Opening and Introduction

Mr Michel Zaffran, Coordinator of WHO’s Expanded Programme on Immunization, officially opened the 8th meeting of IPAC. Dr Shelley Deeks, the Chair, welcomed participants and acknowledged the regrets of Dr Jonathan Colton, Dr Folake Kio-Olayinka, as well as the representative from the Centres of Disease Control, Dr Samir Sodha.

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Session I. Immunization Supply Chain and Logistics (ISCL)

The session began with an introduction by Dr Robin Biellik, the Chair of the Immunization Supply Chain and Logistics (ISCL) working group. Dr Biellik presented the rationale, purpose and structure of the ISCL Working Group. As an outcome of the session, he requested of IPAC the following:

1. Review and endorse in principle the content of the IPAC Call-to-Action on ISCL.
3. Review and endorse the ISCL Key Challenges presentation for the November 2013 SAGE meeting.
4. Consider a coalition of partner agencies that WHO could approach to provide a broader endorsement of the IPAC Call-to-Action on ISCL.

A. Call-to-Action (Robert Steinglass, IPAC member)

Mr Robert Steinglass outlined the mounting challenges faced by national vaccination programmes including but not limited to: a variety of new vaccines and immunization schedules, a diversity of service delivery strategies, a growing target population, and increased cold chain infrastructure requirements. He described the performance of existing ISCL systems by sharing the analysis of Effective Vaccine Management (EVM) scores of 57 countries over the period between 2010 to and 2012, further providing justification for a Call-to-Action on ISCL.
The ISCL Call-to-Action calls upon Ministries of Health to analyze the supply chains and logistics components of their national vaccination programmes, to plan for change, and to implement effective strategies to ensure the efficient and uninterrupted supply of quality vaccines at the right place, at the right time, in the right quantities, and at affordable cost. Further, the document calls upon countries and global partners to increase awareness, identify and resolve knowledge gaps, address ISCL when formulating immunization recommendations, invest in ISCL systems, and harmonize SCL systems in public health service delivery.

C. Key ISCL Challenges (Diana Chang-Blanc and Patrick Lydon, WHO)

Ms Diana Chang Blanc and Mr Patrick Lydon presented a preview of the presentation to the November 2013 SAGE meeting. This presentation is related to the ISCL Call-to-Action in content, will be presented as information-only to SAGE in November, and is a key precursor to the ISCL Call-to-Action presentation to the April 2014 SAGE meeting.

Ms Chang Blanc presented the global challenges facing ISCL systems, such as inadequate investment, limited storage capacity, undesirable characteristics of some new vaccines, inadequate human resources, and increasing complexity in vaccination schedules.

Mr Lydon presented the in-country challenges using a photo story illustrating the field realities of the nine criteria of an EVM assessment. Mr Lydon also presented components of the WHO and UNICEF response to current ISCL challenges, including the work of the Vaccine Product and Packaging Advisory Group (VPPAG), the WHO/UNICEF ISCL Hub, and the EVM strategy to achieve improved service delivery through assessing performance, planning for action, and implementing change.

Discussion:

Members and observers agreed on the timeliness and content of the ISCL Call-to-Action and presentation to SAGE with some modifications. There was consensus concerning the evidence of supply chain challenges and proven innovations, the recommendations presented to the national vaccination programmes and the global community, and the need to heighten global awareness.

Concerning the ISCL Call-to-Action, IPAC members and observers requested the following revisions:

1. Reconfigure the Abstract as an Executive Summary of the Call-to-Action that lists all of the Recommendations. Use this 1-2 page document as the IPAC endorsement. Treat the remaining pages of the document as the background for the Call-to-Action.
2. Add an acronym definition and glossary of terms to the document.
3. Treat harmonization of commodities in ISCL in the context of broader health systems.
4. Align the “Plan for Change” recommendation with the EVM Joint Statement to highlight the importance of implementing change.
5. Improve the outline of the steps countries should undertake concerning their ISCL system improvements.

Members and observers suggested the names of other agencies that could be invited to endorse the Call-to-Action, such as the International Federation of the Red Cross, Medecins Sans Frontieres, and UNICEF. Instead of deciding on expanding the endorsement at this time, it was proposed that the Call-to-Action be presented to SAGE initially with an IPAC endorsement. The GAVI Board could be invited to endorse the Call-to-Action at their meeting in June 2014, and WHO could consider adding a statement regarding the Call-to-Action in the GVAP.

Concerning the SAGE presentation, IPAC requested the following revisions:

1. Define more clearly the purpose and objective of this presentation for SAGE.
2. Reduce the photo essay to one slide per EVM component.
3. Avoid a response that focuses on investing on additional data collection, rather focus on the increased direct investment in supply chains.
4. Highlight the role of IPAC in developing the entire ISCL session presented to SAGE.

Concerning the WHO/UNICEF EVM Joint Statement, IPAC observed the following:

1. The development of human Resources is an important component that needs greater investment in national vaccination programmes, but the analysis of human resource gaps and requirements is difficult to determine through the EVM process.

**Recommendations and Decisions by IPAC**

1. IPAC unanimously endorsed in principle the draft IPAC Call-to-Action for national programmes and the global community, noting that minor changes to the format and structure will be made prior to the SAGE meeting in April 2014.

**Session II. Immunization Management Group**

**Polio Eradication and Endgame Strategy: IPV introduction (Michel Zaffran, WHO)**

Immunization Strengthening and OPV withdrawal (OBJECTIVE 2) is one of four objectives of the Polio Eradication & Endgame Strategic Plan 2013 – 2018. In April 2013, the Immunization Management Group (IMG) was established to manage and coordinate partners’ activities related to objective 2 including: 1) conveying the rationale and urgency across respective agencies, 2) increasing immunization coverage in focus countries, 2) ensuring the availability of appropriate IPV, bOPV, and mOPV products, 3) introducing one dose of IPV in the immunization programme of all countries by 2015, and 4) withdrawing OPV2 from Routine and Supplementary Immunization Activities, by 2016. To manage these activities, the following five cross-agency workgroups were organized: 1) implementation (readiness, supply & demand), 2) regulatory, 3) financing, 4) communications, and 5) routine immunization strengthening. Key areas of work for IPV introduction include identifying priority countries, forecasting IPV demand, assessing country readiness, initiating policy dialogue with countries, implementing a communication plan, and budgeting costs. In addition, technical oversight is being provided for ten focus countries identified for strengthening routine immunization using polio assets.

**Discussion:**

The IPAC chair, members, and observers appreciated the comprehensive update. The following technical queries were raised: 1) why is it recommended to give IPV with the 3rd DPT dose instead of the 1st DPT dose when it could have a greater potential to prevent Vaccine Associated Paralytic Polio; 2) has it been considered to give IPV at the same time as measles vaccination; 3) will providing 3 injections at one visit create problems with health provider or caregiver acceptance; will it create difficulty attributing AEFI – especially regarding local reactions if two injections are given in same limb; and 4) would it be beneficial to extend the target age group to include additional older birth cohorts or administer IPV to children presenting late for vaccination. It was noted that these are preliminary recommendations that have undergone substantial discussion and review of existing evidence. However, they will be considered at the upcoming SAGE meeting and could therefore be further refined. It was also noted that communication is critical at this time. Members were directed to a website that has been launched on the WHO Immunization website ([http://www.who.int/immunization_delivery/adc/inactivated_polio_vaccine/en/](http://www.who.int/immunization_delivery/adc/inactivated_polio_vaccine/en/)) that contains fact sheets and resources. All were invited to provide comments and suggestions for enhancing messages and communicating resources and strategies.
Session III. Global Updates

A. Vaccine Presentation and Packaging (VPPAG): vaccine labelling work
(Drew Meek, WHO)

Dr Meek summarized the key findings of the “Guidelines for the Labelling of Vaccines Proposed amendments to the TRS 822 document & Requirements for Pre-Qualified Products.” This report was commissioned following presentations to IPAC and ECBS in 2011 of the VPPAG proposal entitled “VPPAG Position on Labels for Vaccine Containers.”

The report recommended:

- Improved design features to minimize HCW errors in vaccine delivery;
- Minimum font size of 6pt;
- Expiry date format of MM-YYYY;
- Omission of some information from primary container labels of <10mL, full list of ingredients and quantities, address of manufacturer, and nature and amount of any substance used in the preparation of the biological product that is likely to give rise to an adverse reaction in some recipients;
- Minimum viewing area of contents;
- Generic name should be more prominent than brand name;
- Action to be taken through ECBS on establishment of agreed international abbreviations of generic names; and
- Use of GS1 compliant 2D barcode on secondary container (with GTIN [global trade identification number] batch number and expiry date).

The overall review process for Technical Review Series is underway and a labeling revision will be included in the process. A review by ECBS is scheduled for 2014. For prequalified vaccines, the PSPQ characteristics will be used to promote TRS 822 overall.

B. Update on changes to visual cue strategy (Michel Zaffran, WHO)

Mr Zaffran explained the rationale behind the decision made by WHO in June 2013 to cease further investment in the visual cue for multi-dose vaccine vials. He cited the following combined factors that lead to the final conclusion:

- Difficulty with implementing the field pilot of the visual cue;
- Momentum to launch, execute, and train on visual cue would be extended over years, with high barriers to implementation;
- Uncertain benefit of the visual cue to address the problem; and
- Limited financial resources and capacity of EPI staff to dedicate attention to this intense initiative given competing priorities.

Mr Zaffran reinforced strongly the point that the decision was not a questioning of IPAC’s recommendations to date or of the value of their expertise, but an internal agency choice to re-assess its investment and cut losses. IPAC acknowledged the justification for WHO to curtail further investment but also urged WHO to continue to seek alternative solutions to the problem, as it continues to be an ongoing issue. Certain members expressed the frustration of having invested significant time to address an issue through evidence review, with a final decision being based largely on internal factors. Because the development and review process was lengthy, IPAC reflected whether deliberations over the visual cue, with closer monitoring, might have been stopped sooner. All agreed that lessons could be learned from the process and supported the idea of a future evaluation of IPAC’s functioning.

The agreed solution to use the placement location of the vaccine vial monitors (VVMs) as visual triggers for the 6 hour or 28 day categorization will be reflected in the revised multi-dose vial policy.
Session IV. Vaccine Wastage Modeling

A. Vaccine Wastage: Session Overview (Diana Chang Blanc, WHO)

Ms Chang Blanc explained that estimates of vaccine wastage (combined open and closed vial) vary dramatically across countries for the same vaccine and presentation and across years within the same country. In the absence of reliable data, countries are encouraged to use the WHO indicative wastage rates when forecasting their vaccine needs. WHO provides indicative values for closed vial wastage for each level of the national supply chain, and for opened vial wastage for different vial sizes and multi-dose vial policies (discard after session or after 28 days). The indicative opened vial wastage values include all sources of opened vial wastage, both the avoidable programmatic wastage and the “unavoidable” wastage due to the discard of unfinished opened vials. These indicative wastage rates, closed and opened, represent best-guesses of typical wastage rates across all countries. It is understood that in certain contexts the indicative opened vial wastage rates may be far from the actual values; for some countries the indicative rate may be higher than the actual, whereas for others it may be lower. The purpose of this session was to:

- Share with IPAC work-to-date on methodology on how to estimate opened vial wastage;
- Demonstrate through country examples that session sizes are governed by binomial statistics which allows expected opened vial wastage rate to be determined from the mean session size; and
- Get feedback from IPAC on how this knowledge can be converted to practical field application.

B. Opened Vial Wastage: From Indicative to Expected (Paul Colrain, WHO consultant)

Mr Paul Colrain presented the results of a study of immunization session size distributions and the associated unavoidable opened vial wastage rates. The hypothesis that session size distributions are governed by binomial statistics, and consequently that the expected session size distribution is determined purely by the expected mean session size, was tested using session size distribution data from 272 immunization locations, fixed and outreach, in four different countries (Bangladesh, Ethiopia, Cambodia, Burkina Faso). The two underlying assumptions are that: a) births are uniformly distributed throughout the calendar year and b) children are immunized according to the national immunization schedule, without day preference.

The hypothesis is validated in the vast majority of the 272 locations. Where the hypothesis does not hold up, it can be shown that this is primarily due to the violation of the underlying assumption that children are immunized according to the immunization schedule without day preference. For instance, in certain locations that hold more than one session per week, a particular session is much more popular than the others, leading to non-binomial session size distributions.

Given that session size distributions are governed by binomial statistics, and that the expected session size distribution is determined by the mean session size, it is therefore possible to determine the expected value of the unavoidable part of the opened vial wastage rate from the mean session size alone. This corollary was tested using the Bangladesh DTP 10-dose and Cambodia DTP-HepB 10-dose session size data (148 and 8 locations respectively, both fixed and outreach) and the associated unavoidable opened vial wastage rate data. The expected opened vial wastage rates, determined from the mean session sizes alone, are within 5% of the actual value for 95% of the 156 locations.

There are three potential implications of session size distributions being governed by Binomial statistics. Firstly, given the expected number of doses to be administered in the next year and the planned number of sessions, one can estimate, with reasonable precision and confidence,
the next year’s expected opened vial wastage rate, allowing for more accurate forecasting of vaccine needs. Secondly, given the number of doses administered last year and the number of sessions conducted, one can determine a 95% or 99% confidence interval for last year’s expected opened vial wastage rate, allowing vaccine wastage rates to be monitored against their expected values rather than against zero, thus reducing undue pressure to reduce wastage below acceptable values. Lastly, the wastage rate implications of session frequency choice and vial size choice are now known, allowing more informed choices of session frequency and vial size, in an attempt to control wastage.

Mr Colrain further demonstrated three pilot tools. The simplest way to package the results of this study is in a look-up table showing the expected opened vial wastage rates as a function of vial size, mean session size, and immunization policy (discard at end of session or after 28 days). If further validated, this tool could be used at national or sub-national levels to better understand the wastage implications of session frequency choice and vial size choice when planning immunization delivery and to monitor facility wastage rates. The second tool presented was a simple Excel tool which calculates the expected opened vial wastage for a given annual birth rate, session frequency and vial size, which also showed how the calculation is made. This tool could be used for educational purposes. Lastly, Mr Colrain presented a tool for estimating the national level opened vial wastage rate, based on the annual birth rates and session frequencies of all immunization locations, or estimates thereof. The tool may also be used, for example, to investigate the implications of different session frequency policies on the national opened vial wastage rate.

Ms Chang Blanc closed the session by describing how the different components of vaccine wastage (closed vial, avoidable opened vial, and unavoidable opened vial wastage) may be combined to give the overall national wastage rate. WHO has provided indicative values for the closed vial wastage at each level of the supply chain; for multi-dose vials, the opened vial wastage rate is primarily dominated by the proportion due to the discard of unfinished vials. With the results presented in this session, it now may be possible to more adequately calculate unavoidable opened vial wastage rate for each facility and to aggregate this to national level, in combination with the two smaller components which would remain indicative estimates.

IPAC Discussion

The IPAC chair, members, and observers were appreciative of the stimulating presentation, enthusiastic about the possible implications, and commended WHO on its innovative work.

There was a lively discussion about the validity of the underlying assumptions, that births are uniformly distributed throughout the year, and that children are immunized according to the national schedule. Mr Colrain reiterated that if either assumption is violated, the session size distributions would not be well described by the expected binomial distributions, and that for the vast majority of immunization locations for which data are available, the session size distributions are well described – the empirical data validates these assumptions. However, meeting participants were in agreement that additional session size data should be collected from other countries and analyzed to further validate the model. It was emphasized that programme data from the peripheral levels to fully validate the approach is not easily available and would continue to be sought after by WHO.

An observation was made that in order to determine mean session sizes, a country may need to review previous consumption in terms of absolute number of doses administered, which may be more reliable than birth cohort estimates and coverage data in certain countries.

WHO clarified that any tools developed to facilitate vaccine forecasting based on the knowledge that session size distributions are governed by binomial statistics would be adapted to the level of the system at which they were used, both in terms of objective and functional complexity.

Members and observers advised caution in deciding how to communicate any message or guidance on how to use this information, and that countries should be encouraged to continue to collect and analyze wastage data for routine monitoring.
Recommendations and Decisions by IPAC

2. IPAC commended WHO on this useful initiative, and recommended that WHO continue to seek more country level data to test the validity of the underlying assumptions. IPAC looks forward to next steps.

Session V. Programmatic Suitability of Prequalified vaccines

A. Update on Programmatic Suitability of Vaccine Candidates for WHO Prequalification (PSPQ): Update on implementation of PSPQ process (Robin Biellik, IPAC member)

Dr Biellik presented on the activities of the PSPQ Steering Committee since its establishment in September 2011. He described the evaluation process of the Steering Committee. Nine products with deviations have been reviewed to date with opinions submitted to the PSPQ Secretariat:

- 4 pre-qualified multi-dose unpreserved products (1 liquid, 3 lyophilized/non-live);
- 1 pre-qualified single-dose product with poor thermostability and no VVM;
- 1 new single-dose product in pre-filled, non-AD syringe;
- 2 new two-dose unpreserved products; and
- 1 new single-dose liquid unpreserved product for which prequalification was requested for fractionated (multi-dose) delivery.

Five of these nine products are previously prequalified products (all vaccines pre-qualified before the establishment of PSPQ are scheduled to review).

Recommendations by the PSPQ Steering Committee to the WHO PSPQ Secretariat to improve processes of and deliberations included: a) providing timely and complete background information to facilitate review; b) revising PSPQ guidelines to take 2-dose unpreserved liquid/non-live products off the critical list, on condition that manufacturers apply a VVM and that national programmes provide extra training on discard in <6 hours and AEFIs monitoring; c) providing information on the 28-day multi-challenge test for preserved vaccines, with a view to reviewing non-thiomersal preservatives; d) expanding criteria by which products indicated for non-pediatric populations may be considered compatible with existing vaccination schedules; and d) conducting Steering Committee meetings once annually.

B. Revision of Programmatic Suitability of Vaccine Candidates for WHO Prequalification (PSPQ) characteristics, procedure and document (Rudi Eggers, WHO)

Dr Eggers outlined the planned procedure of the revision of the standing PSPQ document (WHO/IVB/12.10) including the characteristics and the process. At the initiation of the PSPQ guidelines in 2012, it was intended to schedule a review of the process after two years of implementation. During the upcoming revision, some existing characteristics will be reviewed, including the multi-dose inadequately preserved liquid vaccines, scheduling characteristics for older children, further information on the 28 day multi-challenge test for PSPQ SC guidance, and the exclusion of the visual cue requirement. Potential new characteristics may include vaccines which indicate that a half dose (0.25 ml) can be given to younger children, fractional dose characteristics and the review of liquid products that are not live attenuated vaccines. Changes in the procedure of the PSPQ and in the Standing Committee’s composition and size will also be considered. It is anticipated that the revised PSPQ document will be presented to IPAC in a teleconference in April 2014, and a finalized document in the next face to face IPAC meeting for endorsement.
Closing

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

In closing, Mr Zaffran presented Dr Deeks with a certificate of appreciation to acknowledge her excellent stewardship as Chairperson of IPAC since April 2010. WHO, and specifically the Department of Immunization, Vaccines and Biologicals, greatly benefitted from Dr Deek’s committed leadership and expertise. Dr Deeks will continue to serve as IPAC member until November 2015. Mr Zaffran welcomed Dr Chris Morgan as the incoming chair of IPAC, effective December 2013.

The next IPAC meeting will be held 11-13 June 2014.