

A note from the Chair:

Dear colleagues,

Welcome to this slightly belated IPAC bulletin, the second for 2018. It was excellent to see members and others at the July IPAC meeting in Geneva. This meeting was characterized by discussion of how to make the most of the increasing number of innovations becoming available to immunization programmes: such as deployment of vaccines in a Controlled Temperature Chain, new technologies for vaccine delivery (both injection and non-injection), new information on optimal vaccine presentations (such as the dose-per-container), expansion of work on Total Systems Effectiveness to better understand both costs and programmatic benefits, revision to the Effective Vaccine Management (EVM) toolkit, and new thinking on calculation of vaccine wastage.

Such innovations are essential as long-established vaccination schedules, management techniques and service delivery arrangements, are challenged by the increased volume of new vaccines, expansion of the age groups they target, and the need to sustain confidence and investment. Critically important is the short programme of work on the Vaccine Innovation Prioritization Strategy in which key immunization partners support the assessment and ranking of first 'antigen-agnostic' and then antigen-specific

innovations in the provision of vaccination, oriented to the most needy settings.

A sharp reality check has come as I write from the annual meeting of the Paediatric Society of Papua New Guinea, where the emergence of polio (as VDPV-1) shines a harsh spotlight upon persistently low coverage with routine immunization. This group of concerned clinicians discussed the urgent need to re-establish immunization basics, and the immense difficulty of overcoming chronic under-investment in human and other resources. Characteristic of emergency responses everywhere, the key challenge is to meet the immediate need (in this case through the large-scale outbreak response by the government with support by WHO and other partners) while also building for lasting change. Programme innovations have a part to play, but many are more long-term propositions; although updates to EVM and related tools can contribute immediately by providing accurate evidence on what is needed to develop a stronger sustained programme.

Some broader reflections, such as those from the Global Immunization Meeting two months ago, seem pertinent. These include the need to better apply disciplines beyond public health, especially communications or political sciences, to

strengthen community confidence in and demand for immunization. Can we find ways to help local politicians understand the dangers that an under-vaccinated community represents? Can we look differently at resource disparities, perhaps using tools such as Dollar Street (<https://www.gapminder.org/dollar-street/>) to better understand how these limit or potentiate vaccination?

Before I close, I would like to add my appreciation of the contribution made to IPAC by Dr Amani Mustafa, whose term completes this month. I am so grateful for her thoughtful, considered reflections on what is needed to make our ideas relevant to national programmes and national managers. We will greatly miss her involvement in IPAC.

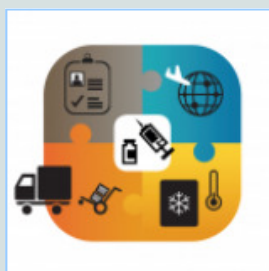
Best wishes

Chris Morgan

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C.Morgan : IPAC Chair



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From the Working Group frontlines

CTC Working Group update
by Anna-Lea Kahn (CTC focal point at WHO and part of the CTC-WG Secretariat)

The IPAC Working Group on the Controlled Temperature Chain (CTC-WG) met by teleconference on June 13th, 2018 to have a focused discussion on the prospects for **Hepatitis B licensure and uptake for use in a CTC**. It has been acknowledged that while progress in gaining industry interest in such a label variation has been notable, clear challenges remain in defining the user case and optimal, yet realistic product profile. Recent momentum in this work stream has been marked by the February 2018 licensure of the LG Chem Hepatitis B product, Euvax B Inj. Vaccine in 0.5ML presentation, by the Korean MFDS. The specific CTC indication allows for storage up to “45°C for 4 days immediately prior to administration, provided the vaccine has not reached expiry date.” This new

indication has yet to obtain approval from the WHO Prequalification team, however. The product labelling also allows for 28 days at a 37°C threshold, which is just below the standard required for CTC.

A second vaccine manufacturer, based in India, remains also committed to seeking CTC certification for its Hepatitis B product, though it is still working on generating the required stability data and does not expect to be able to seek regulatory approval before 2019.

In the meantime, WHO and PATH, through the guidance of the CTC-WG, have drafted a comprehensive document detailing the research in support of delivering Hepatitis B Birth Dose (HepB-BD) outside of the traditional cold chain, as well as the associated challenges and the specific product characteristics sought of a vaccine for this purpose. (This document should be finalized and available online on the WHO-IVB website's dedicated CTC pages by early September 2018.)

From these recent efforts has emerged a clear gap in information currently available on the potential market and value proposition for CTC-qualified Hepatitis B vaccines. Much debate also persists around the acceptable product profile characteristics to promote, especially with respect to **CTC duration** (number of days the vaccine needs to be able to tolerate ambient temperatures) and **threshold temperature** (the minimum value that the upper

threshold temperature for use out of the cold chain should be.)

It has been noted that four days meets generic CTC requirements for minimum duration allowance of end-of-distribution temperature excursion from the traditional cold chain. However, it does not meet the programmatic needs in the specific context of out of facility HepB-BD delivery. Even if this could be extended to 7 days, the CTC-WG questioned whether a full week offers sufficient utility and agreed that additional input from relevant country-level programs, as well as more implementation research is required to properly address this matter.

Potential options to lengthen the CTC duration for HepB vaccine were also discussed by the WG, including decreasing the acceptable threshold to 37°C, decreasing product shelf-lives, and/or increasing antigen content. It was concluded that more data from both country programs and manufacturers were required before any recommendations could be made. Exploring the feasibility and cost benefits of varied compact, prefilled autodisable devices (CPAD) was also encouraged.

The next teleconference of the CTC-WG is scheduled for the final week of September. Anyone interested is welcome to join these calls. For further details, please contact Rachel Bauquerez (bauquerezr@who.int) or Anna-Lea Kahn (kahna@whot.int).



WHO/C.Black— vaccinating babies born at home

Working Groups (Cont'd from page 2)

Summary of outcomes from June 2018 GACVS meeting

by Ian Gemmill (IPAC Member, attended on behalf of IPAC)

The **Global Advisory Committee on Vaccine Safety (GACVS)** recently discussed 2 vaccine safety issues: pharmacovigilance in the RTS,S malaria vaccine pilot study and data on dengue vaccine from the Philippines. It also reviewed three generic issues: progress in the Global Vaccine Safety Initiative (GVSI), communication about vaccine safety and new developments in the Vaccine Safety Net (VSN).

RTS,S malaria vaccine pilot study

Following a joint review convened by the African Vaccine Regulatory Forum (AVAREF), the national regulatory authorities of Ghana, Kenya and Malawi granted special authorization in May 2018 for use of the RTS,S malaria vaccine in the planned pilot implementation programme. As monitoring of safety of new vaccines is a key part of implementation, safety data will be derived from: (i) post-marketing monitoring of cohort events by the manufacturer GlaxoSmithKline (GSK), with detailed active follow-up; (ii) surveillance of mortality throughout the pilot area and surveillance of meningitis and cerebral malaria in sentinel hospitals in both control and RTS,S areas; (iii) active surveillance of adverse events of special interest (AESI); and (iv) pharmacovigilance through passive reports of adverse events following immuniza-

tion (AEFI) with all vaccines from each country.

Data on dengue vaccine from the Philippines

GACVS reviewed long-term follow-up in clinical efficacy trials of dengue vaccine in the Philippines, which indicated that, overall, vaccinated trial participants had a reduced risk of virologically confirmed severe dengue and hospitalization; however, a subset of trial participants who had not been infected with dengue virus before vaccination (i.e. dengue-naïve, seronegative according to the NS1 assay) had a higher risk of severe dengue and hospitalization. As a result of these findings, GACVS has recommended that CYD-TDV not be administered to individuals who have not been previously infected with wild dengue virus. GACVS also noted that no data are currently available to allow an analysis of risk according to the number of vaccine doses received by people who are seronegative at baseline. GACVS will continue to monitor this issue.

Progress in the Global Vaccine Safety Initiative (GVSI)

The Global Vaccine Safety Blueprint (GVSB), a framework of 8 objectives for enhancing global vaccine safety activities, has a vision of effective vaccine pharmacovigilance systems established in all countries, which has progressed steadily. Countries are reporting AEFI and are meeting indicators of improvement in safety surveillance capacity. Resources, training packages on basic vaccine safety, guidelines, AEFI surveillance and manage-

ment, signal detection and communications are integral to robust building and maintenance of capacity for vaccine pharmacovigilance and trust in immunization programmes.

The concept of the Global Vaccine Safety Observatory also was discussed. It was conceived as a clearinghouse for data on vaccine safety systems to assist member countries in achieving the Blueprint objectives. The Observatory will start with 4 regional nodes that provide academic, programmatic, regulatory and technical expertise. The expected outputs of the Observatory include presentation and analysis of relevant data, a website to provide indicators of vaccine safety capacity and links to relevant activities for vaccine vigilance, and an annual report.

Communication about vaccine safety

A new GACVS subcommittee on vaccine safety communication has been established to integrate safety assessments with better capacity to communicate them. It is proposed that a framework and templates for communication on vaccine safety be prepared by mapping vaccine safety communication activities throughout the life cycle of products, examining current vaccine safety communication tools and identifying gaps, and proposing approaches to fill the gaps. The first task of this subcommittee was to prepare a more detailed action plan, including case studies to illustrate how safety is communicated under various circumstances. (Cont'd on page 4.)

Working Groups (Cont'd from page 3)

New developments in the Vaccine Safety Net (VSN)

The Vaccine Safety Net (VSN) is a WHO initiative initially launched to identify trustworthy information on vaccine safety and immunization on the Internet. GACVS supports the VSN by providing advice and criteria for website quality and content, thereby facilitating access by public health authorities, health professionals and the public to reliable information on vaccine safety. There are currently 58 member websites in 16 languages, covering the 6 WHO regions.

The good alignment of VSN mem-

bers provides new opportunities for research. A recently explored area is web analytics to document patterns of web-searching on specific vaccine safety issues around the globe and at each VSN site. Web analytics could also be used to monitor the effects of digital communication strategies in real time. Research on measuring, understanding, tracking and addressing vaccine confidence was identified as another important area. A digital toolkit or news-letter would provide updates, tips, lessons learnt and risk communication guidance and resources for responding to vaccine safety events that occur

locally in member countries.

Readers who would like to read the full proceedings of this meeting may do so at:

<http://www.who.int/wer/2018/wer932930/en/>



WHO/O. Asselin—Vaccine safety

New!

WHO EPI announces new resources on vaccine demand, acceptance, and hesitancy

Two new groups of resources are now available for the areas of demand, acceptance, and hesitancy:

- 1) **New Gavi programming guidance on demand;** Developed by the Gavi demand 'strategic focus area' group, with support from UNICEF, CDC, JSI, IFRC, and WHO/EPI.

These documents are all available on the following GAVI web pages: <https://www.gavi.org/library/gavi-documents/guidelines-forms/>

This guidance should serve as useful references during joint appraisals or any other similar planning activities.

It makes the case for investing in this area, and outlines the main areas of work to be considered:

- Enhancing service quality and accountability
- Engaging communities and shaping social norms
- Managing risks & building resilience

- Advocating and political will
- Using social data for learning and decision-making

The documents also offer suggestions for planning processes and stakeholder involvement, outcome indicators, and includes numerous examples of approaches and interventions, with links to further information.

It should be noted that the scope of this area goes beyond traditional communications, social mobilization, and community engagement, also encompassing service quality improvements, planning to mitigate and respond to vaccine related events (e.g. rumours, misinformation, and AEFIs), and the importance of generating social/behavioural data for specific population groups to diagnose and address under-vaccination. The value of tailored and targeted approaches is also emphasized.

- 2) **Updated WHO tools and resources to support efforts to**

assess and address hesitancy, and to build demand.

This revised WHO guidance and material can be found on the WHO vaccine hesitancy web page: http://www.who.int/immunization/programmes_systems/vaccine_hesitancy/en/

This update includes the following new resources:

- Global information on the updated *Tailoring Immunization Programmes* (TIP) approach, based on TIP guidance from EURO;
- An evaluation tool for research to explore caregiver / health worker interactions;
- Health worker training materials on:
 1. managing pain during vaccination, and
 2. conversations with hesitant individuals.

IPAC's 12th Meeting— a brief summary

by Gill Mayers (meeting rapporteur)

The Immunization Practices Advisory Committee (IPAC) convened for the 12th time on 10-11 July 2018 in Geneva, Switzerland to support and advise the Director and staff of the WHO Department for Immunization, Vaccines and Biologicals (IVB) with the review and/or formulation of immunization practices, operational standards, tools and technologies. Advice aimed to strengthen and improve the delivery of immunization programmes at the country level to realize the goals of the Global Vaccine Action Plan (GVAP).

Special thanks were conveyed to Dr Chris Morgan, the IPAC Chair, who has extended his term by one year to provide continuity to IPAC during the management transition currently ongoing in the IVB Department. IPAC members were also thanked for the valuable and generous contribution of their time.

This year's agenda emphasized innovation, a theme which, in light of the WHO Director General's commitment to reach one billion more people with access to universal health coverage (UHC), is now more essential than ever. The topics deliberated over the two days related to:

1. **Improving coverage and equity by better facilitating access to vaccine innovations;**
2. **Receiving an update on the activities of the different working groups and committees;**
3. **Optimizing vaccine delivery through better financing, access, and supply chains.**

"This year's agenda emphasized innovation, a theme which is now more essential than ever."

A closed session for IPAC members only was held on the third day to discuss how to ensure IPAC's work remains relevant and impactful, one of the key issues being the linkages between IPAC and the Strategic Advisory Group of Experts (SAGE) on Immunization.

During his opening remarks, Chris Morgan highlighted that immunization is going through a time of change – administrative changes in WHO, and changes in the complexity of

process of immunization – and that as such, the immunization community needs to focus on navigating these transitions. He noted that vaccination is key to disease control, and that the Expanded Programme on Immunization (EPI) is one of the world's most successful public health platforms. EPI has always been characterized by simplicity and predictability, but this is no longer the case. There are new vaccines and new ways of delivering them that are to be embraced if ambitious global goals are to be met. He remarked on a possible tension in the meeting agenda of how to accommodate new opportunities and innovations while remaining oriented to the needs of field programmes at all levels, that is: how to combine current complexity and historical simplicity.

The full meeting report can be accessed through the following link to the IPAC page of the WHO/IVB website:

http://www.who.int/immunization/programmes_systems/policies_strategies/ipac/en/

The report will also be published shortly in WHO's *Weekly Epidemiological Review*.

IPAC bids farewell to Amani Mustafa



Dr Amani Mustafa will be unfortunately completing her term as a valued IPAC member in September 2018. Dr Mustafa, a Public Health and Community Medicine specialist from Sudan, currently works with the Carter Center. She played a key role in offering country-level perspective to IPAC discussions, with particular expertise on national policy and regulatory issues. In addition to her service on IPAC, Dr Mustafa contributes to WHO's immunization agenda through the SAGE Working Group on the Global Vaccine Action Plan.

It is with much regret that the IPAC Secretariat is launching a new call for nominations in August 2018 to replace Amani, as finding a candidate as distinguished as her and with as rich a professional profile will be very challenging.

It is with sincere gratitude and best wishes that we part ways.

Upcoming Meetings & Events:

- ⇒ 28 - 30 Aug 2018 — Geneva, Switzerland:
Decade of Vaccines SAGE WG Meeting
- ⇒ 24 -26 Sept 2018 — Annecy, France:
Immunization and Vaccines-related Implementation Research (IVIR) Advisory Committee Meeting
- ⇒ 27 - 28 Sept 2018 — Annecy, France:
SAGE WG on HPV Vaccines Meeting
- ⇒ 8 -10 Oct 2018 — Santiago, Chile:
7th Global Vaccine Safety Initiative Meeting
- ⇒ 9-12 Oct 2018 — Copenhagen, Denmark:
WHO/UNICEF Meeting on Monitoring National Immunization Systems
- ⇒ 23 - 25 Oct 2018 — Geneva, Switzerland:
Strategic Advisory Group of Experts (SAGE) on Immunization



A final word from the IPAC Secretariat

The past month was a very busy one, highlighted by our annual meeting. We wish to thank you for your active participation in this meeting and ongoing support of this Committee. As IPAC members will recall, you elected to have this Bulletin continue and as such we rely on your inputs and suggestions, with respect to preferred content. Such contributions become all the more essential when you represent IPAC on other working groups and sub-committees. We look forward to sharing your views and concerns, as well as taking on your new ideas. Please send all relevant correspondence to Chivonne Tambourlas (tambourlasc@who.int).

In the meantime, we wish you a pleasant end to the summer!

The IPAC Secretariat Team