



**WORLD HEALTH ORGANIZATION  
IMMUNIZATIONS, VACCINES AND BIOLOGICALS**

**IMMUNIZATION PRACTICES ADVISORY COMMITTEE  
(IPAC)**

**14-15 October 2015**

**Final meeting report and recommendations**

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## **Opening and Introduction**

Ms Diana Chang Blanc, Programme Operations Manager in the Expanded Programme of Immunization (EPI), under the Department of Immunization, Vaccines and Biologicals (IVB) officially opened the meeting on behalf of Dr Jean-Marie Okwo-Bele, Director of IVB. This represents the first formal meeting of the Immunization Practices Advisory Committee (IPAC) since a novel operating modality was adopted in November 2014 as part of a new grant from the Bill and Melinda Gates Foundation. This new modality involves less frequent face-to-face meetings and a more virtual approach to Committee dynamics, including an online discussion and document-sharing forum, quarterly bulletins, teleconferences, and IPAC representation on relevant working groups. Ms Chang Blanc welcomed the three members who have joined IPAC since the June 2014 meeting: Dr Adelaide Shearley, Dr Craig Burgess, and Dr Brad Gessner, as well as new CDC Observer, Dr Laura Conklin.

### **IPAC Members present:**

Chris Morgan (Chair)  
K.O. Antwi-Agyei  
Robin Biellik  
Craig Burgess  
Shelley Deeks  
Francois Gasse  
Brad Gessner  
Jean Marc Olivé  
Adelaide Shearley  
Robert Steinglass  
Carla Vizzotti

IPAC continues to be active and productive, as demonstrated by the selected activities and outputs presented by the Chair, Dr Chris Morgan, during his introduction, including:

- IPAC advocacy on Supply Chain and Logistics from 2013, with finalised Call to Action published in October 2014;
- The review of grandfathered vaccines completed for Programmatic Suitability for Pre-Qualification (PSPQ);
- The selection and integration of six new members; and
- Input to: WHO Policy Statement: Multi-Dose Vial Policy (MDVP), WHO Guidance Note: Vaccine Diluents, Tetanus and Voluntary Medical Male Circumcision report, a vaccine wastage study protocol, the Global Immunization Routine Immunization Strategies and Practices (GRISP), Programmatic Options for Implementation of

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Malaria RTS,S Vaccination Schedule for Infants, and a Strategy and Guide on Enhanced Cascade trainings.

Dr Morgan welcomed participants, expressed the regrets of Dr Jon Colton, IPAC member, and of IPAC observers Ms Debbie Kristensen, on behalf of PATH, and Dr Mary Allin, on behalf of the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA). He announced the recent appointment of a further three new IPAC members: Mr David Brown, Dr Ian Gemmill, and Dr Amani Mustafa. It was with regret that the group had to bid farewell to Mr Robert Steinglass and Dr Shelley Deeks who will reach the end of their second terms on IPAC at the end of November 2015. It was also acknowledged that Dr Robin Biellik and Dr Jon Colton will be reaching the end of their second terms in June 2016, which could be prior to a subsequent meeting of IPAC.

## **Session I. Global Updates**

### **A. Report back from SAGE** (*Chris Morgan, IPAC Chair*)

Dr Morgan reported back on the April 2015 SAGE meeting, noting the high proportion of topics considered that were directly related to programmatic issues. These included: evidence on multiple vaccinations at a single session and pain mitigation in immunization, both of which have resulted in new evidence collations and guidance documents. There were also clear programmatic implications from other SAGE discussions, including: the need to broaden the work on Ebola vaccines to general emergency responses that include vaccines; the strategy for middle-income countries; a review of evidence for maternal vaccination during pregnancy; and the acceleration of polio eradication. The review of evidence on pertussis schedules reaffirmed pertussis immunogenicity as a prime driver of standard vaccine schedules in the first year of life. IPAC members' attention was drawn to the use of a 'Good Practice Statement' on multiple injections as an approach to evidence review, a strategy that is likely to apply to the consolidation and use of evidence for other service delivery topics. The April SAGE meeting was also notable for the increased discussion of the potential of implementation science to study programmatic innovation. IPAC members were encouraged to review the April SAGE meeting report published in the Weekly Epidemiological Record.

Members were also alerted to the agenda for the October SAGE meeting immediately after IPAC, noting this would be dominated by polio, Ebola and malaria vaccine considerations, as well as discussion of the current status of global measles and rubella control and regional elimination. Measles and rubella elimination is closely aligned with the need for stronger routine immunization platforms and it was noted that SAGE would discuss plans for a Midterm Review of the Measles and Rubella Strategic plan, including how existing data could be used to better determine optimum target age ranges for measles and measles-rubella Supplementary Immunization Activities.

**B. Programmatic Suitability of Vaccine Candidates for WHO Prequalification (PSPQ): Update from the Standing Committee on PSPQ** (Dr. Robin Biellik, IPAC Member)

Dr Biellik summarized the objectives and operating procedures of the PSPQ Standing Committee (SC)<sup>1</sup>. For the benefit of new members, he also explained that operational characteristics of vaccines submitted to WHO for pre-qualification (PQ) are reviewed for compliance with the PSPQ mandatory and/or critical characteristics in order to generate a recommendation to the WHO PQ Secretariat on whether PQ should proceed or not, clarifying that the final decision on each application rests with the PQ Secretariat.

Since the last IPAC meeting in June 2014, the SC reviewed six products which were pre-qualified before PSPQ was introduced but which are out of compliance with one or more PSPQ criteria. The assessments covered two oral cholera vaccines, two Hib vaccines, one seasonal influenza vaccine and one oral rotavirus vaccine.

The first oral cholera vaccine failed a critical characteristic because its recommended schedule is at variance with standard WHO recommended schedules. However, the SC recommended that PQ status be maintained on the grounds that keeping this vaccine prequalified will help to meet worldwide demand for oral cholera vaccines by 2017.

The second oral cholera vaccine failed three critical characteristics: the absence of stability data to permit attachment of a vaccine vial monitor (VVM), the vaccine is not ready-to-use and requires non-standard administration, and the recommended schedule is at variance with standard WHO schedules. However, the SC recommended that PQ status be maintained on the grounds that keeping this vaccine prequalified will help to meet worldwide demand for oral cholera vaccines by 2017, but on condition that the manufacturer provide stability data and attach VVMs, and provide adequate health worker training on non-standard administration.

Both multi-dose Hib products failed a mandatory characteristic because they lack preservative. The SC recommended that PQ status for both products be withdrawn on the grounds that alternate products are available, the products have not been procured by UNICEF since 2012, the use of monovalent Hib vaccines where multivalent alternatives are available is not encouraged by WHO, and safety concerns are associated with use of unpreserved multi-dose vaccines.

The multi-dose seasonal influenza vaccine failed a mandatory characteristic because it is at variance with the WHO recommendation related to preservative efficacy. The SC recommended that PQ status be withdrawn, but the PQ Secretariat overruled the recommendation after the manufacturer subsequently provided data demonstrating that the concentration of preservative complies with the European Union pharmacopoeia preservative efficacy test.

The oral rotavirus product failed a critical characteristic because it is not ready-to-use and requires non-standard reconstitution. Also, the presentation has an unusually large per-dose volume. The SC recommended that PQ status be withdrawn on the grounds that the product is not ready-to-use, it requires unusually large cold chain capacity, and reconstitution requires additional health worker training. Countries have demonstrated a strong preference for alternative all-liquid products that are currently available.

<sup>1</sup> As per the 2014 Revision of *Assessing the programmatic suitability of vaccine candidates for WHO prequalification* (WHO publication WHO/IVB/14.10) available at: [http://apps.who.int/iris/bitstream/10665/148168/1/WHO\\_IVB\\_14.10\\_eng.pdf?ua=1](http://apps.who.int/iris/bitstream/10665/148168/1/WHO_IVB_14.10_eng.pdf?ua=1)

## Discussion:

IPAC members asked for clarification regarding situations where the PQ Secretariat chooses not to accept a PSPQ SC recommendation, and also questioned whether the PSPQ critical characteristic regarding standard vaccination schedules will eventually need to be reviewed as more new products enter the market with significantly different recommended schedules. Finally, IPAC members expressed concurrence with these six SC recommendations.

### C. Vaccine Packaging and Presentation Advisory Group (*Anna-Lea Kahn, WHO*)

In the absence of Ms Debbie Kristensen, IPAC Observer on behalf of PATH and Chair of the Vaccine Packaging and Presentation Advisory Group (VPPAG), Ms Kahn, who also serves as WHO Representative to VPPAG, provided an update on developments within the VPPAG since the last IPAC meeting, noting that its governance and operating structure had undergone revisions following a face-to-face meeting of the group in October 2014<sup>2</sup> and its membership expanded to include Médecins Sans Frontières (MSF) and additional members representing the Developing Country Vaccine Manufacturers Network (DCVMN).

The four main mechanisms by which VPPAG is active consist of:

1. Topic specific-working groups to generate and review evidence, as well as advance consensus recommendations;
2. Generating generic preferred product profile recommendations for vaccines, the latest version of which were recently updated and posted online;
3. Responding to industry requests for guidance on specific product presentation issues; and
4. Serving as a standing subcommittee of the WHO IPAC.

Among the key aspects of recent modifications to VPPAG is the expansion of its mandate to include consideration of new vaccine delivery technology, which allowed for the successful establishment of a new working group dedicated to this subject. This working group, chaired jointly by Dr Birgitte Giersing of WHO/IVB and Mr Darin Zehrung of PATH, as well as the newly established Packaging working group, chaired by Mr Denis Maire of WHO/EMP, have benefited from VPPAG's broad private sector engagement to develop a well-balanced membership reflecting varied representation and expertise. IPAC members were encouraged to participate in either. A third working group under VPPAG, dedicated to Barcoding, has been working on facilitating adoption by vaccine manufacturers of GS1 standard barcodes on secondary and tertiary vaccine packaging.

### D. Global Routine Immunization Strategies and Practices (*Diana Chang Blanc, WHO*)

Ms Chang Blanc presented on the Global Routine Immunization Strategies and Practices (GRISP) framework, which is soon to be launched by WHO. This document serves as a companion to the Global Vaccine Action Plan 2011-2020 (GVAP) and outlines the specific strategies and activities required to strengthen routine immunization systems and to expand immunization coverage in order to achieve the Decade of Vaccine's (DoV) vision.

<sup>2</sup> The revised VPPAG terms of reference are available online at:  
[http://www.who.int/immunization/policy/committees/VPPAG\\_terms\\_of\\_reference.pdf?ua=1](http://www.who.int/immunization/policy/committees/VPPAG_terms_of_reference.pdf?ua=1)

The GRISP is not a plan, but a comprehensive framework that interprets overall GVAP direction into concrete actions to strengthen routine immunization, highlighting nine transformative areas in which national governments, global partners, and donors should invest for sustained improvements. The document clearly differentiates between the long-term approach of strengthening immunization systems and short-range activities that can boost coverage, both of which are important improving coverage outcomes.

The nine transformative areas identified in GRISP are:

1. A capable national team with sufficient resources and authority to expertly manage each country's national immunization programme.
2. Tailored strategies that identify and reach under-vaccinated and unvaccinated persons.
3. A coherent planning cycle, with strategic, comprehensive, multi-year and operational annual plans outlining and coordinating strategies and activities, which are monitored quarterly.
4. Sufficient and adequately appropriated funds reaching the operational level of the programme regularly.
5. Vaccinators' and district managers' capacity regularly and systematically built, strengthening their performance and providing supportive supervision.
6. Modernized vaccine supply chains and management to ensure that the correct amounts of the right potent vaccines are available at each vaccination session.
7. An information system that identifies and tracks each person's vaccination status.
8. Sustainably expanded routine vaccination schedules to cover people's entire lives.
9. Responsibility for immunization delivery shared between communities and the immunization programme to reach uniformly high coverage through high demand and quality services.

Underlying strategies to support these key investment areas include Maximizing reach, Managing the program, Mobilizing people, and Monitoring progress. The document is currently under finalisation for translation and publication.

### **Discussion:**

IPAC members expressed satisfaction with WHO for its recognition of the urgency for such an advocacy piece, as well as for the actual structure and content. The document was recognised for its comprehensiveness and the conceptual thinking behind it. It was agreed that GRISP's linkages with DoV and GVAP must be clarified, as members emphasised the critical importance of building up political buy-in and finding strategic opportunities to help the global community and countries translate the priorities into action.

### **Session II – Immunization Management Group: IPV introduction and tOPV-bOPV switch**

Dr Olivé provided background on the Immunization Management Group (IMG) and its role in coordinating the work under Objective 2 of *Polio Strategic Plan, 2013-18*. He noted that the World Health Assembly endorsed the tOPV-bOPV switch in May 2015 and that SAGE would be making key decisions on 20 October 2015 to reaffirm OPV2

withdrawal dates in April 2016 (17 April to 1 May), after assessment of progress in eliminating all persistent cVDPV2 and overall preparedness for OPV2 withdrawal.

**A. IPV introduction and progress on Objective 2 of the Polio Eradication and Endgame strategic plan** (*Alejandro Ramirez Gonzalez, WHO*)

Mr Alejandro Ramirez Gonzalez provided an update on the programmatic preparedness for conducting the 'switch' from tOPV to bOPV in April 2016. He outlined the readiness criteria for the switch (IPV introduction, bOPV licensing for routine immunization use, monovalent OPV2 stockpile, containment, eradication of wild poliovirus type 2) and the critical aspect of the progress in stopping persistent cVDPV2.

In general, there has been significant progress in all areas and the recent Certification of Global Eradication of Wild Poliovirus type 2 and the removal of Nigeria from the endemic countries list was highlighted as a key milestone.

One area that remains challenging is the IPV introduction in all countries by the original timeline. Due to global supply constraints, some low-risk countries will have to introduce after the switch has taken place in April 2016. WHO and UNICEF continue to monitor the situation closely, as the global supply scenario is fluid.

Regarding the cessation of the persistent cVDPV2 outbreaks, the programme has successfully stopped the 2 existing strains in Nigeria and Pakistan. In the last 6 months, there have only been 2 cases of cVDPV2 (non-persistent), in Guinea and Nigeria. This also supports 2016 timing as ideal momentum to proceed with the switch.

**B. Monitoring framework for the tOPV-bOPV switch** (*Diana Chang Blanc, WHO*)

Ms Chang Blanc presented the framework that has been developed by the implementation sub-group in order to monitor the withdrawal of tOPV from the field at the time of the switch.

The switch from tOPV to bOPV will be globally synchronized in 2 weeks in April 2016 in order to minimize the risk associated with the withdrawal, as countries with continued use of tOPV might pose a risk to other countries. Therefore, the objective of the monitoring is to ensure that tOPV is no longer administered after the switch takes place in a given country. The disposal of the tOPV is not an obligatory part of the switch monitoring, although countries are encouraged to conduct disposal-monitoring if feasible and in accordance with their national priorities.

The strategy proposes that starting on the national switch day, independent monitors – staff not directly involved in the implementation of the switch- will visit storage and delivery points in the country. From national to district level, it is recommended that 100% of these locations be visited and 10% of health centers in each district should be purposively selected (non-random selection based on higher risk factors such as population size – more vaccine kept-, low routine performance or other issues identified the national programme). If tOPV is found in any of the health centers, then an additional 5% of centers should be selected and visited. A full district monitor will be recommended if tOPV vials are still found in any of the additional 5% of health centers.

The reporting mechanism should be designed in such a manner as to allow information to flow from districts to higher levels, with the respective national government in charge of the final report that has to be submitted to the WHO country office.

Ms Chang Blanc also provided information on the GPEI funds that will be made available to partially support targeted low and low-middle income countries in the preparation, implementation and validation of the switch.

### **Discussion:**

IPAC unanimously emphasised the critical importance of having a good communication strategy in place to ensure a successful switch process and called for a greater effort in this area. This communication strategy should assure that messages and proper information reach all levels, including the health worker staff. Care givers and the community in general should have a correct understanding of the switch. Messages should be constructed to emphasize the benefits of the switch, and communications should be presented in a positive manner and through carefully selected channels in order not to jeopardize the broader immunization programme.

Other areas for which IPAC members expressed concern were the importance of country intelligence on stock levels of tOPV and bOPV, as well as proper disposal of unused vaccines after the switch. WHO reassured that current levels of stocks are being monitored by WHO or UNICEF in most of the countries that are preparing for the switch. Countries procuring through UNICEF or the revolving fund (PAHO) are being monitored as forecasting orders are being placed for 2016. Other countries that self-procure are also being monitored by a working group from UNICEF and WHO that is working closely with these countries in planning for the switch. With respect to disposal of tOPV, the current switch guidelines advise countries to dispose of excess quantities of tOPV according to national guidelines on waste management; in the absence of such policy, the switch guidelines provide options based on best practice determined by the International Solid Waste Association, an advisory body to WHO's healthcare waste department.

## **Session III - Routine Immunization Strengthening**

Dr Morgan introduced the session's purpose:

1. Provide feedback on a reference guide on data collection, use, and assessment that is being drafted by WHO;
2. Review and endorse recommendations made by multiple global, regional and country-level stakeholders during a workgroup session at the Global Immunization Meeting (GIM) in June 2015 on aligning country immunization assessments;
3. Receive information on, and provide input to plans and activities related to strengthening 2nd year of life (2YL) platforms for vaccination and child health visits.

### **A. Collecting, assessing, and using immunization data** *(Jan Grevendonk, WHO)*

Mr Jan Grevendonk presented on the progress made thus far on draft guidance on collecting, assessing, and using immunization data. This guidance document aims to strengthen national level capacity to improve immunization data quality and systems,

and will become available in the first half of 2016. Mr Grevendonk emphasized the objectives and rationale behind the guidance on data collection, use and assessment, and sought feedback on the current structure and high level content of the document.

### **Discussion:**

Overall, IPAC members confirmed the usefulness of this guidance and provided inputs on improving the draft across the three areas of data collection, use and assessment.

Regarding data collection, IPAC members suggested that the guidance take account of the current heavy burden of data collection requirements on staff especially at the health facility level, and the additional training, skills and equipment needed. Decisions on which data to collect should balance the burden on staff and the potential value of those data. It was noted that the design and use of immunization registers merit more detailed discussion. IPAC members noted that the topic of surveillance was missing and should be included.

Regarding data assessments, it was recommended that the guidance not only present common problems identified in assessments but also potential solutions to address them. Periodic data review meetings constitute an important approach for data assessment, training, correcting problems, sharing solutions. Suggestions were made on how the document could better explain different approaches to routine monitoring, surveys and assessments.

Regarding data use, several IPAC members emphasized the importance of instituting systematic feedback mechanisms to influence practices and behaviour. The guidance should go beyond the idea of creating data dashboards, as they may be underused. Data may be presented in modular fashion in order to match data to the levels where they are needed.

IPAC members commended the use of the WHO Health Systems framework but also encouraged the Secretariat to address missing components: efficiency and community engagement. The methods should be tailored to regions and be sensitive to country-specific contexts. Going forward, the level of acceptance that the guidance enjoys will depend to a large extent on its usefulness and user-friendliness to the target audience. Finally, dissemination should include academic and vocational institutions (including pre-service training), to ensure that the guidance is incorporated into academic and vocational curricula in order to rapidly reinforce good practice.

Additional detailed inputs were provided off-line through members' comments on the document.

### **B. Aligning country immunization programme assessments** (*Carsten Mantel, WHO*)

Dr Carsten Mantel presented the dilemma that an increasing number of countries are facing in terms of the burden of assessments. Specifically, the number of country assessments of immunization programs has increased considerably in the past few years. It is estimated that a national immunization programme could be engaged in assessments during 40% - 70% of the working year if all assessments recommended by global level were implemented.



## Discussion:

IPAC members recognised the significance of the outcome of discussions on programme assessments at the GIM 2015 and highlighted the broader context of increasing volume and complexity of immunization programme assessments that are often insufficiently harmonised in timing or resource requirements. IPAC agreed that EPI reviews should be an immunization programme's core assessment to which other assessments should be integrated or supplanted. While IPAC agreed in principle that countries should strive for a "moratorium" of assessments between comprehensive EPI reviews, the duration of this depended on the quality of those assessments. Members were keen to retain broad acknowledgement of the value of good quality monitoring data.

IPAC recognised the increasing quantity and magnitude of assessments being imposed on countries. Several members noted that countries may need to recruit additional EPI staff with skills appropriate to programme monitoring and assessment, rather than expecting programme managers to automatically assume this responsibility. It was noted that if specialized staff are dedicated to monitoring and assessments, it would be important that programme managers and decision-makers are fully engaged in the process.

## Recommendations and Decisions by IPAC

IPAC endorses WHO's efforts to harmonize and streamline programmatic assessments, including work to:

1. Integrate assessments aiming for a core set of three discrete immunization programme assessments: comprehensive EPI Reviews, Effective Vaccine Management Assessments and Data Quality Reviews;
2. Reinforce the recommended timing of comprehensive EPI reviews as every three to five years to coordinate assessments so as to best contribute to broader sector-wide country planning cycles and decrease duplication;
3. Ensure that all programme assessment outcomes inform cMYP development and implementation;
4. Establish a country-specific moratorium on further assessments shortly after a good quality comprehensive EPI review, recognizing that in some cases it may be essential to conduct an assessment if a new initiative or situational change requires it;
5. Revisit the recommendations to routinely conduct PIEs after every new vaccine introduction, with PIEs to be made optional unless the new vaccine necessitates a significant change to current practice (e.g. HPV or measles 2nd dose) or existing data quality is poor.

## C. Plans and progress for strengthening second year of life (2YL) platforms (Karen Hennessey, WHO and Laura Conklin, CDC)

Dr Karen Hennessey described the intent of WHO to conduct the following activities relating to a platform for reaching children in the 2YL over the next three years: conduct a global landscape analysis in conjunction with UNICEF; support two country demonstration projects in countries that had already established a 2YL platform; draft global guidance using information gathered from landscape analysis and country projects; and support four countries to use and provide feedback on the guidance. Dr

Hennessey emphasized that while immunization may be the driver to establish 2YL child health visits, this work is expressly meant to provide a platform for the delivery of other non-immunization preventive health interventions. The plan to seek input from IPAC in the future on draft guidance was presented.

Dr Conklin complemented Dr Hennessey's presentation by describing similar country demonstration projects (Ghana, Malawi) being undertaken by CDC that could also inform such global guidance.

### **Discussion:**

IPAC members expressed interest in the 2YL portfolio of activities and highlighted the importance of this work in helping increase coverage and reach under-vaccinated children. The Committee expressed that 2YL work should be linked with on-going immunization strengthening efforts such as to vaccinate throughout the life cycle, to decrease missed opportunities to vaccinate (including a new project to reach siblings accompanying a child scheduled for vaccination), and to integrate immunization for varied diseases with other health interventions, such as those promoting child growth and development.

Regarding the potential for a 2YL platform to support interventions beyond vaccination, it was noted that valuable lessons may come from Ghana since the country has had a long-standing platform in place for growth monitoring covering children up to five years of age. Vitamin A supplementation was also mentioned as an intervention often recommended during 2YL but not well monitored; IPAC members remarked that strengthening 2YL platforms could support both Vitamin A distribution and monitoring.

Members cautioned that providing an opportunity for late vaccination in 2YL should not encourage late vaccination. IPAC stated that it would be valuable for the demonstration projects to include a measure of costing and efficiency in terms of time savings for the provider and caregiver where services are integrated. The experience gained from conducting a literature review for hepatitis B birth dose vaccination (i.e., searching for publications related to vaccination outside a traditional age range) can be of value for the literature review planned as part of the global landscape analysis.

The Committee is not only interested in providing feedback on draft guidance but also requested to receive progress updates of activities.

### **Session IV. Estimating National Vaccine Wastage**

Dr Shelley Deeks introduced the session, reminding IPAC that the Committee was previously presented with country-specific data which illustrated that opened vial wastage rates can be accurately estimated using the mathematical logic that session size distributions are governed by binomial statistics (see October 2013 meeting report). IPAC had been appreciative and enthusiastic about the work and its possible implications, and requested further follow-up steps. The objective of this session was to present the additional sensitivity analysis on two underlying assumptions, and to seek IPAC endorsement on the underlying logic and methodology for estimating national vaccine wastage rates.

In the absence of reliable national data systems, countries use the WHO indicative vaccine wastage rates to forecast annual vaccine needs. WHO seeks to use a new methodology to replace the existing WHO indicative wastage rate tables with better tuned country specific estimates.

#### **A. Vaccine Wastage Modelling: Recap and Sensitivity Analysis** *(Paul Colrain, WHO)*

Mr Paul Colrain recapitulated the session size model presented to IPAC in 2013, where data from 272 locations in four countries (Bangladesh, Burkina Faso, Cambodia, and Ethiopia) demonstrates that expected session size distributions are governed by binomial statistics. As a consequence, the expected wastage rate for opened vials can be calculated using the mean session size (number of doses administered per timeframe divided by the number of sessions per timeframe), vial size, and application of multi-dose vial policy time limitations.

The new vaccine wastage model for estimating opened vials wastage based on binomial distribution of session size incorporates two core assumptions: a) births are uniformly randomly distributed throughout the year and b) children are immunized according to the immunization schedule, without day preference. Mr Colrain demonstrated that the vaccine wastage model remains robust even when these two assumptions are significantly violated. Firstly, modelling a birth rate variation of 40% amplitude (based on literature, typical variation amplitude ranges from 10% to 30%), the distortion between the expected binomial curve and revised curve is quite minimal for all vial sizes (less than 3%), except for the 20 dose vial for which the difference peaks at approximately 5% for mean session sizes close to the vial size (20 doses). Secondly, while modelling one immunization session as four times more popular than another immunization session (e.g. Friday session preferred to Monday session) generates some distortion between the expected and revised binomial curves, this is still relatively small. In this latter case, the discrepancy between the curves is most evident for 10-dose and 20-dose vials when the mean session size is close to the vial size and vials have a 6 hour discard time limit, but does not in general exceed a 10% difference. Where a 28-day discard is applied, the expected and the revised curves for both sensitivity analyses are in close alignment.

The robustness of the model despite violations of these assumptions follows logically from the generally smooth, downward sloping, convex shape of the curves of wastage rate (y) versus mean session size (x). Where the curves deviate significantly from this shape the model is expected to be less accurate. It is noteworthy that the curves generally follow this shape, except for the 20 dose vial (and to a lesser extent the 10 dose vial) for mean session sizes close to the vial size, and it is for this reason the model estimates are slightly offset from the actual values when there is a significant day preference.

In conclusion, it can be demonstrated that the vaccine wastage model is robust to violations of the two core assumptions.

There are a range of potential uses for this model, such as improved estimation of procurement or distribution volumes for multi-dose vials, better understanding of the effect of altering immunization session frequency, the impact of vial size choices, less pressure on vaccinators to reduce wastage below reasonable norms, and more accurate

wastage monitoring tools. Outputs could include simple look-up tables or opened vial wastage estimation tools.

## **B. Estimating National Vaccine Wastage Rates** (*Paul Colrain, WHO*)

Mr Colrain then presented on one application of the new vaccine wastage model: the better estimation of national vaccine open vial wastage rates. This is a critical improvement, as miscalculations in vaccine wastage rates can have substantial impact on the vaccine wastage factor used in vaccine forecasting, particularly at higher estimations of vaccine wastage rates.

While WHO encourages countries to record, monitor and review vaccine wastage rates at all levels of the supply chain, systems are absent in many countries to be able to do this effectively. Furthermore changes in the programme – such as introduction of a new vaccine or change in vial size – make it difficult for countries to project what the national wastage rate could be.

In situations where reliable empirical data is lacking, WHO proposes that the national wastage rate be estimated as a function of closed vial wastage rate and opened vial wastage rate (both “unavoidable” and “avoidable”):

*Where:*

- Closed vial wastage rate  $(1-w_c)^n$  is set by the WHO-UNICEF Effective Vaccine Management strategy to 1% per storage level, where  $n$ = number of storage levels;
- Unavoidable opened vial wastage rate  $(1-w_{UO})$  is estimated using the Binomial model and country specific program data;
- Avoidable opened vial wastage rate  $(1-w_{AO})$  is set at 5%.

For estimating the national unavoidable opened vial wastage rates, two country specific programme estimates are required: the annual number of births; and the nominal number of sessions per week or month, both for fixed sites and outreach strategies. The most accurate estimates would be obtained when these estimates are available for each immunization location, but this is resource-intensive to collect systematically. Alternatively, aggregated data (annual births and nominal session frequencies) could be generated for each district, province or for the country as a whole, with the trade-off being between accuracy and feasibility.

Given the inputs (birth rates and session frequencies) *per location*, the accuracy of the resulting national wastage rate estimates would be limited only by the reliability of the input data. Given aggregate inputs per district, province or nationally, the accuracy of the estimates will also depend on the heterogeneity of birth rates and session frequencies within each district, province or nation. Simulations presented, contrasting disaggregated and aggregated estimates, show that the aggregate estimates do provide reliable estimates of national wastage rates, even in countries with significant heterogeneity.

This revised methodology is proposed to replace the current WHO indicative wastage rate table for vaccine forecasting. Countries with existing systems to calculate vaccine wastage rates using reliable empirical data would not be encouraged to displace their system with this new approach.

## Discussion

IPAC members commended the excellent analytical work conducted to date and expressed enthusiasm for the predictive power of the binomial vaccine wastage model. Members expressed reassurance that even where the core assumptions fail, the model remains robust. The utility of replacing the current WHO indicative vaccine wastage table with this more refined methodology was well-accepted and understood by the Committee.

Discussion about the consequences and implications of the model was lively and centred around the following concepts:

- **Implementation practice** - While national policy may exist, application of policy can be variable due to human behaviour. Health worker reluctance to open multi-dose vials for small session sizes and client-preference for certain immunization days will persist, and is largely unquantifiable. While the model cannot fully account for human behaviour or errors, it does accommodate a margin of buffer in the formula assumptions. It should be noted that the proposed methodology is used to project *planned* forecasted needs, which must remain aspirational and assume the application of stated goals (e.g. attaining 100% coverage).
- **Avoid stock-outs** - Because the model is being used for vaccine forecasting, the bias must be that over-forecasting is more desirable than under-forecasting. In shifting to this recommended methodology, countries should not risk stock-outs.
- **Appropriate Messaging** - WHO should exercise caution in terms of rolling-out the model such that countries are not putting undue pressure on manipulating session sizes, or foregoing their existing recording and reporting systems for vaccine wastage. Special care is needed in countries where the model may lead to procurement estimates that significantly vary from historical practice.
- **Complexity of the model** - The mathematical logic behind the model is complex and will be difficult for laypersons to understand. The look-up tables or other tools (front-end) should embed the mathematics so the user is not confronted with intimidating theory or formulas.
- **Relationship to coverage achievements** - There is an important link between vaccine wastage and immunization coverage. Countries should not be putting coverage rates at risk when trying to minimise wastage rates.

Feasibility of the model: Several members queried how easily countries could actually provide data on session frequency and session size. While it would be easiest to estimate the data from national level, there will be an obvious challenge around assuring the precision of the data. Several members suggested continuing to try to gain more country experience to understand how this methodology could work in countries with poor quality data.

## Recommendations and Decisions by IPAC

IPAC commended WHO for the innovative work. The Committee unanimously endorsed the underlying mathematical logic and proposed use of this methodology for new estimation of indicative national vaccine wastage rates. IPAC further recommended to WHO the following:

1. To maintain the principle that reducing vaccine wastage should not jeopardise immunization coverage goals;
2. To apply in countries where data and vaccine management systems are notably weak to assess whether the data inputs (number of births and number of projected sessions) can be gathered accurately;
3. To view this model as only one part of the solution to improving programme efficiency and performance;
4. To continue to validate the model in additional country settings and encourage countries to improve data collection so that session size data is obtainable.

## **Session V - Sustaining Maternal and Neonatal Tetanus Elimination (MNTE)**

Mr Robert Steinglass introduced the session by highlighting the specificity of maternal and neonatal tetanus, the major achievements and the need to address strategies to sustain elimination on the short and long term and in particular of a high level of tetanus protection through school age booster doses.

Three presentations were given during this session to provide the background and evidence for developing guidelines to sustain MNTE once achieved, and to highlight critical elements of the guidelines where IPAC members' were expected to review, comment and endorse. Dr Francois Gasse recused himself from this session.

### **A. Status of MNTE elimination efforts** (*Ahmadu Yakubu, WHO*)

Dr Ahmadu Yakubu presented an update on MNTE achievements by September 2015 and the challenges to complete and sustain MNTE. He underlined the dramatic reduction of neonatal tetanus deaths between 1988 and 2013 through the progress made in skilled birth attendance coverage; delivery of tetanus toxoid (TT) containing vaccines (TTCV) to pregnant women through routine immunization; and the effective implementation of TT SIAs in high risk district that have led to the elimination of MNT in 38 out of 59 priority countries between 2000 and September 2015. The low notification efficiency for neonatal tetanus (NT) cases has persisted in most countries. He emphasized the need to implement strategies to sustain MNTE especially in countries that have achieved MNTE through targeting childbearing age women with TT SIAs in a substantial number of districts particularly in the African and South Asian regions. The draft guidelines shared with IPAC members was intended to fulfill this need. The guideline document has two main chapters: MNT risk assessment and MNT risk response. The document also contains annexes with facilitating tools to review district performance and select optimal strategies based upon local country context.

### **B. Development of draft guidelines on Sustaining MNTE** (*Francois Gasse, Donna Espeut and Hilde Sleurs, WHO consultants*)

Dr Francois Gasse presented the specific guidance on the suggested annual MNT district risk assessment using core risk indicators (TT2+ coverage, Skilled Birth Attendant

coverage, Neonatal tetanus rate per 1000 live births) and surrogate risk indicators (antenatal care first visit coverage, DPT/PENTA 1 coverage, DPT/PENTA 3 coverage, MCV1 coverage and urban vs rural status for the district). An algorithm for the MNT risk assessment with risk cut off points for the core indicators (through routine reporting) was suggested to classify districts into low risk and at risk status. Risk cut off points take into account the results of MNTE validation surveys and differences noted between survey data and routinely reported data. A second algorithm is included to guide the selection of most appropriate corrective strategy to sustain a high level of TT protection based upon the districts' risk status and TT protection levels with a menu of options to consider (RED/REC, PIRI, TT SIAs) and their implementation and sustainability issues to overcome.

The major inaccuracies in reported TT coverage are a growing concern and the guideline recommends use of the WHO method of monitoring using the Protection at Birth (PAB) indicator. This method assesses protection against tetanus, at birth, based on a mother's history of doses of TT administered during and outside of pregnancies. However, experiences with the PAB monitoring method have revealed some programmatic challenges to effectively implementing the method nationwide.

Dr Donna Espeut summarized points of intervention along the maternal, newborn, and child health (MNCH) continuum of care that are of greatest relevance to MNTE. Those points of intervention include antenatal care (routine TT immunization of pregnant women based on vaccination history and TT vaccination schedule to ensure protection of a pregnancy against tetanus); delivery care (skilled birth attendance); and postnatal care (clean umbilical cord care; use of chlorhexidine on the cord stump in selected settings). She also underscored that there are missed opportunities due to suboptimal collaboration between EPI and MNCH programs. A major constraint for the guidance document on sustaining MNTE is that its content must be limited to WHO-endorsed policies and recommendations. She posed a question to IPAC seeking guidance on practical modifications to the Annexes of the document to jump-start functional relationships between MNCH and EPI.

Dr Hilde Sleurs presented the challenges of improving the sensitivity of NT surveillance to help monitor the sustainability of the elimination status through a reliable reported NT rate below 1/1000 live births. Critical suggestions are to improve the sensitivity of NT surveillance and reporting, investigation and response requirements, accountability, role of community involvement in surveillance and vital event registration. The guidelines also address vital events surveillance including registration of every pregnant woman and birth, and of every maternal and neonatal death, by Community Health Workers or midwives. This approach is aligned to the WHO WHA action plan to end preventable newborn deaths of May 2014.

Dr Sleurs also presented on the guidance provided to implement school age booster doses for TTCV as recommended by WHO to ensure diphtheria and tetanus long term protection of all age groups and gender. This aims for a total of 6 doses of TTCV if the primary series started in childhood, and 5 doses when immunization started later in life (e.g. pregnancy).

The two strategic school immunization options are: Strategy 1 (the 2 dose option): provide boys and girls with a Td booster dose in grade 1 (5-7 years) and a Td booster in the highest primary or secondary grade where the number of female students exceeds

80% of the number of these students in grade 1. Strategy 2 (the 3 dose option): provide boys and girls with a Td booster in grade 1, Td booster in grade 2 + Td in the highest primary or secondary grade where the number of female students exceeds 80% of the number of female students in grade 2. The variability in coverage within countries can lend itself to different rollout times for this initiative once it is backed by the appropriate national policies. Adverse events following immunization (AEFI) also needs to be monitored.

### **Discussion:**

IPAC welcomed the guidance and acknowledged the significant work that had contributed to its development so far. The difficulties of establishing definite reported cut-off points for considering a district at low risk for MNTE were acknowledged. It was also stressed that the challenge of guidelines are their operationalization and that mechanisms to implement the guidance should be included in the document.

IPAC emphasized that school immunization of tetanus should not stand alone but that the school health platform needs to be strengthened in order to both provide other preventive health services and establish links to other sectors such as nutrition, education and water, sanitation, and hygiene (WASH). Members also commented on the district approach versus national strategy, to seek alternative approaches beyond schools in areas where school enrolment of girls is very low.

Given that in some countries many reported NT cases are still not investigated, it was proposed that case investigation should be a priority for NT surveillance. It was further highlighted that countries will continue to see a few NT cases even after attaining elimination. Chad, Cameroon and Zimbabwe were discussed as examples. The Committee noted the concerning situation in Cameroon where cases continue after having attained elimination, and the shifting policies in Zimbabwe around skilled birth attendance, which in some cases has not increased access to clean delivery.

Other comments included the importance of working with health staff to record pertinent vaccination information on health cards, and promotion of greater availability of those cards to mothers. Doing so would facilitate accurate TT vaccination of women and assessment of protection at birth. MNTE efforts in Ghana were discussed to illustrate the above. IPAC noted the difficulties in coordination between EPI and MNCH programmes in many countries, commenting that this was not restricted to MNTE but is also seen in relation to other priorities such as human papillomavirus and availability of oxytocin. The Committee noted the relevance of other guidance that addressed issues of integration, such as the WHO/IVB 2012 publication *Practices to improve coverage of the hepatitis B birth dose vaccine*.

IPAC concluded that MNTE, and the control of tetanus, needs more "allies". It has become a neglected disease, and it is important to adopt a partnership approach to raise the profile of these efforts. Tapping into the burgeoning newborn health agenda is one avenue. IPAC welcomed the plans for rapid finalization of the guidance, including advice on its implementation. IPAC members were invited to provide additional written comments on the document by mid-November 2015.



**Closing**

Dr Morgan thanked all in attendance and summarised the proceedings. All members were thanked for their important contributions and dedication of service. In closing, Dr Morgan presented Dr Robert Steinglass and Dr Shelley Deeks with a certificate of appreciation to acknowledge the end of their second term of service since April 2010. WHO, and specifically, the Department of Immunization, Vaccines and Biologicals, greatly benefitted from the insights and contributions of Drs Steinglass and Deeks.

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