



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

**IMMUNIZATION PRACTICES ADVISORY COMMITTEE
(IPAC) 12th Meeting
10 – 11 July 2018**

Final meeting report and recommendations

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Opening and Introduction

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

IPAC Members present:

Chris Morgan (Chair)
David Brown
Craig Burgess
Nora Dellepiane
Michael Free
Ian Gemmill
Masahiko Hachiya
Kelly Moore
Adelaide Shearley
Carla Vizzotti

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:

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

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.

The Chair opened the meeting by highlighting 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.

Session I. Innovation for improved coverage and equity

IPAC reviewed reports on the slowing of improvements in global immunization coverage. Although the Expanded Programme on Immunization (EPI) is successfully vaccinating increasing numbers of children every year, the effect of population growth in settings such as sub-Saharan Africa means that it is unlikely that the current coverage with the third dose of diphtheria-tetanus-pertussis containing vaccine (DTP3) of 85% will rise to the global goal of 90% by 2020. IPAC noted that **better subnational data** to identify under-vaccinated groups is increasingly available at the global level. This enables new thinking on tailored solutions, but also calls for new tools and methods to translate this data into innovative immunization strategies and practices to reach under-served populations. Adaptation of existing approaches such as Reaching Every District (RED), the transformative actions within the Global Routine Immunization Strategies and Practices (GRISP) guidance, and examples such as an 'urban toolkit', can also support setting-specific responses.

Three recent initiatives were discussed, all seeking broader alignment between programme needs and product innovation. The **Total System Effectiveness (TSE)** approach aims to support countries in reaching coverage and equity targets by strengthening informed, transparent and holistic decision-making for national immunization programmes, and by ensuring that global policy, market shaping and research and development (R&D) priorities reflect the needs and priorities of low and middle-income countries. The current testing of this approach in Asian and African settings was discussed, noting that formal reporting to the Immunization and Vaccines Implementation Research Advisory Committee (IVIRAC) took place in March 2018 and an update is scheduled for September 2018. IPAC supported the use of TSE in generating a flexible toolkit to be used by countries to analyse barriers to progress and decide which vaccines and related technologies to introduce. The potential value of TSE in providing assessments that can be used in other prioritization efforts was also noted. IPAC noted the conceptual links with the **Doses Per Container Partnership (DCP)** that aims to help country decision-makers include consideration of how differing numbers of doses per multi-dose vaccine vial could optimize equitable and cost-effective coverage; and to strengthen the feedback to developers and manufacturers.

The **Vaccine Innovation Prioritization Strategy (VIPS)** is a new programme of work sponsored by global immunization partners to incorporate the needs of countries into the projected impact of vaccine product innovations to help prioritize those that will more clearly address the barriers countries face in achieving optimal immunization coverage. This accompaniment to Gavi's Vaccine Investment Strategy will support prioritization of innovations in vaccine product attributes, such as primary containers, delivery technologies (for example micro-array patches), labelling, and packaging. VIPS is a multi-partner initiative that includes formal involvement of IPAC and WHO's Product Development Advisory Committee (PDVAC), and envisages production of a prioritized short-list of vaccine product innovations by the end of 2019. IPAC affirmed the VIPS

approach and provided input to strategic concepts, suggested applying a service delivery framework to analyses and early engagement with manufacturers, as well as providing input to the tools for the first round of country consultations.

IPAC noted that VIPS, TSE and DPCP all reflect an attempt to introduce a properly nuanced country view into global policy, into communications with developers and manufacturers, and into the upstream development of new products and tools. IPAC noted the value in categorizing new products or innovative approaches according to their usefulness in different service delivery platforms, to enable application to various settings and across a range of vaccines. To ensure that Middle Income Countries (MICs) are also able to contribute to, and benefit from, these initiatives the Committee agreed that expanding the scope of VIPS and TSE to include MICs and Gavi transition countries would make the work more relevant and could contribute to a better understanding of potential market for manufacturers.

i. Improving how we collectively address Coverage & Equity and evaluate barriers to immunization. *(Jan Grevendonk, WHO/EPI - presented for Partner Alignment)*

The goal of the global immunization community is to achieve the highest possible levels of equitable vaccination coverage at an affordable cost. While coverage with the third dose of diphtheria-tetanus-pertussis containing vaccine (DTP3) has improved steadily in the past, it is now stagnating at 85-86% - not fast enough to reach the global goal of 90% by 2020, leaving 20 million children vulnerable to death and disability from vaccine-preventable diseases. Of the 20 million under immunized, half of these are in the African Region where population growth means although more children are vaccinated each year, this only suffices to maintain current coverage levels. In order to focus efforts to address these inequities, greater insight is needed into who and where these unvaccinated children are.

WHO and UNICEF now have sub-national immunization coverage data from 141 countries, a key step in understanding inequities between geographical areas, districts and wealth quintiles. In countries with large numbers of unvaccinated children, identification of under-vaccinated groups and establishing tailored strategies to serve them is the next step. The Reaching Every District (RED) Strategy¹ and its operational components remain relevant, however additional planning tools are needed to tailor strategies to reach the urban poor, rural remote and conflict-afflicted populations in particular. The Global Routine Immunization Strategies and Practices (GRISP) Framework² encompasses nine transformative investments that can be coupled with innovation in systems and products. New assessment tools, including Total System Effectiveness (TSE) and the Vaccine Innovation Prioritization Strategy (VIPS) will need to demonstrate how product innovations can meet the needs of specific settings and communities, if further advances in equitable coverage are to be achieved.

Discussion:

IPAC members welcomed the overview provided on global coverage and the reminder that there are continuing pockets of unreached populations whose vaccination is key to achieving coverage and equity goals. It was noted that implementation of the tailored approaches needed to access these hard to reach populations is challenging, and that adopting a health systems approach, integrating with other health programmes, to deliver a package of interventions for these populations would be more cost-effective. The Committee supported increased dissemination and uptake of tools to support

¹ http://www.who.int/immunization/programmes_systems/service_delivery/red/en/

² http://www.who.int/immunization/programmes_systems/policies_strategies/GRISP/en/

countries in devising tailored approaches. The “urban toolkit” being rolled out in African countries is one example of a first step for reaching chronically under-immunized populations in urban areas and its adoption was encouraged.

ii. (a) Country use case for Total System Effectiveness (TSE). *(Siobhan Botwright, WHO/IVR – presented for Strategic Guidance)*

IPAC received a further update of TSE, focusing on the development of the country use cases, which applies TSE to national immunization programme prioritization decisions. The overall intent of TSE is to support countries in reaching coverage and equity targets. TSE is an approach to identify the value of products from a country immunization programme perspective, both to support national decision-making on uptake and to direct market shaping at the global level so that country demand informs product development and create a ‘pull’ for new products that meet the needs of low and middle income countries (LMICs). TSE started out as a partnership between the Bill and Melinda Gates Foundation (BMGF), Gavi, UNICEF, PATH and WHO. Other partners have subsequently joined the initiative to enlist expertise in modelling and multi-dimensional criteria analysis, and partners for country implementation.

TSE is currently being piloted through analysis of rotavirus vaccine introduction, to establish whether low- and middle-income countries (LMICs) see benefit in a TSE approach to decision-making and, if so, what tools would be needed and what might be the constraints on data or capacity. In 2018, TSE workshops are being held in Indonesia, Thailand, Mali, Rwanda, with the objective of developing a long-term proposal and recommendation by the Immunization and Vaccines Related Implementation Research Advisory Committee (IVIRAC) in September 2018.

Initial results from Indonesia and Thailand varied in accordance with the maturity and nature of their national decision-making processes. Country stakeholders identified value in using TSE to support the review of different presentations of the same vaccine, to inform the local research and development agenda, and to assess vaccination within broader disease control programmes and/or for considering interventions across the EPI programme. While there is potentially broad applicability for TSE, better flexibility is needed to link TSE to existing country guidelines, studies and methods. Immediate next steps are to complete the country pilots, especially in an African context, and to understand how TSE can influence research and development. In the longer term, the group will develop a “TSE toolkit” for country use, devise a mechanism for the analysis of barriers, develop tools and processes for global use of TSE to direct market shaping, and implement the TSE approach, including an evaluation framework.

IPAC was asked to consider several issues during the meeting, and offline through suggestions to the Secretariat. For the analysis of barriers to TSE, these included which ongoing initiatives and forums should be leveraged, and which important partners should be engaged. In relation to country use of TSE, questions included whether it is feasible to consider “archetype countries” as TSE is developed, and how representative countries should be selected.

ii. (b) Dose per Container Partnership (DPCP) *(Craig Burgess, JSI and IPAC Member – presented for information)*

IPAC received an update on the DPCP, noting completion of Phase 1 and near completion of Phase 2 of this initiative. The DPCP acknowledges that while countries need access to affordable and appropriate vaccine products there is a risk that products are supply driven and there is an over-reliance on multi-dose presentations to maintain low costs. At the service delivery level, fear of wastage and stock-outs leads to missed opportunities to immunize, for example if health care workers only open a 10-dose measles vial if more than five children are present and otherwise instruct a caregiver to

return later for a dedicated measles vaccination session. Historically, there has been little focus on the impact of dose per container (DPC) on coverage, and DPC trade-offs between system savings and performance. The goal of the Dose per Container Partnership (DPCP) is to support vaccine product and programme decision-making in considering the impact of DPC on equitable, timely, safe, and cost-effective coverage. The Technical Advisory Group of the DPCP includes representatives from WHO, UNICEF SD, Gavi, industry, academia, and countries.

In Phase I, from April to October 2015, country consultations and literature reviews indicated that most EPI Managers prefer a 5-dose measles vial and are interested in allowing different DPC presentations of the same vaccine to be in the system at the same time. There was also strong interest from countries in strengthening the feedback loop to manufacturers to inform product development to meet their needs.

IPAC heard that in Phase II, findings suggest that national decision-making processes are based on global availability of products and are reliant on options proposed by procurement agents. As cold chain requirements and vaccine price are more easily quantifiable than the impact of failing to reach coverage and equity goals, national decisions on vaccine products are influenced more by budget than by national goals. However, in countries where vaccine is locally produced, manufacturers can play a key role in the decision-making and can be responsive to DPC requests.

The next steps for the DPCP are to translate the evidence gathered into tools that support national decision-making by helping countries consider the impact of different vaccine DPC sizes on the various system components and to understand the trade-offs involved. Incorporating DPC into a tool that is already owned and used by countries, e.g. the UNICEF Supply Division (SD) ordering form, the Effective Vaccine Management (EVM) tool, the Comprehensive Multi-Year Plan (cMYP) or the new TSE tools, would contribute to easier uptake.

IPAC was asked to consider how DPCP results (processes, interventions and guide) could make a difference to the front line, how DPCP evidence could strengthen links to industry and increase choice of product development, and how to ensure synthesis and communications influence policy making.

Discussion on TSE and DPCP:

IPAC Members expressed interest in seeing how adaptable the final TSE tool is to countries' situations, and how flexible it is to countries uploading existing country data. While it may be difficult for countries to adapt the tool, the intent should be to make a generic flexible tool in which countries can select their own criteria for decision making, insert their own data, and be able to run the analyses. The 'tool-kit' approach was encouraged, such as that adopted by the Global Routine Immunization Strategies and Practices (GRISP) guidance, in order that countries have access to a menu of instruments from which they can choose. The Committee also urged the TSE Partnership to articulate clearly the gap in tools for country decision-making at country level, and how TSE will address this.

Although there was some caution expressed about the expansion of TSE beyond its original mandate of focusing on assisting countries to choose between different products for a specific vaccine, the responsiveness of the initiative to the interest expressed by countries in a framework to choose between vaccines and other interventions was welcomed.

IPAC Members applauded the linkages between downstream implementers and upstream manufacturers evident in these two presentations, and also recognized that the TSE and DPCP are important tools to use to advocate for political commitment for immunization. As TSE has broader inputs than other existing decision-making models, it would be useful if

it could also be used to assess the trade-offs between different service delivery platforms, to consolidate information for a country on their barriers to increasing immunization coverage, and link this with the work of the DPCP. IPAC also noted and welcomed the adoption of TSE within the IVIRAC agenda of work.

iii. Vaccine Innovation Prioritization Strategy (VIPS).

(a) Overview of initiative, rationale and objectives. *(Marion Menozzi-Arnaud, Gavi – presented for strategic feedback)*

Innovation is one of the Alliance priorities for shaping markets to the benefit of Gavi-supported countries. Vaccine product innovation, using new technologies, has been identified as one of the levers to achieving coverage and equity goals by driving product innovations to better meet country needs. As vaccine development occurs on a long time horizon, that exceeds Gavi's strategic and funding cycle, and as Alliance partners sometimes lack alignment and clarity around longer-term priorities, manufacturers have indicated that even a non-binding indication of the interests of the Alliance in this area could inform their decision-making.

The objective of the Vaccine Innovation Prioritization Strategy (VIPS) is to develop a common language for valuing innovation and to identify common priorities by convening the market-shaping community. The scope of the VIPS covers innovations in vaccine products' attributes, i.e. delivery technologies (for example micro-array patches), formulations, for example heat stability, primary containers, labelling, and packaging.

VIPS will first prioritize antigen-agnostic innovations then vaccine-specific innovations. The first phase includes landscaping of all innovations, assessment of country needs, development of methodology and criteria for assessing innovations, and an initial prioritization of antigen-agnostic innovations. A second phase applies product innovations to specific antigens, conducts further consultations, in-depth analyses (including usage of relevant TSE assessments), and finalizes the priority listing.

Governance of the VIPS is through an Alliance Working Group, comprising representatives from WHO, UNICEF, Gavi, BMGF, and PATH. This is supported by a Steering Committee with designated seats for members of IPAC and PDVAC (Product Development Vaccine Advisory Committee), whose mandate will be to review the VIPS analyses and make recommendations to the VIPS Alliance Working Group.

The work of the VIPS will take place in 2018 and 2019 with a final set of prioritizations expected at the end of 2019 that articulate the Alliance perspective on what innovations to be prioritized and the rationale to make investment decisions.

(b) Country consultation approach. *(Anna Osborne, Gavi – presented for strategic feedback)*

One of the key pillars of the VIPS mandate is to understand countries' needs by leveraging countries' and technical partners' field experience to consider financial and non-financial impact of innovations. Currently there is no formal process to articulate country needs and communicate these to developers and manufacturers to inform product development. There will be three main touchpoints with countries: firstly to provide input into the development of the evaluation criteria; secondly to review the draft conclusions on country needs for product innovation; and thirdly to validate the analysis conclusions and identify additional considerations.

Initial country consultations are expected to generate a broad range in level of detail and differing opinions across a large number of reported barriers to equitable coverage. The challenge will be to condense these into usable inputs for the VIPS evaluation framework

and definition of quantitative weighting criteria. It will also be important to document country insights into the likelihood of product uptake, including characterization of the trade-offs inherent in an innovation and its relative importance in addressing specific barriers. Two further country-level inputs are planned. Once the preliminary analysis of all innovations in scope is finalised, a short-list of the most promising will be presented to countries to discuss their potential to address implementation challenges, and their known trade-offs. Country inputs will also be incorporated into the final scoring of each innovation to guide final prioritization of antigen-agnostic innovations.

The next step in the VIPS work is the launch of the online survey in August 2018, targeting a large audience including EPI Managers, National Immunization Technical Advisory Groups (NITAGS), national logisticians, and similar stakeholders. As healthcare workers (HCWs) are a key respondent group who may not have access to an online survey, face to face interviews with 10-15 HCWs will be conducted in October 2018 in 4-5 countries. The analysis of results will be presented in November 2018 to the first Steering Committee meeting.

IPAC was requested to consider the focus of country consultations, their format, target countries and audience, and other possible support.

Discussion:

IPAC recommended allowing collection of information on innovations that will solve barriers in different sub-populations, including areas where government service delivery is weak, to evaluate innovations needed in fragile settings. The Committee also recommended including consultations with Civil Society Organizations (CSOs) or Non-Governmental Organizations (NGOs) who are delivering immunization in such settings to obtain their perspective on the innovations that could be most effective.

IPAC Members suggested that the VIPS develop a common taxonomy of service delivery platforms, for use in categorizing data collection and analysis. Platform types may include facility-based, outreach, and campaign service delivery; possibly also considering outbreak response, community-based service delivery, vaccination in later ages of life, and school health platforms. Considering how product innovations could apply to various typologies of service delivery could also enable the findings to be tailored in application and possibly be applied beyond Gavi vaccines and countries, for example to overcome barriers in middle-income countries (MICs).

The Committee highlighted the importance of including the perspective of manufacturers early in consideration of innovations, both to specify target populations and potential market, and to identify likely trade-offs inherent in manufacturing processes of product innovations, such as the time to market. In order to avoid any conflict of interest, VIPS will present the findings to the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) and the Developing Countries Vaccine Manufacturers Network (DCVMN), including a specific session on VIPS at the DCVMN conference in October 2018. In addition, both IPAC and PDVAC deliberations provide forums where these groups, and other manufacturers can access information on VIPs.

IPAC members were also requested to email to VIPS any suggested changes to the tools and to the country consultations approach, and on possible support that could be provided from IPAC Members.

Session II. IPAC working groups and other advisory committee updates

IPAC's **Controlled Temperature Chain Working Group (CTC-WG)** presented progress against the GVAP strategic objective for increasing the number of vaccines licensed under CTC for deployment beyond the standard cold chain. This included review of the four priority vaccines highlighted in the CTC Strategic Roadmap, which IPAC had endorsed in 2017. IPAC noted the recent prequalification of Shanchol® oral cholera vaccine, that one human papilloma vaccine (HPV, Gardasil®) is already licensed and prequalified for use in CTC, two different manufacturers have committed to relabelling hepatitis B birth-dose vaccines and, for tetanus toxoid-containing vaccines, one manufacturer has committed to CTC, but has yet to generate all data required. More advocacy and financial resources are required to achieve further progress with this and other vaccines, noting the potential for CTC deployment to advance coverage and equity in a variety of service delivery scenarios.

Pilots of CTC deployment of HPV vaccine in Uganda were discussed, noting the overall high level of acceptability and increased ease of use, supporting CTC as a strategy likely to improve coverage and efficiency in HPV vaccination programmes. The main drawback noted was difficulties in target population estimation, which requires improved micro-planning to optimize CTC deployment. IPAC provided input into ideal format and scope of guidance documents for country use. Among recommendations on usage, IPAC supported flexibility in decisions on whether local pilots are needed prior to CTC implementation, but reinforced the CTC principle that only one excursion outside the cold chain be allowed. IPAC noted the HPV vaccine deployment in CTC as a valuable demonstration of how aligning interests across regulators, manufacturers and national planners can enable the expansion of vaccine service delivery beyond traditional parameters.

IPAC reviewed the potential for **CTC strategies for oral cholera vaccine**, to improve coverage, accelerate response times, and reduce operational costs. Discussions focused on the limitations of the current CTC timing of 14 days, and the types of data that will be most informative in proposed pilot studies in planned (non-crisis) campaigns in endemic settings.

Defining demand and usage scenarios for **hepatitis B vaccine birth-dose in a CTC** is the most challenging of the four priority vaccines and this remains under discussion. IPAC noted that known thermostability data of potential candidates does not yet match ideal usages and reviewed several options for re-defining CTC for this vaccine. IPAC recognized the unique difficulties of reaching new-borns with timely vaccination and noted that the CTC-WG will need to continue work to better characterize the likely demand and feasibility of HepB-BD in a CTC, recognizing that this may require tighter focus on very specific usage scenarios such as community outreach.

IPAC appreciated the achievements of the **Delivery Technologies Working Group (DTWG)** over 2017-2018, including: development of and reporting against a delivery innovation indicator for the Global Vaccine Action Plan (GVAP indicator G4.2); country assessments on the potential of micro-array patches (MAP); review of a broad range of pipeline technologies; and contributions to the TSE and VIPS initiatives. IPAC heard updates on acceptability studies of the measles-rubella vaccine MAP (MR-MAP), contributed to a revision of its Target Product Profile (TPP), welcomed the establishment of a PATH MAP centre of excellence, and recommended additional work on public health need and implementation potential to sustain momentum on MR-MAP.

Other reports included the Standing Committee of PSPQ and updates on the work of PDVAC and IVIRAC. IPAC considered how evidence and discussion for implementation issues can be coordinated across PDVAC, IVIRAC and IPAC. Discussions recognized clear

demarcations between the roles of the three Advisory Committees, and also identified potential for increased synergy through work on linked topics. Examples include the cross-cutting work of the TSE initiative across all three committees, and the mixture of 'upstream' and 'downstream' inputs to the VIPS process provided by PDVAC and IPAC respectively. In consideration of the reporting on progress in GVAP, IPAC noted the need for future global strategies to balance aspirational with achievable goals, and the potential for richer, possibly less frequent, analyses to help contextualize and inform country-level reflections on their programmes.

i. Delivery Technologies Working Group

(a) Update on working group activities. *(Darin Zehrung, PATH - presented for information)*

The Delivery Technologies Working Group (DTWG), established in 2015, provides feedback to developers of technologies on product development considerations and programmatic suitability of their products for use in LMICs. This contact happens through meetings and through a dedicated discussion group on the TechNet 21 Forum. IPAC noted with appreciation that the DTWG's accomplishments over 2017-2018, included: development of an indicator for the Global Vaccine Action Plan (GVAP) Platform Delivery Technology (Indicator G4.2) along with a contribution for the 2018 report on progress and recommendations; country assessments by PATH and Agence de Médecine Préventive (AMP) on the potential usage of micro-array patches (MAP); review of a broad range of pipeline technologies (including glass cartridges, MAPs, prefill/blow-fill-seal vaccine presentations, and electroporation); and contributions to the TSE and VIPS initiatives.

(b) Report from the WHO workshop on measles-rubella vaccine micro-array patch (MR-MAP) product development. *Birgitte Giersing, WHO/IVR - presented for strategic guidance*

Microarray patches (MAPs) are needle free patches that deliver a dry formulation of vaccine into the upper layers of the skin. MAPs require no reconstitution, remove needle waste, potentially reduce cold chain storage, and are perceived to be easier to administer, possibly by community health workers, or even through self-administration. These attributes could aid the global immunization community to accelerate progress towards measles-rubella elimination goals. Previous work reported to IPAC includes the 2015 consultation held to assess the potential for MAP vaccine delivery in LMICs, which concluded that the value proposition for low cost, well established EPI vaccines such as measles and rubella (MR) was weak, with poor incentives for development of innovative products. One of the recommendations from that meeting was to develop the Target Product Profile (TPP) for MR-MAP, and this was presented to IPAC in 2016. Following this, in 2016, the Strategic Advisory Group of Experts (SAGE) for Immunization issued a recommendation that licensure of measles containing vaccines in MAPs be expedited.

IPAC heard that, while the planning for the first MR-MAPS is expected to enter Phase I clinical studies in 2019 and that PATH is forming a MAP Centre of Excellence, other initiatives to define public health need and create momentum for MAPs are required to establish pathways to licensure and prequalification, identify manufacturing and implementation barriers, and forecast uptake of MR-MAPS in LMICs. IPAC was updated on the main conclusions from MAP acceptability studies conducted by PATH and AMP: there is much interest and enthusiasm for MAPs, but assumptions about how these products will be adopted in countries cannot be made. There are important trade-offs between the potential benefits in ease of delivery and increased access, and the additional cost of the MAP. Modelling is underway for five different potential demand scenarios for a measles-containing vaccine (MCV)-MAP, however the realistic timeline for product availability is

10 years, and much will be required, especially in estimating demand, to incentivize manufacturers and developers to invest in this.

Discussion:

IPAC Members were pleased to learn of the progress made in this area and recognized the possibilities of using microarray patches to reach the fifth child, especially in settings where it is possible to expand cadres of lesser-qualified vaccinators capable of delivering immunization through MAPs. IPAC noted that while articulating a TPP is one clear and effective way to communicate with manufacturers, additional tools to help describe usage cases in more detail may be helpful to developers in understanding programmatic issues involved in rolling out MAPs. IPAC members also provided, through a separate survey and document review, detailed suggestions on a revision to the MR-MAP TPP, with a focus on issues such as optimal wear time and acceptable temperature ranges.

ii. Product Development for Vaccines Advisory Committee (PDVAC) update. *(Birgitte Giersing, WHO/IVR – presented for information)*

The mission of PDVAC is to accelerate product development of urgently needed vaccines and technologies and ensure they are appropriately targeted for use in low- and middle-income contexts. This recognises that on average it takes several years from vaccine licensure to first introduction in LMICs, and over a decade for implementation of the vaccine to reach 50% coverage. PDVAC reviews vaccines in early clinical development, evaluates the probability of technical and regulatory success, and ensures the pipeline will meet the unmet public health need for a vaccine from an LMIC perspective. PDVAC communicates priorities by articulating the public health value and preferred product characteristics (PPCs); developing roadmaps early in product development to help define a value proposition; encouraging investment; and reducing the implementation gap.

IPAC was updated on candidate vaccines and initiatives under PDVAC consideration, including: HIV, Tuberculosis, Malaria, Influenza, Enterotoxigenic *E.coli* (ETEC), Shigella, Respiratory Syncytial Virus (RSV), Group B and Group A streptococcus, Herpes Simplex Virus (HSV), Microarray patch product development for MR vaccines, TSE and VIPS. IPAC acknowledged the importance of ensuring new vaccines meet the needs of the end-users such as national immunization programmes, and noted the benefit of mechanisms (such as VIPS) that can communicate learning on service delivery and antigen-agnostic issues to manufacturers for incorporation in their development plans. IPAC also discussed how research and deliberation on implementation issues can be coordinated across PDVAC, IVIRAC and IPAC.

iii. Immunization and Vaccine related Implementation Research Advisory Committee (IVIRAC) update. *(Raymond Hutubessy, WHO/IVR – presented for Information)*

IVIRAC provides guidance on implementation research relevant to immunization policies and practices, reviews implementation research, advises research groups, and reviews best practices related to research methods. IPAC was updated on IVIRAC's current agenda, including: firstly to minimize barriers through work on rotavirus vaccine impact, the global research agenda for HPV vaccines, and the global research on Vaccine Demand and Acceptance update; and secondly to maximize impact of vaccines in use through work on Malaria RTS,S Policy Decision Making Framework and impact modelling, the optimal intervals between measles SIAs model, the WHO Guide on standardization of economic evaluations of vaccines, the development of Full Public Health Value Proposition, TSE, and the standardization of vaccine delivery cost.

IPAC noted clear demarcations between the roles of the three Advisory Committees, with IVIRAC considering implementation research issues, PDVAC more upstream research and development issues, and IPAC focused on the programmatic aspects of implementation.

There are also useful synergies, such as the cross-cutting work of the TSE initiative. IPAC encouraged IVIRAC to continue to relay programmatic applications to IPAC once they had reached a sufficient level of maturity, so that the evidence-based approach to recommendations is maintained.

iv. Programmatic Suitability of Vaccine Candidates for WHO Prequalification (PSPQ) update. *(Kelly Moore, IPAC & PSPQ Standing Committee Member – presented for information)*

The PSPQ process works within WHO's Essential Medicines Programme to define characteristics that determine the programmatic suitability of vaccine products, define the process for assessing compliance with these characteristics, and indicate programmatic characteristic preferences to industry and other vaccine development stakeholders. The PSPQ Standing Committee, a standing report to IPAC, comprises two IPAC Members and three independent experts, and is responsible for reviewing applications where a vaccine falls outside standard PSPQ criteria, but has potential public health benefit, as referred by the PSPQ Secretariat. IPAC was updated that in 2018, prior to official submission for review by the PQ Secretariat, an advance opinion was requested from the Standing Committee on a pentavalent meningococcal conjugate vaccine. This request doubled as a training opportunity for new members on PSPQ Standing Committee criteria and processes. IPAC confirmed continuation of their representation on the PSPQ Standing Committee.

v. SAGE Decade of Vaccines Working Group – Assessing progress on Global Vaccine Action Plan (GVAP). *Christoph Steffen, WHO/DIR – presented for information)*

The SAGE Decade of Vaccines Working Group (SAGE DoV WG) facilitates a yearly assessment of progress of the implementation of the Global Vaccine Action Plan (GVAP) 2011-2020³ and prepares the annual assessment report that is presented to the SAGE meeting in October, the WHO Executive Board in January, and to the World Health Assembly in May. As the GVAP comes to an end, it will be reported on to the WHA in 2020, and in 2022 to unveil the new strategy. GVAP's five main goals (Polio, Maternal and Neonatal Tetanus and Measles elimination, introduction of new vaccines, and increasing routine immunization coverage), six strategic objectives and 16 sub-objectives, are monitored through indicators largely based on data submitted by countries through the WHO-UNICEF Joint Reporting Form (JRF)⁴. IPAC heard that approximately 150 recommendations have been made through GVAP assessments, and the results for 2016 show that only the goal on new vaccine introduction is on track. The GVAP Secretariat is now aiming to reduce the number of recommendations being made and is discussing how to make them more impactful to achieve results.

Discussion:

IPAC Members recognized the tremendous achievement of having the GVAP report on the agenda of the World Health Assembly every year. It was noted that most efforts towards achieving the GVAP goals need to take place at country level and that the Regional Vaccine Action Plans developed by countries with support from WHO Regional Offices are key to holding countries accountable for the goals they have endorsed. IPAC also appreciated the increasing clarity and detail in the most recent assessment reporting.

IPAC agreed that in the setting of goals for the future strategy, balance needs to be achieved between setting aspirational and ambitious goals, setting achievable goals that

³ http://www.who.int/immunization/global_vaccine_action_plan/en/

⁴ http://www.who.int/immunization/monitoring_surveillance/routine/reporting/en/

countries can work towards and document achievements that contribute to high-level advocacy. IPAC Members suggested that a future global strategy could be reshaped so that not only can the annual reports serve to showcase the successes of immunization and garner international support, but also that countries can use the data for their own monitoring and advocacy. IPAC also suggested consideration in the new strategy of less frequent reporting, such as every other year, that could facilitate more in-depth and provocative analysis examining, for example, the causes of low coverage and high drop-out rates, which may be more useful to countries.

vi. Controlled Temperature Chain Working Group

(a) Progress towards GVAP Indicator. *(Rachel Bauquerez, WHO/EPI – presented for information)*

WHO defines the controlled temperature chain (CTC) as “a single excursion of a vaccine into ambient temperatures typically not exceeding a set threshold of 40°C, for a limited number of days before administration.” The GVAP includes CTC within a strategic objective on research and development, measuring progress against the indicator “Number of vaccines that have either been re-licensed or licensed for use in a controlled-temperature chain at temperatures above the traditional +2°C - +8°C range”. The CTC Working Group was established within IPAC in 2016 to expand on earlier work by the five year Project Optimize collaboration of WHO and PATH that successfully supported CTC re-licensing and deployment of a meningococcal A vaccine (MenAfriVac™). IPAC reviewed the main activity of the CTC-WG over the last year: the development of the Strategic Roadmap for Priority Vaccines 2017-2020⁵, which identifies the way forward for vaccines to be considered for use in a controlled temperature environment. This document focuses primarily on the following four vaccine types selected by the CTC-WG and endorsed by IPAC in February 2017: Human Papilloma Virus (HPV) vaccine, Oral Cholera Vaccine (OCV), Hepatitis B birth dose (HepB-BD) and Tetanus toxoid containing vaccine (TT).

IPAC noted that progress against the GVAP CTC indicator remains on track following the recent prequalification of Shanchol® OCV for use in a CTC of 40°C for up to 14 days. IPAC also heard updates on progress by other priority CTC candidate vaccines. For the HPV vaccine, Gardasil® is already licensed and prequalified for use in CTC (up to three days at 42°C) and has been piloted in Uganda, with additional guidance under development. For HepB-BD, two different manufacturers have committed to relabelling their respective HepB-BD presentations, in order to be compatible with CTC minimum criteria (tolerance up to 40°C for at least three days). One product remains in the pipeline and another has been licensed for use up to four days at 45°C, or for up to 28 days at 37°C, and is currently under review for prequalification. HepB-BD has been shortlisted by Gavi for consideration in their next Vaccine Investment Strategy (VIS). If successful, this may help to increase demand for a CTC-approved product. For TT, no product has been re-licensed under CTC to date. One manufacturer has committed to relabelling its tetanus-containing vaccines for CTC compliance, but has yet to generate the full data required for this. More advocacy and financial resources are required to achieve further progress with this vaccine, noting that potential combined delivery with HPV may provide additional incentive.

As a cornerstone to its work, the CTC-WG favours open dialogue with manufacturers and the WHO Prequalification team to accelerate progress towards approving existing and new vaccines, acknowledging the cost and time commitments this represents for manufacturers, and the importance of continuing to work for clearer forecasts of demand

⁵http://www.who.int/immunization/programmes_systems/supply_chain/ctc_strategic_roadmap_priority_vaccines.pdf?ua=1

for CTC vaccine. Despite a current gap in funding, the CTC-WG, in conjunction with the main partners (PATH, MSF, Gavi and UNICEF), will continue to support countries in the implementation of CTC and generate additional evidence to inform guidance on this approach.

Discussion:

IFPMA expressed its satisfaction with the work WHO is doing in this area for which there are clearly expressed objectives and welcomed a continuation of an open and two-way dialogue.

(b)HPV/CTC Implementation

Lessons learned from the Pilot in Uganda.

(Andrew Bakanaiga, WHO Uganda - presented for information)

In order to assess impact and optimize the implementation methodology for using the CTC approach in the provision of HPV vaccine, a pilot study was carried out by the Uganda Ministry of Health, PATH and WHO in Uganda in Q4 of 2017. The pilot was conducted mainly in two districts (plus two control districts) with the objectives to: determine optimal conditions for integrating CTC into HPV vaccine delivery so as to improve coverage and equity and alleviate burden on healthcare workers; generate information and lessons learned to shape WHO's guidance to countries on appropriate use of CTC in HPV vaccination; and evaluate how to use the CTC flexibility for HPV vaccines and generate evidence on the experience and impact of delivering HPC vaccine.

IPAC was presented with the findings from the pilot, noting that: CTC was well understood and accepted in both districts and facilitated the work of EPI staff; CTC helps overcome poor cold chain practices and insufficient capacity, especially in reducing the risk of freezing of vaccines; the success of any CTC approach depends on effective training of healthcare workers prior to introduction, appropriate forecasting of vaccine and monitoring/supervision on the job; the CTC approach appears to have a positive effect on the number of girls vaccinated per session, but additional coverage data is necessary; and that the CTC implementation effort was undermined by a significant problem of unclear HPV target population and confusion around eligibility criteria, associated with poor forecasting of vaccine quantities and inadequate microplanning.

Implementation Guidelines

Anna-Lea Kahn, WHO/IVR presented for strategic guidance

Along with facilitating licensure of vaccines for CTC and piloting CTC deployment, WHO's commitment as outlined in the CTC Strategic Roadmap is to draft guidelines for implementation in a CTC of the designated priority vaccines. The purpose of these antigen-specific guidelines is to: empower countries to decide whether CTC is the appropriate choice; enable countries to implement CTC without external technical support; and ensure CTC offers more advantages than constraints. IPAC was updated on the current draft of **the HPV/CTC guidelines' objectives**, that is: to define standard operating procedures (SOPs) for implementation of HPV with CTC; assist country decision-makers and healthcare workers through all phases of HPV delivery using the CTC strategy, incorporate lessons learned from Uganda pilots; be adaptable for all HPV products approved for administration in a CTC, irrespective of product brand. IPAC also reviewed the **document development process**, that is: draft guidance has been prepared following on from the pilot implementation in Uganda, has undergone internal review and is currently in the process of two rounds of external review by the CTC-WG. Once the document is finalized, it will be submitted for endorsement by IPAC.

IPAC was asked to provide input on three main points where consensus within the CTC-WG had proven difficult, comprising: firstly whether the guidelines should be

comprehensive and detailed, or streamlined standard operating procedures (SOPs); secondly guidance on what constitutes acceptable wastage levels versus programmatic gains, recognizing that more cost-effectiveness data is needed to clarify trade-offs; and thirdly whether combined vaccine delivery (e.g. HPV + TT) should be encouraged, even though it potentially undermines the benefits of CTC by having a cold chain dependent vaccine. IPAC was also asked to consider three additional issues:

- Given the experience in Uganda, should CTC be implemented only after a country has delivery experience with the given antigen, e.g. HPV, or immediately to allow CTC application in constrained areas?
- Should the application of the CTC strategy be recommended nation-wide, or only at district level? Can the strategy be adopted only by select health facilities, or would this pose too high a risk of confusion and inefficient use of resources?
- As HPV vaccine is expensive and in short supply, should any leftover vaccine that has been taken out of the traditional cold chain for a CTC excursion be used to vaccinate older girls rather than discarding?

Discussion:

There was agreement among IPAC Members that the most important documents are those that support the national or subnational health planner, and the frontline healthcare worker; these could contain links to information sources for those health professionals interested in obtaining more information on the evidence base. As national level policy makers and National Immunization Technical Advisory Groups (NITAGs) also need to understand the CTC strategy and the scientific basis for its recommendation, such information could be provided separately or in an annex. Another option would be a generic guidance document for decision-makers that applies to CTC for all vaccines, and shorter documents for vaccine-specific indications to be used by healthcare workers.

The possibility of coupling delivery of HPV vaccine with other vaccines that need cold chain was discussed and IPAC members agreed that while the benefits of combining CTC with cold chain delivery appear limited, this should be a decision taken at national level based on the immunization schedule and proposed delivery strategy.

The Committee also noted that, when assessing whether or not to introduce the CTC strategy for HPV, countries should be empowered to also decide whether or not a trial introduction of HPV prior to introducing the CTC strategy is warranted. IPAC Members suggested that if the generic programmatic shortfalls highlighted in the Uganda pilot, especially problems with forecasting the total vaccine needed and lack of clarity over the target population, are overcome, then countries should be fully able to use the CTC strategy when they first introduce HPV vaccine. Routine monitoring arrangements could be expanded to include monitoring of CTC usage issues including wastage. Likewise, it should be decided at national level whether to apply the CTC strategy to HPV vaccination nation-wide or to limit it to certain geographic areas or populations.

Although the possible benefits of re-using left-over vaccine rather than discarding it are appreciated, on balance the Committee felt that such vaccine should not be returned to the cold chain after deployment in CTC; that is: that programmes should adhere to the original definition of CTC as allowing only one excursion outside the cold chain. IPAC noted that re-use of left-over vaccine is not recommended in other campaign-based usages, and there was concern among Committee Members that recommending this practice could divert attention from important improvements in micro-planning prior to introduction to assess demand and target population.

(c) Planning for OCV/CTC Pilots in Zambia and Uganda. *(Francisco Luquero, MSF-EpiCentre, and Lorenzo Pezzoli, WHO/WHE – presented for strategic guidance)*

Oral cholera vaccine (OCV) is usually administered in response to a cholera outbreak or during a humanitarian crisis. Its use is also being promoted preventively in cholera “hot

spots”, that is: in settings that predictably experience cholera epidemics on a regular basis. Piloting CTC for OCV would be better placed in these non-emergency uses rather than in a humanitarian crisis situation. Zambia, Malawi, Haiti and Uganda are examples of countries containing cholera hotspots, with plans for OCV preventive campaigns in the near future. Those with potential to inform the CTC deployment of OCV are: Zambia, which plans to vaccinate with OCV in September and October 2018 and in April and June 2019; Uganda, which plans to vaccinate with OCV in July and October 2018; and Malawi, which plans to vaccinate with OCV in July and August 2018. It is anticipated that all upcoming campaigns can generate useful information for CTC pilot planning, with a formal CTC pilot possible in early 2019.

CTC can help address some of the challenges specific to OCV campaigns, given the vaccine is relatively more complicated than other vaccines in cold chain logistics and requires a two-dose schedule. Using OCV in CTC has the potential to increase the performance of the vaccination teams, reduce the time required to vaccinate an at-risk community, increase the vaccination coverage and reduce the cost of vaccine delivery. The fact that OCV is relatively expensive and often in short supply reinforces the need for accurate micro-planning and demand estimation.

IPAC was provided with reports on the limited experience with “off-label” use of OCV out of the cold chain during distribution, and while vaccine effectiveness studies have shown good protection of OCV using this strategy, the disadvantages of off-label use, in terms of liability born by the country and the lack of controlled and validated implementation measures, reinforce the importance of pursuing CTC deployment and licensing additional OCV products for use in CTC. As noted, the Shanchol™ vaccine is now prequalified for use in CTC, and Eubiotics is also working on obtaining CTC labelling for their OCV product Euvichol. It was noted that the maximum 14 day excursion, as in the license for Shanchol™, is not ideal when the two dose schedule calls for a two week interval, especially given the desirability of allowing the second dose to be self-administered.

Discussion:

The Committee suggested that examination of existing data, including whether interpolation is possible, may help assess the potential for additional time out of the cold chain. It was noted that an additional barrier to extending the CTC duration is the vaccine vial monitor (VVM). While the VVM 30 can be exposed to 30 days at 37°C before it reaches its endpoint, if OCV is stored up to the 40°C that its licensure permits, the VVM 30 may reach its endpoint as early as day 14, thus requiring the vaccine to be discarded. This may require manufacturers seeking extended CTC durations to also seek other VVM types, the market for which is limited.

IPAC noted that, given many countries have significant experience of OCV preventive campaigns using the traditional cold chain, it will be important for OCV-CTC pilots to demonstrate that CTC can improve coverage, accelerate response times, and reduce operational costs. IPAC suggested that the CTC-WG, and others, could provide input to methods for future pilots, to assist with identifying core questions that will test the feasibility, acceptability, and cost savings in the CTC approach.

(d)The Hepatitis B licensure/programmatic needs challenge. *(Nora Dellepiane, CTC-WG Chair and IPAC Member – presented for strategic guidance)*

The Global Health Sector Strategy on Viral Hepatitis for 2016–2021 has set targets for global coverage of hepatitis B vaccine birth dose (HepB-BD) of 50% by 2020 and 90% by 2030, along with other approaches to prevent mother-to-child transmission. In 2016, SAGE also reinforced their earlier recommendation for vaccination within 24 hours of birth. As of 2016, 101 countries had a policy to administer hepatitis B vaccine birth doses to all infants and another 20 countries administer the birth dose only to infants born to mothers with chronic HBV infection. Seventy-three countries (38% of the WHO Member

States) do not have a HepB-BD policy. Hepatitis B vaccine is both highly freeze sensitive and highly heat stable. As a VVM30 suggests, the vaccine can be maintained at 37°C for 30 days without a harmful reduction in potency, some countries have elected to use the vaccine out of the cold chain (OCC); however this remains an off-label usage, not supported by vaccine manufacturers' licensing, and not acceptable to many countries. The challenges to the timely provision of HepB-BD relate to reaching newborns with an equipped, trained vaccinator within 24 hours of birth; most logistically difficult for births outside of health facilities, and in settings with infrequent births where multi-dose presentations and short re-supply times are less feasible.

WHO has been promoting the use of HepB-BD in a CTC to help overcome these barriers, and in 2016 SAGE urged all vaccine manufacturers to pursue regulatory approval for CTC use of their prequalified monovalent HepB vaccine. As reported, only one has succeeded so far. A major constraint is the lack of clarity in the demand forecast for a HepB-BD in a CTC. IPAC heard that the CTC Working Group is working on draft product profile characteristics for HepB-CTC which focus on time, temperature and dose per container. One currently proposed optimal operational target is 28 days at 40°C. At present, available thermostability data for vaccines that are potential candidates for CTC do not match this aspiration; for example: one is documented as stable for four days at 45°C or for 28 days at 37°C. The absence of data on stability at 40°C, raises questions regarding the potential interpolation of temperature data which cannot yet be answered. Other options under discussion include making a special variation to the standard CTC minimum temperature, for example to 37°C. Other CTC-WG discussions have suggested preferences for single dose containers, and/or possibly single dose compact Prefilled Autodisable Devices (cPADs) that could be used by lesser trained health workers based perhaps in the community.

IPAC guidance was sought on the following aspects of use of Hepatitis B vaccine in a controlled temperature chain: the potential market and value proposition for CTC qualified vaccines; comments on the suggested key product profile characteristics for Hep B birth dose (BD) in use in CTC; and recommended next steps.

Discussion:

IPAC Members noted that the success of bringing an affordable meningitis vaccine in a CTC (MenAfriVac) to market was due to the predictability in meningitis campaigns, with a clear demand that could be signalled to manufacturers. However, service planning for vaccination bound in time to an event that is inherently unpredictable (childbirth), is very difficult, especially in the African Region where 50% of births occur in the community. Although HepB-BD administration is a target in the African Regional Strategic Plan, to date, relatively few countries have introduced it due to the challenge of having a trained healthcare worker to administer the birth dose to infants within 24 hours.

The Committee also highlighted the challenge of supply, as much of the monovalent hepatitis B antigen is used to formulate the pentavalent HepB-Hib vaccine and some bulk manufacturers are discontinuing their production of monovalent HepB vaccines. UNICEF Supply Division have issued a new tender for HepB monovalent and have agreed with the WHO Prequalification Team that they will accept new applications of this product for prequalification to encourage increased production. IPAC Members also noted that the majority of settings in the region most advanced in HepB-BD, the Western Pacific, have been able to link vaccination to scaled up facility-based childbirth, where CTC is less applicable. Given that HepB-BD usages are limited in special settings such as community-based childbirth, this may reduce the incentive for manufacturers to engage in CTC re-licensing.

IPAC noted that the CTC-WG will need to continue work to better characterize the likely demand and feasibility of HepB-BD in a CTC, recognizing that this may require tighter focus on very specific usage scenarios such as community outreach.

Session III. Optimizing vaccine supply

IPAC noted that improved global monitoring of Immunization Financing shows a clearer picture of the shortfall between what is currently being spent and what needs to be spent to achieve immunization goals. The Committee noted the progress that is needed by national governments to take up immunization financing, and the importance of communicating the risk of failure in preventive health to decision-makers. IPAC also added to the discussion of global financing, the recognition of the risks posed by polio transition to operational budgets.

IPAC Members welcome the MI4A Initiative's provision of more nuanced data in the area of supply and access which is providing vital information to countries to increase their understanding of whom they are buying vaccines from and at what price. The benefits to Middle Income Countries (MICs) in particular was applauded. The Committee noted with concern continuing national stock-outs, and stressed the importance of engaging with countries to understand better the programmatic issues, such as poor supplies management, that may exacerbate this issue. IPAC recommended collation of different country responses to vaccine shortages and providing a menu of alternatives that can be employed in the face of global shortages; such as fractional dosing, improving forecasting, and modifying immunization session sizes.

IPAC was presented with updates on the global calculation of indicative wastage rates, including a refinement to the new method for estimation of immunization session sizes, previously reviewed and endorsed by the Committee. This was welcomed, with the well-recognized caveat that some wastage is unavoidable if coverage is to improve. IPAC was also presented with an update on the major revision to the Effective Vaccine Management (EVM) assessments (EVM 2.0). The Committee acknowledged the major role that EVM assessments have played in helping countries improve their supply chain. They also commended the different perspective in the EVM analyses that could facilitate evaluation of other aspects of service delivery such as waste management. IPAC urged that among the increased number of indicators, the focus remain on those with direct relevance to informing local improvement plans, and provided additional ideas on how to ensure trends remain comparable across assessments conducted under EVM 1.0 and 2.0.

i. Global Immunization Financing update. *(Claudio Politi, WHO/EPI – presented for information)*

IPAC was presented with an update on WHO's work on the monitoring of global immunization financing. At the global and regional level, the GVAP and the Addis Declaration⁶ ask countries to commit to, and increase financing for, immunization. At the country level there are four key approaches countries can take to do this: efficient use of existing resources, mobilization of additional resources over time, increasing share of domestic resources, and ensuring country driven decisions and ownership.

The status of immunization financing globally is monitored through the GVAP immunization financing indicator that measures domestic expenditure for immunization per person targeted, based on data collected in the WHO/UNICEF Joint Reporting Form (JRF). Between 2010-2016, based on data from 127 countries, this figure increased globally from US\$31 to US\$39.⁷ In 2016, globally, governments were funding around 71% of total expenditure on routine immunization (both vaccine and operational costs)

⁶ <http://immunizationafrica2016.org/ministerial-declaration-english>

⁷ http://www.who.int/immunization/programmes_systems/financing/en/

although LMICs funded on average 26% of their immunization programme needs through domestic sources. Moving towards financial sustainability and introducing new vaccines requires government ownership and strong political commitment.

The main challenges in immunization financing at the global level, include an unfinished agenda on securing basic immunization, limited access to affordable vaccines by Middle Income Countries (MICs), relatively high prices for new vaccine, and problems for countries transitioning out of traditional support mechanisms such as Gavi, the Global Fund and support from the Global Polio Eradication Initiative (GPEI). At the country level issues relate to: limited fiscal space (the budgetary room that allows a government to provide resources for public purposes without undermining fiscal sustainability); inadequate budget allocation for the health sector in general; and the risk of either catastrophic health spending or inability to access health care by poor populations.

To translate the financing goals articulated in the GVAP into country plans, the comprehensive Multi-Year Plan (cMYP)⁸ provides countries with an analytical and budgeting tool to assist in the area of planning, budgeting, financing and sustainability which can be used at national level to plan for, advocate for and secure financing for vaccine and operational costs of immunization. The cMYP is critical for securing appropriate funding for immunization both at the country level and in discussions with donors.

Discussion:

IPAC Members also noted that a significant threat to immunization operational funding is coming from the polio transition⁹ as many countries' health systems have been built or strengthened around efforts to end the disease, and with the withdrawal of donor funding, will be dependent on domestic funding. Key areas such as disease surveillance, historically funded by the GPEI, may face serious budget cuts and no longer be able to operate. Countries are developing transition plans to enumerate costs and figures for what other donors or the countries themselves need to start financing.

The Committee also noted the additional pressures on countries as they transition out of Gavi support once their Gross National Income (GNI) per capita rises above US\$ 41,580, and they take on full responsibility for their vaccine costs. Gavi provides support to countries to plan for and achieve financial sustainability for vaccine and immunization costs; they urged WHO and UNICEF to continue to support countries in this endeavour.

IPAC urged those working in immunization financing to strengthen the link between the Ministries of Health and Financing so that commitments made to introduce new vaccines (a key driver of increased immunization budgets), are supported by transparent information available to all concerned. The Committee pointed out that national governments have made commitments to increase health and immunization financing through the Abuja and Addis Declarations, and noted that efforts need to be made to bring these issues to Parliamentary bodies, where funding decisions are made, and not limit advocacy efforts to the Ministries of Health.

ii. Improving Vaccine Access. *(Tania Cernuschi, WHO/EPI – presented for strategic guidance)*

The WHO 13th General Programme of Work (GPW), approved by the Seventy-first World Health Assembly (WHA), foresees achievement of Universal Health Coverage (UHC) as one of three key goals aiming at saving, making safer and improving the quality of lives. A corner stone of the UHC is access to safe, effective, quality and affordable essential

⁸ http://www.who.int/immunization/programmes_systems/financing/tools/cmyp/en/

⁹ <http://polioeradication.org/polio-today/preparing-for-a-polio-free-world/transition-planning/>

medicines and vaccines for all, without suffering the risk of financial hardship. In response, the WHA mandated WHO to design an Access Roadmap, for 2019-23, in consultation with Member States to facilitate access to medicines and vaccines.

WHO's Market Information for Access to Vaccines (MI4A) initiative aims to advance UHC through enhanced access to safe, effective, quality, and affordable vaccines for all. This responds to specific requests from Member States and SAGE to address vaccine market information gaps. MI4A focuses on vaccines that have availability constraints, affordability issues, or that are subject to important policy or vaccine pipeline changes. In particular, MI4A aims to address the needs of self-procuring countries that do not benefit from international financing or procurement support. WHO is working with stakeholders to provide guidance and strategies to enhance affordability and availability of vaccines. Country fact sheets¹⁰ have been developed to allow countries to see self-procuring prices, other products, and options from other manufacturers. Meningitis and HPV vaccines have been chosen for study in 2018, based on the current shortages of these vaccines and the importance of vaccination with these vaccines to reach elimination goals and respond to outbreaks and emergencies.

With respect to availability of vaccines, the global immunization community is far from reaching GVAP targets for reducing the number of stock-outs at country level. Although there is great variability between countries, globally, 35% of national-level stock-outs are reported as being due to global vaccine availability issues and 36% due to funding or procurement delays. Only 6% of countries report having national level stock management issues that contribute to vaccine stock-outs.

IPAC was asked to consider how best to engage countries in these initiatives, what kind of support countries need to leverage available information and analysis (noting that resources to engage with non-Gavi MICs and HICs are extremely limited), how best to use available fora to share information, and what might be other opportunities for engagement.

Discussion:

IPAC Members congratulated the MI4A Initiative for helping to bring the data on pricing, availability and procurement of vaccines out of the realm of research and health economics and make it available to programme managers and decision makers. IPAC noted that due to limited financial resources, MICs are lagging behind both high-income countries (HICs) and LMICs in introducing new vaccines, in increasing their routine immunization coverage, and are not conducting the preventive health actions needed to secure the health of their populations. The Committee expressed its hope that the support behind the WHO/GPW 13 will bring about additional change and more interest in this area.

The Committee noted with concern continuing national stock-outs, and stressed the importance of engaging with countries to understand better the programmatic issues, such as poor supplies management, that may exacerbate this issue. IPAC recommended collation of different country responses to vaccine shortages and providing a menu of alternatives that can be employed in the face of global shortages, such as fractional dosing, improving forecasting, and modifying immunization session sizes. Improved wastage management is also a contributor, with caveats that some wastage is unavoidable if coverage is to improve.

In terms of additional resources or fora to further intelligence in this area, IPAC Members suggested that the MI4A contact the Sustainable Immunization Financing Programme at

¹⁰ http://www.who.int/immunization/programmes_systems/procurement/v3p/platform/en/

the Sabin Vaccine Institute, UNITAID and other entities involved in procuring commodities for MICs, as well as the Community of Practice in Immunization Value, Costing, Financing and Economics¹¹ initiated by the Bill & Melinda Gates Foundation.

iii. EVM 2.0 Progress. (*Souleymane Kone, WHO/EPI – presented for information*)

Update on Global Wastage Rates:

Improving vaccine forecasting by countries results in more accurate production from manufacturers, avoids global shortages, and facilitates procurement of accurate quantities of vaccine at country level, ensuring availability of potent vaccines at the service delivery level. Correctly estimating vaccine wastage is crucial in any vaccine forecast but systems for wastage monitoring at country level are weak, and the 2002 WHO global indicative vaccine wastage rates are generic and fail to account for national and sub-national variations. In 2016 a new model was developed to estimate more accurate open vial wastage, and in 2018 this has been refined to apply to normative immunization policies, such as universal coverage targets, session frequency, number of doses in schedule and number of service points (1:10,000 population being a common WHO target). This new approach, draws on the binomial distribution of session size methodology previously reviewed and endorsed by IPAC.

Based on this updated methodology, WHO will revise the global estimated wastage rates, and in consultation with countries and Regional Offices, develop a process for tailoring wastage rates for countries. Application of the new wastage rates will be submitted for endorsement by IPAC in 2019.

Update on the Status of EVM 2.0:

IPAC received an update on the major revisions to the Effective Vaccine Management (EVM) initiative; a joint WHO and UNICEF effort to provide guidance and tools to countries to assess the performance of their supply chain.¹² The EVM Assessment evaluates each level of the supply chain, from the national store down to the health facility level. The results of the assessment provide scores by programmatic area, the analysis of which then leads to an EVM Improvement Plan to bring about improvements in the supply chain. IPAC noted that 151 assessments have now been conducted in 89 countries, but of these, only 17 countries reached the target composite score of 80%.

Version 2.0 of the EVM assessment tool is intended to be a deeper and wider assessment process that will add assessment of waste management, warehousing practices, and include a more holistic view of managerial capacity. It is expected that EVM 2.0 will be better able to establish root causes of problems to guide action plans. EVM 2.0 can be administered using a mobile device and has other features that facilitate a faster more streamlined enquiry process. A WHO core technical team constituted in February 2018 is carrying out virtual and field tests in July and August of this year. A Global Partners' Consultation will be held in September 2018 and the final version of EVM 2.0 is expected to be launched for use by countries in December 2018.

IPAC was alerted to several challenges to rolling out EVM 2.0. Firstly, while the performance measurement scores between EVM 1.0 and EVM 2.0 are largely comparable, care needs to be taken in comparing quantitative scores that may now not accurately reflect true trends in countries' performance. Secondly, more investment and commitment from partners is needed to provide and disseminate guidance materials,

¹¹ <http://immunizationeconomics.org/>

¹² http://www.who.int/immunization/programmes_systems/supply_chain/evm/en/

conduct assessments, develop and support improvement plans and build capacity in countries to carry out self-assessments.

Discussion:

The Committee noted that the revised vaccine wastage rates and accompanying tool under development by WHO to help tailor vaccine wastage rates to realities in countries reflects a different approach to service planning, useful for informing a more efficient use of resources. IPAC Members cautioned those working in this field to exercise caution and not to encourage countries to focus solely on reducing their wastage rates, at the expense of not reaching children.

IPAC Members recognized the major value of EVM assessments to date in helping countries improve their supply chain. They also commended the different perspective in the EVM analyses that could facilitate evaluation of other aspects of service delivery such as waste management. The Committee urged that among the increased number of indicators, the focus remain on those with direct relevance to informing local improvement plans. The Committee also suggested that quick qualitative assessments in different categories (e.g. very good, good, poor) may also facilitate meaningful assessment of trends, for countries comparing assessments conducted under EVM 1.0 and 2.0.

Conclusion and closing remarks by the Chair

The IPAC Chair closed the meeting by summarizing key aspects of the discussions as noted above. He expressed his thanks to all participants, especially noted the engagement of staff from the Gavi Secretariat, the contributions from vaccine manufacturers, and from USCDC and UNICEF. He also thanked the Regional partners for providing a key country perspective to these global level discussions. On behalf of the Committee, he recognized the immense amount of work undertaken by WHO's IPAC secretariat and Working Groups, and by WHO staff working on immunization in general.
