IPAC BULLETIN

October 2017

QUARTERLY UPDATE OF THE IMMUNIZATION PRACTICES ADVISORY COMMITEE

Volume 3, Issue 3 **WORLD HEALTH ORGANIZATION**

A note from the Chair:

Dear IPAC members and observers,

Welcome to the third IPAC bulletin for 2017 – you'll see some interesting updates in the pages that follow, reflecting the busy time over recent months, including an update on the TechNet21 conference, and the accelerating work on the Controlled Temperature Chain. I wanted to share some reflections on the October SAGE meeting that I attended on behalf of IPAC several weeks ago. These are my own thoughts of course, and the formal report on SAGE will appear in an upcoming Weekly Epidemiological Review. At present, all the presentations made at SAGE are available at http://www.who.int/immunization/sage/meetings/2017/october/ (You will notice there is a tab for presentations).

Among many insights in the global overview by Dr Jean-Marie Okwo Bele, it was interesting to hear how, under new leadership and a new Director General, changing strategic directions for WHO are favourable to maintaining immunization as a global priority. Also notable was the mention of potential tiers for WHO interactions with countries: normative guidance for all countries (something both SAGE and IPAC spend considerable time on); tailored inputs to middle level countries; and on-the-ground intensive input to a number of countries with particular system fragilities. Immunization is playing a key role in the Sustainable Development Goals – with the likelihood of having two immunization indicators helping to track progress towards Universal Health Coverage. There was some debate as to whether the indicators under consideration were sufficiently ambitious, and whether composite measures across a number of vaccines (currently at lower coverage) would generate more momentum.

The update on the Decade of Vaccines noted some particular concerns. While coverage has been sustained overall, it remains insufficient and has actually declined in some jurisdictions. Financing available to immunization was generally increasing, except in the European region, where it fell. The proportion of countries reporting vaccine stockouts has risen back up to 34%, from 29% last year. Some middle-income countries not eligible for Gavi support are struggling to procure and introduce newer vaccines.

New work on data disaggregation also enabled presentation of global consolidation of sub-national data. Especially helpful is the recent **State of Inequality** report that informed much of the global update and displays large variability of coverage within countries. This can direct greater focus on underserved communities and enable better tracking of progress in equity. By the way, this report received first prize in the Digital and Online Resources category at the British Medical Association's (BMA) Medical Book Awards in September 2017. The report is available frome the Global Health Observatory repository: http://www.who.int/gho/ .

Health security was a common theme throughout this SAGE, with frequent mention of the new Coalition for Epidemic Preparedness Innovations (cepi.net), highlighting the role of new vaccines in ensuring bio-security and preparedness against epidemic threats. Reports on active use of the cholera vaccine stockpile, and that for yellow fever, highlighted the importance of such preparedness measures. Linked to this is importance of vaccines in the response to anti-microbial resistance; one example is the importance of typhoid vaccine in averting a rapid increase in extremely drug-resistant organisms. IPAC and others advising on immunization programmes will need to give increased attention to delivery of vaccines under emergency and outbreak conditions. New thinking here may also inform the pressing need for new thinking on immunization campaigns, which remain necessary for measles and polio vaccination.

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Inside this issue:

A note from the Chair (cont'd from page 1)

Progress towards **polio** eradication was discussed, of course, with the high level summary expressed as "polio is not yet eradicated, but it will be…" The current schedule is looking towards 2020, and there was welcome news of improvement in IPV supplies, helped as well with increasing use of fractional dosing (a topic IPAC has dwelt on in the past year).

Of interest was the planning for a consultative approach to development of a **new Global Immunization Strategy for 2021-2030**. This feels a few years away, but the process has started and the clock is ticking. There was acknowledgement of the need for a higher level of integration of immunization with other health programmes, with a strong focus on Universal Health Coverage as part of joint work towards SDGs. I encourage you to check out Carsten Mantel's presentation.

Other important specifics where considered, including: vaccine **hesitancy** (noting the new tools on building community demand and confidence from WHO Euro), **rabies** vaccine (work to update the position paper with new evidence on pre/post exposure prophylaxis), **pneumococcal vaccine** (updates on optimal schedules and new vaccine products), **measles and rubella elimination** (noting the need to consider vaccination earlier in infancy) and on **BCG vaccine.**

This meeting was notable for being Dr Okwo-Bele's final SAGE before moving on from WHO, and he was farewelled with some VERY old photos and other ceremonies after the final session. On behalf of IPAC, we thank him for his leadership and pass on every best wish. The meeting also heard the announcement that Dr Joachim Hombach will assume leadership of the WHO Secretariat for SAGE – taking over from the encyclopaedic Dr Philippe Duclos, who expertly steered this group for so many years.

Happy reading,

Chris Morgan

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Renewal of IPAC Chair

"...it was agreed that Chris Morgan should be invited to exceptionally extend his role as Chair by one year …"

In recognition of the current state of transition the Immunization, Vaccines and Biologicals (IVB) department is confronting, especially with respect to changing leadership, it was proposed that we postpone the selection of a new Chair until the changes within the department are completed.

As you may already know, both the IVB Director, Jean-Marie Okwo-Bele, and the EPI Coordinator, Thomas Cherian, are retiring at the end of next month and their replacements have yet to be recruited. It was thought best to allow the new Coordinator and Director to weigh in on the choice of IPAC Chair, and so consequently that decision must be delayed as the deliberations can't proceed further until those two positions are filled.

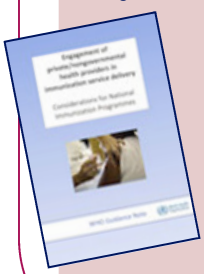
In the interim, it was agreed that Chris Morgan should be invited to exceptionally extend his role as Chair by one year to ensure the continuity needed by the Committee and IVB.

A selection process will be relaunched in the course of that year, most likely around September 2018.

Highlighting new IVB publications!

A number of new guidance documents have recently been published and are now available online. Hard copies upon request!

WHO Guidance Note: Engagement of private providers in immunization service delivery. Considerations for National Immunization Programmes



Published Sept. 2017 (WHO/IVB/17.15)

Available in English and French at:

http://www.who.int/immunization/documents/policies/WHO_IVB_17.15/en/

Vaccination In Acute Humanitarian Emergencies: A Framework For Decision Making and Implementation Guide

Published May / Aug 2017

(WHO/IVB/17.03, WHO/IVB/17.13)

Available in English at:

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

Missed Opportunities for Vaccination (MOV): Planning Guide and Methodology

Published Oct.2017

Guides and field tools available in English at:

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

French and Portuguese coming soon!

From the Working Group frontlines

Update from the Secretariat of the CTC –WG

The main focus of the **Controlled Temperature Chain Working Group** (CTC-WG) over the last three months has been following the progress of the preparations for a pilot implementation of the Human Papilloma Virus (HPV) vaccine through a CTC in Uganda

and the finalization of the CTC Strategic Roadmap for Priority vaccines which was completed in September 2017 and is available on the WHO/IVB website through the following link:

http://www.who.int/immunization/programmes_systems/supply_chain/ctc/en/index2.html

The CTC work in Uganda has been rooted in a study protocol which details the approach to integrating CTC into HPV vaccine delivery strategies in two districts and offers a methodology on specific data to collect. The latter should reveal what kind of impact the strategy has had on HPV immunization efforts in the country and inform decision making both within Uganda, concerning scaling up CTC use to a broader geographic zone, as well as in other countries who could benefit from the lessons learned from this pilot experience. The project just completed actual CTC implementation and has transitioned into the data collection phase during which a qualitative survey will be conducted to assess health worker perceptions

CTC training Photo : A. Kahn

HPV outreach with CTC in Adjumani District Photo : L. Alonso

on HPV vaccine delivery in both the "intervention" districts, where CTC was implemented, as well as in two " control" districts considered to be comparable. Data analysis is expected to be carried out during the first half of November, the results of which will be detailed in a final project report under preparation by the Uganda CTC-HPV Pilot Study Coordinator, Mr Luis Alonso.

A draft version of this project report will be shared with the CTC-WG prior to finalization in order to allow feedback and guidance on recommendations to include.

Update from the Secretariat of the DT–WG

There has been much focus on the end-user acceptability of microarray patches (MAP) in the last few months! The **Delivery Technology Working Group** (DT-WG) have reviewed the results from two separate field studies, that evaluated two different formats of the patch technology. The first was performed by

FIG.1—Georgia Tech/Micron Biomedical MAP Photo : US -CDC

PATH, which assessed the MAP system from Georgia Tech/ Micron Biomedical. This format of patch is based on dissolvable microneedles and does not require an applicator (see fig.1). Activities included an online stakeholder survey of EPI managers in LMICs and other global experts, heuristic human factors analysis, in-house usability testing at PATH and a country level usability assessment in

From the Working Group frontlines (cont'd from page 3)

Ghana. The second study performed by Agence Medicine Preventive (AMP) and funded by WHO assessed the Vaxxas MAP technology, which is based on coated microneedles and requires an applicator (see fig2).

FIG.2: Vaxxas MAP Photo: Vaxxas

This study assessed the perspectives of 4 key stakeholders (healthcare workers, community health volunteers (CHV), community representatives and caretakers) regarding MAP use across 3 immunization strategies, namely healthcare facilities, outreach in fixed posts and house-to-house (HtH) vaccination, in the context of the current measles vaccine schedule. The study was performed in Benin, Nepal and Vietnam. Neither study administered an actual microarray or vaccine but simulated device administration and use in all other ways. Both studies concluded that MAPs have high acceptability and potential applicability by all stakeholders interviewed, across a number of immunization scenarios. Interestingly, both studies also reflected that self-administration of MAP for vaccine delivery is generally not recommended; in the case of the AMP study, this feedback was also received in the case of potential H2H vaccination, from all types of stakeholder interviewed. Data from both studies is ongoing and results will be published in a scientific journal.

A third entity that is developing MAPs also presented the status of their product development to the DT WG. Vaxess (as opposed to Vaxxas) is applying the structural and inherently thermostable properties of silk to develop patches of dissolvable needles, the base of which dissolves instantly to embed slow-release silk-vaccine 'tips' in the intradermal layer, which can deliver active vaccine or drug for 3-4 weeks. Vaxess has seven candidates in early (non-clinical) development, including yellow fever, IPV, influenza and measles containing vaccines. All of three of the MAP technologies mentioned above are currently being supported by the Bill and Melinda Gates Foundation for their potential applicability to administration of measles containing vaccine. All are currently in preclinical or early stage clinical development.

The DT WG has also reviewed the current state of use and optimization of Uniject, branded by the manufacturers Becton Dickinson as Uniject 2.0. BD Uniject technology has been available for some time and is currently used to deliver HepB birth dose vaccines in Indonesia (produced by Bio Farma), was previously used to deliver TT in multiple countries (produced by Bio Farma), and is being introduced in multiple countries for contraception (Sayana Press, produced by Pfizer). Uniject 2.0 is the result of a long-standing programme of continuous improvement; although changes not obvious to the end-user user, the device includes better fit of needle shield and leak reduction by improved seal between port and reservoir and improvements in manufacturing processes. Uniject fill/finish costs have decreased and could ultimately become less than conventional single dose vials depending on scale, but will likely always be higher than cost/dose in multi-dose vials. With this in mind, BD is positioning Uniject 2.0 as a potential solution to reach the sustainable development goal disease elimination and eradication targets by reaching the last mile, particularly in campaigns/ special strategies where SDVs are likely to be considered the most effective, but more costly, vaccination strategy.

"MAPs have high acceptability and potential applicability by all stakeholders interviewed, across a number of immunization scenarios…"

Update from the U.S. Advisory Committee on Immunization Practices (ACIP) – By Kelly Moore

The ACIP is the national immunization technical advisory group that develops recommendations for the use of licensed vaccines in the United States; these recommendations become binding policy upon acceptance and publication by the US Centers for Disease Control and Prevention (CDC). The 25 October 2017 meeting of the ACIP at the CDC headquarters in Atlanta, Georgia, was particularly eventful, with two important decisions voted on: one on a **new 2-dose herpes zoster subunit vaccine** (HZ/su) and another on circumstances warranting a **third dose of measles-mumps-rubella (MMR) vaccine**.

The HZ/su vaccine, recently licensed for the prevention of herpes zoster in adults aged 50 years and older, joins zoster vaccine live (ZVL) which was FDA-licensed in 2006 and recommended by the ACIP for use in adults aged 60 (not 50) and older. To date, 31% of US adults for whom ZVL is recommended have been vaccinated. Clinical trials of HZ/su demonstrated a 97% reduction in zoster among recipients aged 50 and older and sustained >85% protection after 4 years even among persons aged over 70. By contrast, ZVL initially reduces the risk of shingles by about 50% or less, with initial benefit much reduced at older ages; protection is insignificant by 8-10 years after vaccination.

Given the substantial difference in disease prevention and economic models showing that under almost all reasonable assumptions HZ/su would be more cost effective than ZVL, the ACIP made three decisions on HZ/su use: first, it approved the use of HZ/su for all immunocompetent persons aged 50 years and older (recommendations for the immunocompromised will follow in 2018); second, it recommended that all persons who previously received ZVL should now receive HZ/su because it could prevent substantially more disease than ZVL; third, it recommended that clinicians prefer HZ/su over ZVL. Now the focus turns to implementation.

The ACIP chose to address the resurgence of mumps in the US, as this has been a growing issue since 2006 despite high 2-dose coverage with measles-mumps-rubella (MMR) vaccine routinely administered at one year and at 4-6 years. Outbreaks among 2-dose vaccinated persons have become common in recent years on college campuses and in other settings where the force of infection is high due to close prolonged contact among tight-knit groups who often live and socialize in close quarters. Laboratory and epidemiologic evidence suggests that waning vaccine-induced immunity contributes to these outbreaks. Fortunately, complications of mumps illness have been very low among these vaccinated cases, and spillover into the broader community has not resulted in sustained transmission in the general public. Studies of the use of a 3rd dose of MMR in highly vaccinated groups experiencing a mumps outbreak have suggested benefit, but the first study showing a statistically significant benefit was published in the New England Journal of Medicine on September 7, 2017, describing the 2014 outbreak at the University of Iowa and demonstrating that 3rd dose recipients had a 77% reduced risk of mumps compared to their 2-dose counterparts.

The ACIP agreed unanimously to recommend that persons identified by public health authorities as at risk of mumps due to an outbreak should receive a 3rd dose of vaccine. More detailed guidance will soon be developed by the CDC on the identification of at-risk persons, with the recognition that each outbreak is different. Questions concerning the benefit of a routine 3rd dose for a given age group must wait for better evidence of the duration of benefit and the cost-effectiveness of such a broad-based consideration.

Note – *IPAC Member, Kelly Moore, is also a member of ACIP and currently chairs their mumps work group, in addition to serving as a member of the shingles work group.*

Over 300 participants gather in Cascais, Portugal for 15th TechNet Conference

TechNet has a long history dating back to 1990 when the first meeting (or Consultation as it was known at the time) was held in Cyprus and attended by 32 participants representing the four main partners working on cold chain and logistics at the time – namely WHO, UNICEF, PATH, and USAID (REACH/BASICS). Fifteen gatherings later and with a tenfold increase in participation representing over 70 organizations from the public and private sectors, the evolution of the TechNet has moved from a small-scale consultation with key stakeholders to a much larger event with many more players working in this space. It should be noted that in addition to the 340+ participants who joined us in person in Cascais, there were up to 120 participants who joined through the internet to live stream the TechNet Conference from 23 different countries across all five of WHO's regions.

Convened by the WHO-UNICEF Immunization Supply Chain Hub in Portugal on 16-20 October 2017, the overall theme of this 15th TechNet Conference was on **"Building the Next Generation of Immunization Supply Chains"** and emphasised three recent developments since:

Photo: WHO/P. Lydon

TechNet Conference summary (cont'd from page 5)

1. New evidence published in a **Special Issue Vaccine (Elsevier)**: Building the next generation of immunization supply chains. This issue includes evidence-based information on innovative interventions to strengthen and improve immunization supply chains, and thereby allow immunization systems to achieve vaccination coverage goals and reduce inequities in access to services.

2. New **strategies aimed at strengthening immunization supply chains by 2020** across countries according to an endorsed theory of change. If all countries prioritize strengthening five fundamentals (Supply chain leadership, Continuous improvement & planning, Supply chain data for management, Cold chain equipment, and Supply chain system design), immunization supply chains will contribute sustainably to improving the coverage and equity of Immunisation. Interventions focusing on these five fundamentals will invariably:

   - Ensure vaccine **availability** up to the service delivery point with better products and use of accurate data;
   - Safeguard vaccine **potency** with optimized cold chain and temperature management systems;
   - Improve supply chain **efficiency** with system design interventions and improved equipment;
   - **Enable** supply chain improvements and change through leadership, management and coordination.

3. A movement at global level to **collectively accelerate progress towards achieving 2020 goals**. This was initiated in Seattle in November 2016, at a meeting of 72 participants from 20 international organizations. The movement was triggered by the recognition that there is a growing number of key stakeholders vested in strengthening immunization supply chains, and that enhanced efforts are needed for organizations to work more interdependently and collectively across technical areas and countries. Under a collective action framework—a collaborative, systematic approach involving many stakeholders, partners and organizations to achieve significant and lasting change—the organizations represented have committed to work together around a common agenda for change. How to galvanize a wider set of stakeholders—and more importantly, countries— and using the TechNet community, will be an ambition of this conference.

To reflect the overall theme of the conference, the conference format was organized into four *themes* and five daily perspectives.

Themes:

Availability – topics related to vaccine products/ technologies and data systems (LMIS)

Potency – topics related to cold chain and temperature management

Efficiency – topics related to system design, integration and private sector engagement

Enablers – topics related to leadership, management and coordination

Daily perspectives:

Day 1 – Stage-setting during the opening ceremony

Day 2 – Current challenges, successes and lessons learnt

Day 3 – Future innovations, solutions and approaches to address challenges

Day 4 – Getting practical on how to implement improvements

Day 5 – Building a future coalition for collaborative action and change

Complementing the plenary and interactive sessions, the conference hosted many side events including the Manufactures Marketplace, the Innovations Café, the Innovations Pitch Fest and the Poster Gallery.

Throughout the week, the intensity of technical discussions gradually made way for more time to discuss how to use the TechNet community of proactive and create a coalition for immunization supply chain change and action. Session on the last day explored with participants how to attain collaborative action at a local level by connecting dots between country to global and across sector, individuals and communities. Interactive, human -centered design approach breakouts enabled smaller groups synthesize needs and identified opportunities for engagement in the future. The 15th Conference ended with a Call for Collaborative Action and summarized individual commitments and potential collaborators gathered throughout the week. The presentation will be followed by a panel discussion on how these commitments feed into collective action to build the next generation of immunization supply chains.

The TechNet Conference Guide (available at https://www.technet-21.org/en/library/explore/global-initiatives/4170-technet-conference-2017-conference-guide) includes the agenda, session descriptions, list of participants, and other information. If you are wishing you could have been there, you can catch all plenary sessions on the TechNet-21 channel on YouTube.

A summary of the Data Partners Meeting

23-25 October, Cascais, Portugal – **By Jan Grevendonk**

About 50 participants from several Ministries of Health, WHO, UNICEF, CDC, PATH, JSI, AMP, Swiss TPH, and from the newly established SAGE Working Group on data, met in Cascais (the week following the TechNet conference) to discuss on-going collaboration and the need for collective action around immunization data availability, quality, and use. The specific objectives of the meeting were to:

- Finalize a framework for partner collaboration to strengthen immunization and surveillance data for decision-making, brainstorm on its implementation, and start planning for concrete improvement activities.
- Review emerging guidance materials for recording, assessment and use of immunization data, identify gaps, and plan for further development of guidance material.
- Start creating a community of practice around immunization data, and brainstorm on ways to share experiences and collaborate.

The framework for partner collaboration is built around the assumption that if countries and partners invest in the "fundamentals" of data and information systems, this will result in better availability of fit-for-purpose data, that will be used for better programme decision making. During the meeting, small working groups brainstormed on the priority actions that need to be taken to strengthen each of the identified areas, and prioritized these actions. An updated document of the framework will be made available to IPAC by mid-November 2017.

Figure 1: Results of a voting round on "what matters most for better immunization

Next, the meeting focused on identifying the needs for guidance in data and monitoring related areas. A plenary panel discussion highlighted the need for improvement at two levels:

1. Need for more global level clarity and consensus around specific issues, such as levels of disaggregation in administrative systems, ways to measure inequities, ways to deal with population targets in the context of rapid urbanization and migration, etc.
2. Need to translate the guidance better between the global level and the frontline health worker, and develop targeted ways to deliver guidance at all intermediate levels, including the national and subnational programme managers.

Working groups then focused on the

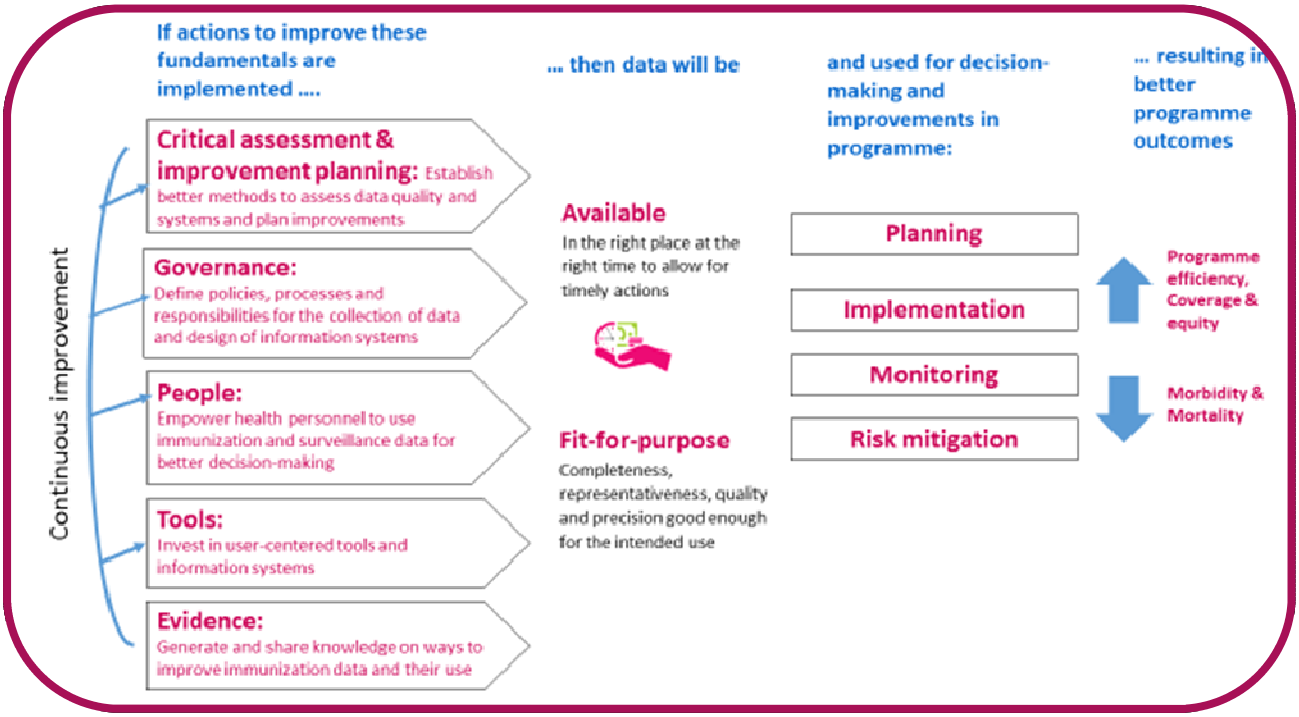


Figure 2: Theory of change for investments in data availability, quality, and use

Data Managers Meeting (Cont'd from page 6)

following areas (more detail to be included in the final report):

- Programmatic data standards: What are the specific areas for which clear global / regional guidance is needed? The group focused on equity, and the need to streamline global and regional level needs, as expressed in the JRF.
- Data use culture: What are the ingredients that foster a positive data use culture? In many cases, this culture is punitive, and characterized by a focus on collection and reporting rather than use. We often assume that the underlying reason for this is lack of knowledge, rather than on other underlying reasons.
- Data quality assessments and improvement planning: much progress has been made, but need for better coordination between HSS and EPI initiatives and methods, more evidence on interventions that work, and follow-up on and support for the single plan.
- Guidance for the development and implementation of electronic tools: programme managers have often only superficial knowledge on what is required for major system implementations. They need support in everything from e-health guidelines to how-to guidance for implementation.
- Denominators: the current situation in which programmes need to rely on census derived estimates for everything from supply chain planning to coverage monitoring, seems to be inadequate. There is a need to investigate alternative methods for target setting at local levels, that acknowledge local issues such as migration, displacement, mobile populations, etc.

The following side meetings were organized:

* Demonstration of a Routine Immunization Module within DHIS2 – a commonly used Health Management Information System, and plans for testing and implementation in 2 Anglophone and 1 Francophone African countries in the next few months. (Tentatively, Kenya, Uganda, and Burkina Faso).
* Building a community of practice: how can we do a better job with Knowledge Management, sharing, use of platforms like Technet-21?
* SAGE Working Group on data – closed meetings
* PATH and PAHO Immunization Learnings project – closed meeting for the advisory group
* WHO and partners to discuss the development and implementation of a common single platform for data management across functional areas of immunization and surveillance of vaccine preventable diseases, and across Regional Offices and Headquarters.

Throughout the meeting, specific topic presentations were made on facility and home-based records, WUENIC and subnational estimates, lessons learned from the BID initiative and PAHO IDQI, and surveillance data, All materials for this meeting can be found here:

https://www.dropbox.com/sh/l66oqyap53shy3q/AAC8GGtI480wvNifYLELX2z0a?dl=0

Upcoming Meetings / Events:

⇒ November 13-17, 2017: Geneva, Switzerland – **Global IB-VPD Surveillance Network Meeting**

⇒ November 28, 2017: Malaga, Spain - **RSV Technical Advisory Group**

⇒ December 14-15, 2017: Geneva, Switzerland – **Meeting on next generation of Cholera vaccines**

⇒ January 10-11, 2018: Kampala, Uganda – **WHO / PATH / UNEPI Investigators Meeting on HPV/CTC Pilot in Uganda**

⇒ March 21-23, 2018: Geneva, Switzerland – **IPAC Annual Meeting**

A final word from the IPAC Secretariat

After much deliberation with respect to when and where our Committee should meet next, I'm happy to confirm that the **next IPAC Annual Meeting** will take place in Geneva, Switzerland at the Chateau de Penthes from the **21st and 22nd of March 2018**. An additional closed session limited to Committee members is scheduled to be hosted on the WHO premises on 23 March 2018. Please mark your calendars and stay tuned for additional details with respect to the agenda. In addition to the usual updates from each of the working groups attached to IPAC, there will also be presentations and discussions on a variety of technical subject matter, including strategies on catch up vaccination. We look forward to seeing you then.

The IPAC Secretariat Team