fully cognizant of the requirements of the PSPQ document by the end of 2011. Several observers representing industry and representatives from manufacturers replied that the revised PSPQ document and the nuances of the transition process needed to be considered. WHO secretariat acknowledged that it was aware of manufacturers' concerns, and had assigned two days for a face-to-face consultation with different manufacturers, during which their specific concerns would be considered.

**Vaccines up for pre-qualification renewal:** Although initially only vaccines presented for the first time for pre-qualification would be subjected to the PSPQ procedure, IPAC was asked if a date should be set by which *all vaccine PQ renewals* needed to comply with the PSPQ process and if some vaccines could be exempted from this demand.

There was unanimous consensus among IPAC members that a date should be specified in the current PSPQ document by which vaccines under renewal would be included in the process. However, it was WHO's prerogative to specify the date.

**Frequency of revision of the document:** Currently, the document did not address the issue of its revision and when it would be revised. IPAC considered that the frequency of revision should be stated in the document itself. Alternatively, IPAC could review the document as a standing issue in its subsequent meetings, and ensure the process of renewal of the PSPQ procedure.

Several members suggested that IPAC could review the document once a year, and re-affirm its principles, or determine which specific issues could be revised as per need and experience. A few members also suggested that the preference of countries should be reflected in the revision of the document. Several observers suggested that the implementation date of the revision should be specified to the manufacturers, and a transition period for the same should be also put in place. WHO accepted this suggestion.

IPAC decided to consider the PSPQ document as a standing issue on the IPAC agenda, and to determine its revision as per need. The frequency of revision was left open-ended.

**Endorsement of the current PSPQ document:** In conclusion, IPAC endorsed in-principle" the PSPQ document dated 27 October 2010. However, before final endorsement, IPAC suggested WHO should revise the document based on present input at this meeting. IPAC would review the modifications in the next teleconference (January 2011) meeting before endorsing the document. An IPAC member suggested that the document should specify volume of dose for oral vaccines administered in infants. IPAC disagreed with this suggestion.

## 5 Vaccine Safety at WHO and interaction with GACVS

Dr Patrick Zuber from WHO/IVB presented this session, outlining the main vaccine safety activities being undertaken by WHO IVB, which included responding to vaccine safety alerts, serving as secretariat for the Global Advisory Committee on Vaccine Safety (GACVS), developing and disseminating training materials, developing a global network for post-marketing surveillance, providing harmonized tools for vaccine safety, and developing a global vaccine safety blueprint. WHO faced several challenges during investigation of crises, including investigation of non-programmatic events, and had to provide substantial external support especially for new and/or pre-qualified vaccines. In many countries, vaccine safety issues are complicated by the limited experience of local staff, resulting in significant delays in investigations along with scarcity of captured evidence.

Dr Zuber discussed the specific functions and role of GACVS, which was established in June 1999, to enable WHO to respond promptly, efficiently, and with scientific rigor to vaccine safety issues. It was composed of 12 to 15 members with expertise in relevant fields. WHO also gave support to programmatic and regulatory activities; for example post-marketing surveillance (PMS) for MenAfriVac in three countries was being conducted by WHO and reviewed by GACVS, along with daily monitoring of AEFI reports, and training of national AEFI review committees.
According to Dr Zuber, 58 countries have a functional National Regulatory Agency (NRA). Overall, PMS/AEFI surveillance function is implemented in countries that account for 52% of the world’s population; countries without functional systems are primarily developing and least developed as of 2009. He also discussed support provided by WHO to countries regarding vaccine PMS and response. These tools included AEFI assessment, basic (vaccine vigilance) and advanced training (causality assessment) for programme staff, and developing a PMS network for pre-qualified vaccines. The PMS network supported the vaccine pre-qualification program with safety data in post-marketing phase; ensured standardized approach to monitoring AEFI; and provided adequate safety information to support vaccination policy and recommendations. Countries from different regions nominated for initial PMS were using pre-qualified vaccines, had a functional PMS, and a DTP3 coverage above 80%.

Lastly, Dr Zuber talked about the Global Safety Blueprint project undertaken to better integrate existing resources for WHO support. WHO task groups, vaccine manufacturers, procurement agencies, other support groups, etc. were part of these different facets of the network. Work was under way in four phases, for successful implementation of the global safety blueprint project. These four phases included systematic situation analysis and assessment, drafting a strategic plan blueprint, global vaccine safety meeting to discuss blueprint components, and finally, a revised blueprint ready for endorsement and implementation.

5.1 Discussions with IPAC on vaccine safety

5.1.1 Interaction of IPAC with GACVS, and IPAC input on vaccine safety issues

IPAC discussed the ways it could function alongside other committees, such as GACVS, and the potential linkages between the two committees. Dr Zuber mentioned that the SAGE Chair was usually invited to attend GACVS, and vice versa. Furthermore, some members had also been on both SAGE and GACVS. Dr Zuber suggested that a similar process could be put in place for IPAC and GACVS. He said that AEFI events were brought to the attention of vaccine safety experts due to mainly programmatic reasons. This was one area where IPAC expertise could be used. Additionally, capacity building of countries to monitor new vaccine introductions, and similar programmatic issues were also potential areas where IPAC could provide input. IPAC and WHO secretariat agreed to these suggestions.

It was suggested to have a periodically published safety report for products, and not only for adverse events. Dr Zuber said that meeting reports for vaccine safety experts and specialists could be sent to IPAC members. WHO secretariat added that it could regularly inform IPAC about programmatic issues related to vaccine safety. IPAC agreed to this.

5.1.2 AEFI surveillance

Members asked about the kind of surveillance support that countries were getting, and whether they were able to use this information for self-assessment. Dr Zuber said that the range of programmatic errors was very large, and could potentially range from type of vaccine product to reconstituted vaccines, lack of disinfection, availability of resources, etc. However, every country had access to NRA tools, and a comprehensive mechanism following AEFI surveillance was available to them. New vaccines were also safety-monitored. Hence, passive PMS, in alignment with NRA assessment, was being done in countries.

Few IPAC members asked whether WHO sent guidelines to countries on improving surveillance and conduct better communication regarding active surveillance. Dr Zuber responded that active surveillance was being done in very selective countries. Moreover, enhanced passive surveillance was also being done. He agreed that communication was indeed a vital component of both training packages that WHO had.

5.1.3 Capacity building

Dr Zuber was asked about help offered to countries that did not have a functional NRA, through the blueprint project. He replied that the aim of the blueprint was to take advantage of other resources outside WHO. In terms of WHO efforts and capacity building, minimal
capacity principle would apply, so that countries could deal with main issues around vaccine safety. WHO IVB anticipated technical competence, regulatory provisions, and available resources, as the key components of capacity building. There were suggestions to have training manuals and materials for field workers. Dr Zuber said that WHO was currently drafting manuals and developing comprehensive training tools, which were expected to be ready in 2011 and translated into different languages by 2012.

6 Routine and Supplemental – definitions and issues in data recording and analysis

The main objectives of this session were to update IPAC about the scope of data recording and analysis problems relating to routine versus supplemental vaccination. Country specific examples were shared to demonstrate these issues. The ultimate aim is to work towards achieving agreement on definitions, and standardization of terminology.

6.1 Evolution of Immunization Paradigms and Presentation of Re-worked definitions

Mr Tony Burton from WHO/IVB/EPI introduced the session for which the background paper "Distinguishing Characteristics of Routine and Supplemental Immunization and Doses" was shared (Annex 3, page 30). Traditionally doses administered have been associated with different strategies (e.g., routine or supplemental). However, in recent years many countries have begun to administer routine doses during campaigns which historically have been used to only to delivery supplemental doses. There is a debate among some who feel that campaigns should not be considered an appropriate strategy for routine "services," although they accept that if proper attention is given to screening for age/dose per the national immunization schedule and recording on the child's vaccination card, then these vaccinations would constitute "routine doses" (even though the strategy used would be considered "non routine" by some).

Mr Burton described the problems in data recording and analysis. Merely to distinguish “routine” doses from “routine” strategies, he proposed that when immunization in the recommended schedule was offered based on assessment of child's immunization history and dose, and when the date of immunization was recorded on personal immunization records, such a strategy could be called- a) BIHAIR – Based on Immunization History And Individual date and dose Recorded, or b) RSBIHIR – Recommended Schedule, Based on Immunization History, Individual date and dose Recorded respectively.

Conceptually, Mr Burton illustrated that there could be two ways of viewing the monitoring of immunization activities:

1. Record vaccinations given by BOTH type of dose (routine or not routine) AND type of delivery strategy (e.g., type of dose and strategy are recorded together); or

<table>
<thead>
<tr>
<th></th>
<th>Dose</th>
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<tbody>
<tr>
<td></td>
<td>Doses give based on immunization history, individual date and dose recorded (&quot;Routine&quot;)</td>
</tr>
<tr>
<td>Delivery strategy</td>
<td>Routine</td>
</tr>
</tbody>
</table>
2. Decouple the concepts of doses and strategies, and monitor these irrespective of one another (e.g., monitor type of dose only).

2.A. | 2.B.  
---|---
**Delivery Strategy** |  
| Routine | $n_1$ |  
| Campaign | $n_3$ |  
| **Doses** |  
| Routine | $n_2$ |  
| Not routine | $n_4$ |  

Lastly, Mr Burton invited IPAC’s views on the possible implications of this conceptualization at service-delivery, sub-national, national, and international levels. The discussion was divided between:

(i) those who were uncomfortable accepting routine doses delivered through non-traditional means such as campaigns, and they felt that for management purposes it was important to know the specific strategy used to deliver the type of dose; and

(ii) those who felt that all strategies were legitimate ways to provide routine vaccinations, therefore the recording of the type of dose (routine or supplemental) was the key monitoring issue (not the strategy that was used). It was argued that strategies were always changing and that it would be too burdensome to monitor the strategy that had been used to deliver each and every dose. For example, a child may get DTP1 through a fixed site; DTP2 through a campaign; and DTP3 through a mobile outreach.

### 6.2 Country-case study—Somalia Child Health Days 2009

Dr Imran Mirza from (UNICEF Somalia) presented the example of Somalia’s Child Health Days (CHDs), and outlined how Somalia, which has a very weak health system, dealt with the immunization data recording challenges.

Dr Imran Mirza said that the UNICEF/WHO Joint Programme on Accelerated Young Child Survival carried out scheduled, population-based activities through CHDs, to deliver key health interventions to women and to children under five years of age. The CHD package included DPT, OPV, Measles, TT, Vitamin A, oral rehydrations salt, de-worming, and water purification tablets. In addition to the twice yearly CHDs, different immunization approaches were employed throughout the year, including implementing the Reaching Every District (RED) approach to strengthen routine EPI, better training and better communication of health workers in the field, as well as employing effective reporting and monitoring methods. Since implementation of CHDs in 2009, Somalia had immunized 51% and 58% children under one year of age against DTP3 and measles (an additional 22% of children were reached with CHDs).

The implementation of the CHDs included development of field operational guidelines, training of health workers, and district-level micro-planning. Each CHD team included two vaccinators, one screener, one health promoter, one crowd controller, and one recorder. Children were vaccinated with DPT only after screening for eligible age and prior vacation history. Administered doses were recorded by age category and dose. The following recording, reporting, and monitoring tools were used in Somalia: (i) recording tools- CHD Card, CHD TT card, CHD Tally Sheet, and TT Tally Sheet, (ii) reporting tools- daily summary sheets at supervisor, district and regional levels respectively, AEFI reporting form, and AEFI investigation form and, (iii) monitoring tools-CHDs preparedness checklist, CHDs monitoring.
checklist, rapid assessment form, and CHD interventions sheet. Dr. Mirza explained that in future Somalia had decided it would record all routine doses given through CHDs on the Child Vaccination Card and would no longer distribute a special CHD vaccination card.

CHD data collected from each site were consolidated at district, regional, and national levels. DPT and MCV doses administered through CHDs were also included in routine administrative data at the district level. Through the use of the CHDs strategy, Somalia achieved a significant increase in routine DPT3 coverage levels in most districts.

In summary, a combination of fixed site, Periodic Intensification of Routine Immunization (e.g., CHD), and RED approach strategies are being effectively employed in Somalia. Somalia's attention to the recording and reporting processes provides an example of CHDs being successfully used as a strategy to deliver routine immunization services.

6.3 PAHO experiences with PIRI-like activities, and the recording of routine immunization activities

Dr Mauricio Landaverde from WHO/PAHO presented experiences of PAHO with PIRI-like immunization activities. Dr Landaverde mentioned that in Latin American and Caribbean countries, where immunization coverage among children under one year of age was already more than 90%, it seemed fruitless to worry about the strategy that helped achieve this high goal. It was also difficult to distinguish if disease control and disease elimination was due to routine or campaign programmes. Dr Landaverde presented the case of Cuba, where poliomyelitis and measles had been eradicated using a combination of immunization strategies.

The Vaccination Week in the Americas (VWA) is an important PAHO initiative, which has vaccinated over 300 million people from a wide variety of ages over the last eight years. Countries have implemented several different types of activities under the framework of VWA, which include polio and measles vaccination, yellow fever campaigns, etc. Some countries also used VWA to introduce new vaccines, while other Caribbean countries used VWA to conduct awareness campaigns. Dr Landaverde presented examples of high coverage achievement in Paraguay, for different vaccines, to demonstrate the benefit of VMA to routine coverage.

During VWA, all routine vaccinations are recorded by age and dose on the child’s immunization card, as well as on tally sheets, and included in the administrative data.

6.4 Discussions by IPAC

6.4.1 Cost-effectiveness of CHDs

Cost effectiveness of CHDs and the impact of the cost of CHD's on the regular government delivery system were discussed. Members agreed that it was important for national governments to realize the value of campaigns such as CHDs, and to avoid the process becoming solely donor-driven. Dr Nadia Teleb from WHO EMRO added that strengthening of the health system was a priority.

6.4.2 Data handling and recording

IPAC agreed that it was important to know the overall contribution of campaigns doses, such as those delivered in Somalia’s CHDs, to routine immunization programmes. In addition, several members also felt that it was important to monitor the incremental contribution to coverage, not just at the district level, but also at the regional level.

The process for following up on vaccinations and the internal quality control practices used for CHD coverage data recording in Somalia were discussed. Dr Mirza replied that all doses were recorded and compiled systematically. All districts, regional, and zonal offices received the summary sheet data. Furthermore, during implementation of the CHDs, the coverage achieved was compared against targets, the number of children vaccinated was compared to the number of vials used, and the doses were registered on the tally sheets. This thorough crosschecking acted as an internal quality control of recorded data.
Several members and observers raised concerns regarding the risk of double counting and inaccurate coverage data. Dr Mirza responded that Somalia was trying to develop methods to improve monitoring accuracy of the data. It was also noted that data recording errors are not exclusive to PIRI-like activities, and that there can be issues with accuracy for fixed-site, mobile, and outreach immunization data recording also.

6.4.3 Definitions and terminology

Some members and observers expressed reservations and concerns about the use of “routine” terminology, and suggested that this term be revised. It was considered that any predictable, sustainable activity could be considered routine. Alternatively, the term “routine campaign” was suggested. There was some disagreement on CHD being used as a strategy to deliver routine immunization. However, other members disagreed, as they considered achieving high coverage, regardless of strategy, to be more important. Some members also suggested that routine services should be used for coverage and monitoring, although recommended doses may be given through whichever strategy was appropriate to the specific case.

IPAC agreed that the real issue was the risk of incorrectly recording the number of doses and of coverage data. Several members appreciated Somalia’s efforts using CHDs to deliver routine doses in order to achieve high coverage in a country where the health system is almost non-existent. It was also noted that in Somalia data recording distinguished between type of dose and age of child through the proper use of tally sheets. However, the quality and accuracy of data recording and monitoring to avoid duplication of data was still a major concern for some members and observers.

A document had been shared to the IPAC members, highlighting in a tabular form, the distinguishing characteristics of routine immunization and supplemental immunization. IPAC members were encouraged to share feedback to the WHO focal persons.

IPAC members agreed that definitions needed to be revised. IPAC members advised that accuracy in coverage measurements was of great importance regardless of delivery strategy.

In conclusion, IPAC accepted that it was important to maintain both routine and campaign strategies. However, IPAC strongly felt that the situation concerning the recording of doses should be clearly disentangled.

7 Closing

IPAC Chair Dr Shelley Deeks summarized the recommendations and endorsements of IPAC as outlined in the document above:

7.1 Administrative issues, planning, and sub-groups

In the first part of this session, Dr Eggers reiterated the responsibilities of IPAC sub-groups and of IPAC’s relationships with other committees, as discussed in the previous IPAC meeting.

7.2.1 IPAC sub-groups and work groups

Dr Eggers expounded on the roles and responsibilities of IPAC sub-groups. Task groups7, or Work groups, when established according to need, would ideally consist of a WHO technical lead, other experts, and one to two IPAC members who would represent IPAC in the task groups. While IPAC members were not expected to be experts in the topic of the task group; rather they would act as topic leaders when the topic was brought to the full IPAC meeting for discussion. Further, time limited sub-groups8 may be formed for a particular task at hand. An IPAC member volunteer, on behalf of IPAC, would also be needed to participate in the ongoing standing committees that meet ad-hoc.

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7 Task Group: Time-limited group to assess and review specific topic.
8 Sub-group: Small time-limited group to oversee distinct part of a task groups review.
According to Dr Eggers, the roles and responsibilities of IPAC members would be defined in the terms of reference, which may differ from one working group to another. He said that a minimum of one, and a maximum of two, IPAC members could play a leading role in each work group, depending on the workload. The size of a work group could vary from six to not more than ten members. The chief difference between a work group and other IPAC groups was that the work group could include relevant topic experts. In terms of operational procedures, a member of the work group would be required to submit a brief on its meeting outcome and decisions, as guidelines for the full IPAC. Any members found in conflict of interest in the work group could not continue to serve in that group.

7.2.2 Potential future topics for IPAC and next meeting dates

Dr Eggers presented IPAC with some potential future topics that could be discussed in the future IPAC meetings. Some of these included baby tracking by engaging existing community-based resources to reach the unreached, developing an adaptable tool kit for reaching the unreached, pay for performance schemes (also known as results based financing), review of programmatic aspects of aerosol route for vaccination, school-based vaccination, vaccination as a legal requirement on school entry, and guidance in needle size in vaccination. The potential topics, their inclusion, as well as consideration of other proposed topics, was open to discussion by IPAC members.

IPAC agreed on the following process for topics to be included as IPAC meeting agendas: the topics were mainly initiated by WHO secretariat and finalized after IPAC Chairperson’s agreement and endorsement. Topics proposed by IPAC members and observers would be communicated between IPAC with rationale for its inclusion. After consensus, the topic would be recommended to WHO secretariat as a future IPAC meeting agenda.

Dr Eggers proposed potential dates for future IPAC meetings, which were aligned to bi-annual SAGE meetings, as much as possible. These dates were as follows:

<table>
<thead>
<tr>
<th></th>
<th>IPAC (2 or 3 days)</th>
<th>SAGE (2 or 3 days)</th>
</tr>
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<tbody>
<tr>
<td>First meeting 2011</td>
<td>Tue 12-Thurs 14 April</td>
<td>Tue 5-Thurs 7 April</td>
</tr>
<tr>
<td>Second meeting 2011</td>
<td>Tue 27-Thurs 29 September</td>
<td>Tue 8-Nov 10 November</td>
</tr>
<tr>
<td>First meeting 2012</td>
<td>Tue 17-Thurs 19 April</td>
<td>Tue 10-Thurs 12 April</td>
</tr>
<tr>
<td>Second meeting 2012</td>
<td>Tue 2-Thurs 4 October</td>
<td>Tue 6-Thurs 8 November</td>
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It was decided that the next IPAC meeting would be held on 12-13 April 2011 at WHO Headquarters in Geneva, and would be a week after the SAGE meeting. Moreover, 14 April 2011 was potentially reserved for IPAC work groups. Dr Eggers also mentioned that the topics which would be discussed in April 2011 IPAC meeting would include visual cue, Hepatitis B birth dose, and Routine/Supplemental strategies, among others.
8  **Annex 1: Initial terms of service for IPAC members**

<table>
<thead>
<tr>
<th>IPAC member</th>
<th>Start</th>
<th>End (incl.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shelley Deeks (chair)</td>
<td>2010</td>
<td>2013</td>
</tr>
<tr>
<td>Robin Biellik</td>
<td>2010</td>
<td>2013</td>
</tr>
<tr>
<td>Xavier Bosch-Caplansch</td>
<td>2010</td>
<td>2011</td>
</tr>
<tr>
<td>Francois Gasse</td>
<td>2010</td>
<td>2013</td>
</tr>
<tr>
<td>Najwa Khuri-Bulos</td>
<td>2010</td>
<td>2011</td>
</tr>
<tr>
<td>Sanath Lamabadusuriya</td>
<td>2010</td>
<td>2012</td>
</tr>
<tr>
<td>Jules Millogo</td>
<td>2010</td>
<td>resigned</td>
</tr>
<tr>
<td>Pieter Neels</td>
<td>2010</td>
<td>2011</td>
</tr>
<tr>
<td>Folake Olayinka</td>
<td>2010</td>
<td>2013</td>
</tr>
<tr>
<td>Jane Soepardi</td>
<td>2010</td>
<td>2012</td>
</tr>
<tr>
<td>Robert Steinglass</td>
<td>2010</td>
<td>2012</td>
</tr>
<tr>
<td>Pierre Van Damme</td>
<td>2010</td>
<td>2012</td>
</tr>
</tbody>
</table>
9 Annex 2: PSPQ Criteria flowchart

Programmatic Suitability for Pre-Qualification Criteria flowchart

This flowchart has to be read in conjunction with the PSPQ document (version 27/10/2010).

CANNOT PROCEED WITH PQ ASSESSMENT

PQ TEAM AND DIRECTOR IVB
Decides to PQ or not

Adminstration

Injectable

Volume of paediatric dose < 1 ml?

PSPQ STANDING COMMITTEE
Recommend

Oral

Ready to use?
(no reconstitution)

Not PPS or AD

Single dose?

Live-attenuated?

Contains any preservative?

Preserved with regular concentration thiomersal?

Passed test for reduced / alternative preservative?

Two dose per vial?

Antigenic stability >= 28 days after reconstitution?

PROCEED WITH PQ ASSESSMENT

* = visual cue requirement will become operative once WHO policy has been finalized.

DRAFT 27/10/2010
### 10 Annex 3: Distinguishing characteristics of Routine/Supplemental immunization and Doses

<table>
<thead>
<tr>
<th>Routine Immunization/Doses</th>
<th>Supplementary Immunization/Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Purpose</strong></td>
<td>To provide broad scale, synchronized, selected vaccines according to a specific accelerated disease control objective.</td>
</tr>
<tr>
<td>Individual protection to reduce mortality and morbidity from VPD through high coverage with all antigens (90% in all districts).</td>
<td><strong>Goal</strong> Boost population level immunity to reduce/interrupt transmission of selected diseases often with the goal of elimination or eradication.</td>
</tr>
<tr>
<td><strong>Target Groups</strong></td>
<td>Expanded to children of other age groups up to 5-15 yrs generally; WCBA; entire populations in high-risk areas e.g., JE, YF, Mening.</td>
</tr>
<tr>
<td>Continuous and Predictable: Daily, weekly, monthly, quarterly, etc.</td>
<td><strong>Frequency</strong> Intermittent defined by disease epidemiology, and level of susceptibles in population.</td>
</tr>
<tr>
<td>Fixed, outreach, mobile, school-based, campaigns, PIRI.</td>
<td><strong>Service Delivery Strategy</strong> Fixed, outreach, door-to-door, extra posts, mobile, school-based, campaigns.</td>
</tr>
<tr>
<td>Yes, for age and vaccination/AEFI history (obtained from card/caregiver); &quot;Routine&quot; dose is given only if due according to the national schedule and child is of eligible age.</td>
<td><strong>Screening and Decision to Vaccinate</strong> Screen only for age eligibility and previous AEFI. Prior vaccination history is not important. &quot;Supplemental&quot; dose is given to all of eligible age irrespective of vaccination history.</td>
</tr>
<tr>
<td>Child Health/Immunization Card, Tally sheet, health facility register, monthly summary.</td>
<td><strong>Recording</strong> Tally sheet disaggregated by age (generally not recorded on child health card but if included must be in section marked &quot;Supplemental&quot;). These &quot;additional&quot; or &quot;extra&quot; doses are not counted towards completion of the routine schedule.</td>
</tr>
<tr>
<td>Routine doses would be included in administrative data collection systems, and included in the &quot;Administrative Coverage&quot; section of the WHO/UNICEF JRF.</td>
<td><strong>Reporting</strong> Supplementary doses should not be included in the routine administrative data collection systems, but should be reported separately. They should be included in the section &quot;Supplemental Activities&quot; of the WHO/UNICEF JRF.</td>
</tr>
</tbody>
</table>