

Note for the Record

5th Meeting of the SAGE Polio Working Group

World Health Organization, Geneva, September 3 - 4, 2012

Introduction

The fifth meeting of the SAGE Polio Working Group (WG) was held on 3 and 4 September, 2012 at the World Health Organization in Geneva, Switzerland. The meeting was attended by the following WG members: Elizabeth Miller (Chair), Peter Figueroa, Jacob John, Francis Nkrumah, Walter Dowdle, Walter Orenstein, Antoine Kabore, Kimberly Thompson and Nicholas Grassly; Hyam Bashour was unable to attend.

Jay Wenger, Bill and Melinda Gates Foundation, and Julian Bilous attended several meeting sessions as an invited expert. Participants from WHO were Bruce Aylward, Jackie Fournier-Caruana, Philippe Duclos, Tracey Goodman, Hamid Jafari, Roland Sutter, Rudi Tangermann, and Chris Wolff.

On the first day, the WG interacted in separate sessions with teams representing four manufacturers of inactivated polio vaccine (IPV) from Glaxo-Smith-Kline, SANOFI, the Serum Institute of India, and the Statens Serum Institut (Denmark). Manufacturers responded to a series of questions previously provided to them by the WG (see Annex III).

This note presents a summary on main findings, conclusions and recommendations from the 5th WG meeting, and summarizes presentations and discussions on main agenda items (see agenda in Annex I).

1 Background and objectives of the fifth meeting

The main objective of the fifth SAGE Polio Working Group meeting was to prepare for renewed interaction with SAGE on the planned cessation of OPV2 (replacing tOPV with bOPV for routine immunization) through:

- (a) detailed review of the current status of the GPEI, of key pre-requisites for OPV2 cessation, and of the GPEI draft 'Endgame and Legacy' strategic plan 2014-2018;
- (b) direct interaction with IPV manufacturers, to learn more about available IPV products, prices and supply options, particularly in view of the need to develop 'affordable' IPV options for low and low-middle income countries as IPV will be the only poliovirus vaccine available for routine immunization after OPV cessation;
- (c) discussion of 4 main questions related to OPV2 cessation: on IPV introduction, ID vs IM application of IPV, timing for implementing OPV2 cessation, and on the duration of IPV use following final cessation of routine OPV.

2 Summary of main findings, conclusions and recommendations

Following discussions at the 5th meeting, the WG agreed on the following main findings, conclusions and recommendations.

- 2.1 *Cessation of OPV2 is central to the new 'polio endgame'.* OPV2 cessation should be a central, prominent and near-term goal of the new 'polio endgame.' Wild poliovirus type 2 has been eradicated for >10 years and OPV2 cessation will eliminate the generation of new outbreaks due to type 2 Sabin viruses and nearly 50% of vaccine-associated paralytic poliomyelitis. OPV2 cessation is a seminal step in the polio endgame culminating in the eradication of all wild polioviruses, the cessation of all routine OPV use (to end vaccine-associated paralytic polio and vaccine-derived poliovirus outbreaks), and the end of all poliomyelitis disease.
- 2.2 *Use of IPV to manage risks associated with OPV2 cessation.* OPV2 cessation will expose the global population to a new, exceptional era in the history of vaccination, in which there will

be a low, but real risk of type 2 polio outbreaks due to circulating vaccine-derived polioviruses, long-term VDPV excretors and reintroduction from containment failures (the last WPV type 2 cases, which occurred in northern India in 2002-2003, were associated with the introduction of a laboratory strain).

The risks of new cVDPV2 emergences extend into the period immediately following OPV2 cessation, because some OPV2 viruses may be circulating silently in populations with relatively low population immunity at the time of cessation. The possibility of sustained transmission of a type 2 virus increases with increasing population susceptibility following cessation of all routine and supplemental use of OPV2. IPV, which is trivalent and includes serotype 2, will be the only poliovirus vaccine available for type 2 protection. At least 1 dose of IPV should be introduced into routine immunization programmes prior to or at the time of OPV2 cessation to yield the following expected benefits:

- a) the prevention of paralytic polio in individuals successfully vaccinated with IPV who get exposed to a cVPDV type 2, Sabin type 2 (VAPP) or wild poliovirus type 2;
- b) improved immunological response in individuals previously vaccinated with IPV when receiving mOPV2 (and potentially IPV) vaccination given in response to a WPV2 or cVDPV2 outbreak that occurs after OPV2 cessation;
- c) reduced transmission of cVDPV2 or WPV2 should they be introduced (i.e. there is evidence to suggest that IPV reduces the titer of fecal virus excretion and duration of shedding and is equivalent to OPV in decreasing oropharyngeal shedding);
- d) boosting of immunity to wild polioviruses type 1 and 3 in vaccine recipients, which may further accelerate wild poliovirus eradication.

For countries at particular risk of cVPDV emergence, the suggested minimum 1-dose IPV policy may need to be complemented with additional measures (e.g. pre-OPV2-cessation boosting with tOPV SIAs to maximize population immunity to serotype 2 or introduction of a 2nd IPV dose, potentially with catch-up campaigns).

- 2.3 *Target price for an affordable IPV.* Based on consultation with manufacturers, volume purchasing, guaranteed procurement and other such approaches can substantially reduce the price of current IPV products below that currently available to Unicef (i.e. US\$2.75/dose) and can play a role in facilitating the early introduction of IPV for OPV2 cessation. Such approaches cannot achieve a target price substantially below US\$1.00/dose for an 'affordable' IPV product for low-income settings due to inherent costs in the production of the current vaccine.

Volume purchasing of whole dose IPV, potentially subsidized to achieve a more affordable near-term price, may be an important part of a global IPV introduction strategy for low and low-middle income countries. The affordable IPV options that have been identified in clinical and preclinical studies, but which current manufacturers have not yet fully developed or licensed, must also be realized to ensure sustainable solutions for low and low-middle income countries. The recommendation to include at least one dose of IPV in routine immunization (with additional use as needed) reflects a risk management perspective independent of cost considerations. However, the lower the price of IPV, the more cost-effective IPV becomes as an option. Based on the interaction with manufacturers, the WG expects the international community to collaborate with manufacturers to work toward a target price of \$0.50/dose of IPV for low-income countries.

- 2.4 *Fractional dose, intradermal (ID) or adjuvanted, intramuscular(IM) IPV as "low cost" IPV options.* Following an extensive review of potential strategies for achieving a low cost trivalent IPV product for OPV2 cessation in the near term, two viable approaches emerged for reducing the cost substantially below US\$ 1 per dose: intradermal (ID) fractional (1/5th) doses

and adjuvanted intramuscular (IM) IPV. Both approaches face substantial regulatory and/or development challenges but these can be addressed in the near-term (24-36 months) with appropriate, intensive support from the international community, the development of a multi-dose vial policy for IPV, active engagement by manufacturers, and rapid mapping of regulatory pathways and options.

- 2.5 *Need to make both fractional intradermal (ID) and adjuvanted intramuscular (IM) options available.* As countries may have different preferences with respect to the ID vs. the adjuvanted IM dose-sparing options, and based on limited evidence about the related risks, costs, and benefits, both options should be pursued. Some immunization program managers identified a potential preference for ID administration if IPV were to be given at an immunization contact during which other IM injections are already given (e.g. DPT, PCV); other immunization programs may prefer not to introduce a new delivery technology.

WHO has been collaborating with the manufacturers of needle-free injection devices for several years, which has resulted in the engineering of two new intradermal devices that are currently being investigated in clinical trials. If successful, these devices could be used to administer fractional-dose IPV intradermally.

- 2.6 *Need to continue IPV for at least 5 years beyond bOPV cessation.* Recognizing that as the risks associated with eventual bOPV cessation may be similar to those following OPV2 cessation, countries should plan to continue IPV vaccination for at least 5 years after bOPV cessation (i.e., after stopping all routine use of OPV). This issue will be reviewed as additional information becomes available, particularly the experience with OPV2 cessation.
- 2.7 *Target synchronous OPV2 cessation by 2015-2016.* As a fundamental step in the polio endgame, synchronous OPV2 cessation should be targeted for the near-term (i.e. 2015 or 2016). Additional consideration of the time frame will be reported back to SAGE in April 2013 following further review of the prerequisites for OPV2 cessation, including the development of affordable IPV options, long-term biocontainment policy, and post-OPV outbreak response policy.

3 Next steps and action points

The WG agreed to the following main next steps and action points:

- a) **Follow-up letter to manufacturers:** the WHO secretariat should write a follow-up communication to IPV manufacturers who had been invited to the WG meeting, to request them to summarize the information they had provided to the WG during the interaction on 3 September. Manufacturers should be asked to describe the strategies which a company is able and willing to pursue to work towards developing an 'affordable' IPV product, to comment on the time-frame for this development work, and most importantly, to provide, as much as possible, specific information on the price per dose that this development may eventually result in.
- b) **Background paper for SAGE:** the WG requests that the secretariat provide an expanded background paper, to be provided to the WG and then to SAGE (and to be included in the SAGE 'yellow book'), in order to summarize as completely as possible the scientific evidence to underpin the recommendation for a 1-dose IPV strategy.
- c) **WG conference call end-October:** the WG should hold a pre-SAGE conference call (end-October / early November) to finalize WG recommendations and the WG presentation to SAGE at their November meeting.
- d) **IPAC presentation on IPV delivery through IM vs. ID injection:** the outcome of the recent 5th WG meeting, as well as the assessment of implications of adding a dose of IPV either through

IM (full or adjuvanted dose) or through ID injection (fractional dose), should be presented to the SAGE Immunization Practices Advisory Committee (IPAC) at their meeting in early October.

- e) **Regional consultations:** the 'polio endgame', including plans for OPV2 cessation, should be explained and discussed at the regional and country level, including at regional EPI manager's meetings (EMR: 18 September; this discussion has happened at the time of writing - 6/20/12, see ANNEX IV; AMR/PAHO: 17 October; SEAR: mid-December)

ANNEX I Presentations and discussions on other agenda items

The following are brief summaries of presentations and key agenda items from the 5th meeting.

3.1 Current status of the GPEI and outcomes of VDPV meeting.

B. Aylward reported on *major developments in the Global Eradication Initiative since the last WG meeting* in early February 2012. Key development in terms of polio epidemiology was that in end-February 2012, India was formally removed from the list of countries with wild poliovirus transmission; the last wild poliovirus case in India was detected in January 2011.

Also, type 3 wild poliovirus cases are only reported from northern Nigeria and Pakistan. The only area reporting type 3 WPV in Asia is a small circumscribed area of Khyber agency, North-West Pakistan.

Following the report of the GPEI's Independent Monitoring Board (IMB) in the fall of 2011 and the subsequent discussion on the status of the GPEI at SAGE in November 2011, the World Health Assembly declared polio eradication as an *emergency for global public health* on 25 May 2012. Since then, efforts have been targeted at the remaining priority countries to establish and improve accountability structures for government and partner agency staff, to identify and recruit more than 6500 additional partner agency staff (WHO: technical assistance, UNICEF: social mobilizers) at the local level in highest risk areas, and to establish multiple new strategies to improve the quality of SIAs to identify and vaccinate children missed by SIAs.

Activities in the three endemic countries Afghanistan, Pakistan and Nigeria have received effective support from the highest political level, including from the Heads of State.

As of 11 September 2012, the majority of the 136 cases reported in 2012 were reported from the endemic countries (Nigeria: 84, Pakistan: 30, Afghanistan: 17, with only 5 cases reported from Chad), while the number of cases reported at this time last year was 379, reported from 11 countries.

Nigeria currently is the only country in the world where the number of cases has considerably increased compared to last year (from 26 in 2011 to 84 cases this year).

Type 2 vaccine-derived poliovirus (cVDPV2) from the known foci of transmission in northern Nigeria and south-east DR Congo had been reported last in April 2012; however, cVDPV2 - with evidence of prolonged undetected transmission - was recently also reported from both sides of the Kenya-Somalia border.

The large remaining financing gap of around 600 million USD to implement the 2012-13 emergency plan is a continued serious problem, which has already led to the cancellation of planned SIAs in more than 30 countries at risk of importation and spread.

Discussions about OPV2 cessation at SAGE and the WHA. In April 2012, SAGE re-affirmed the need for sequential cessation of OPV vaccine serotypes, starting with type 2 (i.e. synchronous replacement of tOPV with bOPV for routine immunization, or OPV2 cessation), and, to mitigate possible associated risks, had recommended for countries to consider to introduce 1 dose of IPV into their routine immunization schedules prior to OPV2 cessation.

While promoting the concept of introducing a universal 1-dose IPV policy in the context of OPV2 cessation, SAGE recognized and accepted that it was highly probable that IPV uptake would be low in low-coverage countries. SAGE requested that WHO and the GPEI continue to work towards making low-cost options for IM and IM IPV available within 1 year, and decided that, while OPV2 cessation was urgent, 2014 was too early as the target date for OPV2 cessation.

In a resolution on polio eradication in May the WHA endorsed the concept of OPV2 cessation, but expressed alarm over current IPV prices, limited IPV supply options, and lack of clear cost-benefit

assessments. The WHA requested WHO to work with partners and manufacturers to enhance IPV affordability and availability.

The Global Certification Commission (GCC), in August 2012, welcomed the benefits of an early cessation of OPV2 use, and recommended a formal process for Regional Certification Commissions (RCCs) to 'conclude' (not certify) that wild poliovirus type 2 was eradicated, based on time since WPV2 was last seen (>10 yrs), and on the quality and sensitivity of surveillance in the Regions. The GCC recommended that Phase I of lab containment of WPVs needs to be completed globally, prior to OPV2 cessation. The GCC is willing to consider evidence to conclude WPV2 was eradicated as early as mid-2013.

3.2 *Development of the Polio Endgame and Legacy Strategy*

A. Freeman introduced the current draft strategic plan for the polio endgame and legacy options. This document is currently being developed in close consultation with GPEI spearheading partners and other initiatives (i.e. GAVI), as well as with WHO Regional Offices; further consultations about this project will be held with the IMB in October and with SAGE in November.

The document will be drafted using three main sections: a) the endgame strategic plan, including the eradication of polio, and management of associated risk, b) the legacy, i.e. to define the broader global health benefits of the global polio programme, as well as c) the financial requirements 2014 to 2018 (i.e. a 2014 to 2018 indicative budget).

Key assumptions of the document will be that WPV transmission will be interrupted globally by end-2014, OPV coverage reaches the necessary thresholds, full financing and effective implementation will be feasible, VDPVs can be eliminated, and affordable IPV will be available for low-income settings.

Major thematic areas, timelines and milestones for the 'Endgame' section will include a) routine immunization, b) SIAs, c) surveillance, d) communications and social mobilization, e) lab containment and f) the certification process. Geographical considerations and risks to be considered will relate to wild poliovirus and vaccine-derived poliovirus. Long-term poliovirus risks during the endgame will be managed with a long-term IPV policy, effective response activities to cVDPV using IPV, and the use of polio anti-viral compounds.

The 'legacy' part of the document will include a discussion of the polio infrastructure (human resources, capacities and infrastructure, social mobilization and knowledge), as well as a discussion of 'broader benefits' of polio eradication - including an expanded global surveillance response capability.

3.3 *Affordable IPV for routine immunization: new study results contributing to policy discussions*

R. Sutter provided updates on new study results that are relevant to the ongoing policy discussions. Three main policy-relevant questions to address were:

- whether recent results from the Indian study on intestinal immunity confirm that IPV boosts intestinal immunity in infants and children with a history of multiple OPV doses;
 - preliminary analyses from this high-quality trial (few drop-outs, high compliance with study procedures and completion of questionnaire data) suggest that a single dose of IPV can significantly decrease excretion in all age groups, but that the greatest benefits are seen in older children because their intestinal immunity has waned; full analysis of the results is expected in the next 3 months;
- whether or not data from the Cuba study (phase 2) show a difference between intestinal immunity induced by fractional-dose IPV compared with full-dose IPV;

- preliminary conclusions include that full-dose IM IPV and fractional-dose ID IPV (1/5 of a full dose) induce a similar immune response, and that tOPV (live virus) can accelerate intestinal immune response in IPV-vaccinated infants (regardless whether vaccinated with a full or fractional IPV dose);
- what evidence can be derived from Hungarian VAPP on the one-dose efficacy of IPV against VAPP;
 - data from Hungary suggest a highly significant reduction of VAPP following the introduction of one dose of IPV.
 - the WG noted however that other data from a WPV1 outbreak in Senegal suggested potentially lower effectiveness of a single dose of IPV.

3.4 ID vs. IM administration of IPV in context of OPV2 cessation

J. Bilous reported on findings of a review of operational differences between using IPV as a full dose (IM) vs. application as fractional dose (ID), comparing differences relating to service delivery, cold chain and logistics, management, training, supervision, and cost. The assessment also included interviews with EPI managers from Asia (India), and Africa (one West and one East African country).

Main conclusions were that:

- ID administration of IPV may be preferred in countries where multiple IM injections are already being given to infants at the time suggested for scheduling the IPV dose (i.e. the 3rd DTP contact at 14 weeks of age);
- training and supervision will be more intensive for ID administration;
- vaccine wastage rates may be higher for ID, but cost of wastage lower;
- countries which already have been successful at introducing several other new vaccines will be most successful in introducing IPV; however, these countries generally have well-performing EPI programmes and will be least likely to be affected by cVDPV following OPV2 cessation;
- large countries without a history of successful nationwide new vaccine introduction will encounter greater difficulties.

3.5 Towards affordable IPV - recent efforts by the BMGF

Jay Wenger, the director of the polio team at the Bill and Melinda Gates Foundation, provided an update on the foundation's current program of work on IPV, including findings and the BMGF position related to four main areas of interest:

- the potential contribution of IPV to polio eradication,
- IPV product options for GAVI-eligible countries and lower middle-income markets,
- the affordability of IPV and supply potential for GAVI-eligible countries and lower middle-income markets, and
- factors enabling affordable IPV for GAVI-eligible countries and lower middle-income markets.

Probably the most critical issues for the BMGF are the 'affordability factors' defining IPV affordability and supply potential.

The BMGF feels that a key factor for success will be clear SAGE recommendations on IPV use in polio eradication, including on

- a) the role of IPV in routine immunization as part of OPV2 cessation,

- b) its role in routine immunization as part of OPV cessation overall, and
- c) the role of IPV during campaign use to help interrupt WPV transmission.

In this context, the BMGF encourages the WG to identify the additional studies or efforts needed in case any of the previous 3 questions cannot yet be answered due to insufficient data.

The second-most critical factor will be for the GPEI to gain sufficient financial support for IPV, including clarification of whether GAVI will be willing to open a 'funding window' for IPV.

Lastly, once SAGE recommendations on IPV use have been made, country acceptance and uptake will depend on establishing a dedicated technical capacity to support countries in the adoption of IPV.

J. Wenger assured the WG that the BMGF is committed to support the availability of IPV for GAVI-eligible and lower middle-income countries, at the lowest possible prices.

3.6 Surveillance strategies to accompany OPV2 cessation

H. Jafari described to the WG the surveillance goals and priorities to accompany and support the 'polio endgame,' including the AFP surveillance and environmental surveillance (ES) systems. The main objectives of surveillance will be to ensure prompt and reliable detection of and response to any wild poliovirus and Sabin 2 virus following OPV2 cessation (i.e. discontinuation of tOPV), and to any VDPV or Sabin virus following cessation of all OPV.

Main surveillance strategies for the 'endgame' will be the AFP system, supplemented by environmental surveillance, as well as, when and where appropriate, special targeted studies, including serosurveys, large scale stool surveys and expanded sampling of case contacts.

For AFP surveillance, certified WHO Regions (Americas, European and Western Pacific Regions) will need to revitalize their AFP system to meet performance standards through global certification. Non-certified Regions (Eastern Med., S.-E. Asian and African Regions) will need to close any remaining AFP quality gaps prior to OPV2 cessation, and subsequently sustain AFP quality at the national and sub-national levels through regional and global certification.

Environmental surveillance of waste or sewage water samples is used to supplement AFP in selected areas; the method can potentially detect infection / transmission before paralytic cases occur. However, ES has to be targeted appropriately and is most successful in detecting polioviruses, i.e. excretion from high-risk population groups, where such groups reside and can be sampled in areas with converging sewage systems.

The GPEI plans to expand ES to

- a) identify residual WPV transmission in endemic areas,
- b) provide early indication of new importations, and
- c) document elimination of Sabin virus following OPV2 cessation and eventual bOPV cessation.

By mid-2014, additional ES sampling sites will be placed in Nigeria and Afghanistan, and other areas at high risk of WPV importation and spread. Also, an additional 10 to 20 sites globally will be established based on history of recurrent cVDPV emergence.

In summary, surveillance systems for poliovirus will be adapted to support the goals and priorities of the 'polio endgame,' including regional and global certification of wild poliovirus eradication and verification of VDPV elimination. To achieve the surveillance objectives, targeted environmental surveillance will be further expanded, and special surveillance activities will be used; also, new diagnostics will be developed to more rapidly detect polioviruses.

3.7 Poliovirus laboratory containment as pre-requisite for OPV2 cessation

C. Wolff noted that the main objective of the Global Action Plan III (GAP III) for laboratory poliovirus containment, the key policy document, is to minimize the risk of reintroducing facility-based wild and Sabin polioviruses into communities following wild poliovirus eradication and OPV cessation.

GAP III relies on two main containment strategies: risk elimination through the destruction of unneeded poliovirus materials, and risk management - activities to manage the risk and consequences of a possible inadvertent poliovirus release through effective management and so-called 'safeguards.'

Primary safeguards minimize risk through facility design, management and oversight (i.e. biosafety level requirements, legal frameworks, national and international accreditation). Secondary safeguards minimize the consequences of poliovirus release through locating facilities in areas with sufficiently high anti-polio immunity, and tertiary safeguards minimize consequences through locating wild poliovirus facilities in areas with low probabilities of poliovirus spread (i.e. with high standards of hygiene and sanitation).

Main implications of / requirements for OPV2 cessation (i.e. replacement of tOPV with bOPV for routine immunization) are:

- finalization of Phase I of lab containment (national survey and inventory);
- determination of all facilities retaining WPV type 2 infectious or potentially infectious materials, and those retaining Sabin 2 materials;
- establishment of national regulatory environment in WHO Member States to encourage destruction of unneeded type 2 poliovirus materials and to facilitate safe handling of type 2 materials that are retained.

The following will be important next steps to assure progress in lab containment commensurate with plans for OPV2 cessation:

- continue completion of lab inventories to finish Phase I containment in polio-free countries (particularly India);
- finalize containment procedures required for phased OPV cessation (serotype containment);
- begin process of Sabin 2 containment;
- finalize GAP III with approval of WHO governing bodies; and
- begin work with Member States on national regulatory frameworks.

3.8 Outbreak response strategies post-OPV

The GPEI has gained experience in responding to more than 100 outbreaks of wild poliovirus (WPV) and of circulating vaccine-derived poliovirus (cVDPV) during the last decade. The intensity and dynamics of response will change with increasing time from the cessation of OPV use, as both population susceptibility and public health response capacity change.

Key principles of response, as recommended by the Advisory Committee on Polio Eradication (ACPE) and endorsed in a WHA resolution, remain to

- a) within 7 days of the report confirming the outbreak, to rapidly conduct an assessment and develop a response plan, to
- b) conduct a large, high-quality and sustained immunization response within 4 weeks of the confirmation of the outbreak, and
- c) to implement a surveillance response through immediate enhancement of surveillance and detailed investigation.

The immediacy, speed and scope of outbreak response has been strongly predictive of the duration of the outbreak and number of immunization rounds needed to control it. Outbreaks for which a quality response immunization was conducted within less than 6 weeks of onset of the index case continued for only half as long as those for which the first immunization round was conducted more than 6 weeks after onset of paralysis of the index case. Similarly, the duration of outbreaks for which response campaigns included children over the age of five years was shorter than outbreaks for which the immunization response targeted five-year olds only.

Based on lessons learned in responding to outbreaks during the last decade, the following key principles are suggested for outbreak response post-OPV cessation:

- Speed – response within less than 6 weeks of index case onset and less than 4 weeks of notification;
- Flexibility – short intervals (2-3 weeks) between rounds, targeting of wider age groups (< 15 years);
- Technical support – initial assessment within 48 hours of report, deployment of teams within 7 days;
- Sustaining response – minimum 5 response rounds
- 'Closing out' – assessment of response quality at 3 months following the first case, and of surveillance quality at 6 months, or when the outbreak appears to be over, to assure transmission has been reliably interrupted.

OPV remains the main vaccine of choice for response even after its routine use has been stopped, since it will be available in stockpiles, is easily used in large-scale campaigns, rapidly triggers and boosts intestinal immunity, and has a proven track record in outbreak response.

Following OPV2 cessation, mOPV2 will be used for type 2 cVDPV outbreaks, and bOPV or mOPV for outbreaks of WPV or cVDPV type 1 and 3. Stand-alone IPV may play a role for responding in contiguous areas affected by the outbreak. Following cessation of all OPV use (i.e. post bOPV cessation), outbreak response will be conducted with the appropriate mOPV from stockpiles, possibly with stand-alone IPV.

Draft Agenda

Fifth Meeting of the SAGE Polio Working Group WHO, Geneva, *Salle D*, 3-4 September, 2012

Monday, 3 September, 2012

8:00 – 8:15	Registration	
8:15 - 8:30	Welcome and opening remarks	E. Miller
8:30 – 9:00	Current status of the GPEI and outcomes of VDPV meeting	B. Aylward
9:00 – 10:00	Affordable IPV for routine immunization: new data strengthening the case, and I.D. vs I.M. IPV administration	R. Sutter J. Bilous
10:00 - 10:30	Towards affordable IPV - recent efforts by the BMGF	J. Wenger
10:30 – 11:00	<i>Coffee break</i>	
11:00 - 11:30	Poliovirus lab containment: GAP III, finalizing facility requirements, and implications for tOPV-bOPV switch	C. Wolff
11:30 - 12:30	IPV products, prices and supply: WG interaction with SANOFI (<i>closed session</i>)	
12:30 - 13:30	<i>Lunch break</i>	
13:30 - 14:30	IPV products, prices and supply: WG interaction with GSK	(<i>closed session</i>)
14:30 - 15:30	IPV products, prices and supply: WG interaction with Serum Institute of India (SII)	(<i>closed session</i>)
15:00 – 15:30	<i>Coffee break</i>	
15:30 - 16:30	IPV products, prices and supply: WG interaction with Staten Serum Institute (Denmark)	(<i>closed session</i>)
16:30 - 17:00	WG discussion	

Tuesday, 4 September 2012

8:30 - 8:45	Recap - day 1	E. Miller
8:45 - 9:30	Surveillance strategies to accompany the switch: AFP, expanding environmental surveillance and targeted studies	H. Jafari
9:30 - 10:00	Outbreak response strategies post-OPV: mOPV stockpile and use, potential role of IPV	WHO C. Wolff
10:00 - 10:30	<i>Coffee break</i>	
10:30 - 11:00	The GPEI 'Endgame and Legacy' strategic plan 2014-2018	A. Freeman
From 11:00	<i>Internal WG discussion on key questions to prepare for renewed interaction with SAGE on the tOPV-bOPV switch (closed session)</i>	
11:00 - 12:30	<u>1 - IPV introduction</u> : should SAGE strengthen its IPV recommendation given the additional information now available on VDPV risks and IPV impact, price, supply and route of administration?	
12:30 – 13:30	<i>Lunch break</i>	

- 13:30 – 14:30 2 - ID vs IM application of IPV: how should SAGE balance its recommendations vis-a-vis ID vs IM IPV use for the purposes of a tOPV-bOPV switch?
- 14:30 – 15:30 3 - Timing for tOPV-bOPV switch: in view of the additional information suggesting that the pre-requisites are likely to be in place, can SAGE now make a specific recommendation on the timing of a tOPV-bOPV switch?
- 15:30 - 16:00 *Coffee break*
- 16:00 - 17:00 4 - IPV post-bOPV cessation: should SAGE recommend 1 routine IPV dose following final cessation of bOPV?
- 17:00 - 18:00 Final WG discussion to prepare for November meeting of SAGE E. Miller

ANNEX III - Letter and questions to IPV manufacturers

Dear

On behalf of Dr Elizabeth Miller, Chair of the SAGE Polio Working Group, I would like to invite you to the Working Group meeting on the afternoon of 3 September, 2012.

In planning for the 'tOPV-bOPV switch' (i.e. cessation of type 2 OPV use), and eventual bOPV cessation, the WG would appreciate your frank perspectives on key issues related to IPV that may affect planning for these critical phases of the polio 'endgame'.

The following are main issues which the Working Group would like to discuss with you:

- (a) what are the quantities of whole dose IPV could your company potentially provide for low-income markets over the coming 5 years, and under what conditions?
- (b) how would volume purchasing translate into price reductions for whole dose IPV from your company?
- (c) how would fractional dosing and the use of adjuvants impact IPV price, and what would your company require to develop such products?
- (d) how does your company envisage the development challenges and timelines for a low-cost, low-IPV dose hexavalent product for low-income settings, and what would your company require to develop such a product?

We would appreciate if you could prepare 15 to 20 minute presentations on these main discussion issues. In preparing for the inter-action with the Working Group please also note the attached more detailed list of relevant questions.

The information you provide and all discussions will be treated as confidential, unless you explicitly inform us otherwise.

Please confirm at your earliest convenience that you will be able to participate in the planned session between the Working Group and your company which has been tentatively scheduled for p.m. on 3 September, 2012.

With best regards,

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Detailed background questions.

1) Current IPV:

- a) what is your current production capacity and what would be your timelines for scale-ups to 50, 100 and 200 million doses per year?
- b) what are the key factors affecting your decisions re scale-up/expansion?
- c) what is your current 'best price' for stand-alone IPV for low-income settings and what would be your rough 'best price' for 10 million doses year? 25, 50, 100?
- d) how would volume purchases and guaranteed minimum purchases affect your price? what other approaches could help you offer a best price?

2) ID IPV: your perspectives on

- a) the licensing pathway for ID (requirements, timelines, feasibility based on discussions to date - if any - with your regulators),
- b) the impact of ID on your company's cost and price of ID per dose; specifically what would be your 'best price' for ID IPV? How - if at all - would volume purchases affect your company's price?

3) 'Low-cost' IM IPV (SAGE's specific request): your perspectives on

- a) potential approaches to developing a low-cost (as well as low price) IM IPV standalone vaccine for low-income settings,

- b) specifically, what would be the potential dose reduction with adjuvanting of IPV?
 - c) what is the feasibility of developing an adjuvanted IM IPV (timelines, regulatory path)?
 - d) what would be the potential cost-savings/price reduction for an adjuvanted standalone product?
- 4) Hexavalent IPV:
- a) do you have a development plan for a 'low-cost' hexavalent product targeted for low-income/GAVI settings?
 - b) if not, what would you need to initiate such a development project?
 - c) how would the price of such a hexavalent compare to your current pentavalent product?
 - d) what approach would your company take to a hexavalent product (e.g. WP vs aP; IPV antigen content?)
 - e) what is your company's best and worst case development timelines for a low-cost hexavalent product?

New Polio end game strategy (tOPV-bOPV switch)

Comments from National EPI managers & chairmen of NITAG, WHO Eastern Mediterranean Region, 27th EPI managers meeting, 20 September, Egypt

As per SAGE request (April 2012 meeting), the “new proposed polio end game” was discussed during the 27th inter-country meeting of national EPI managers in the WHO Eastern Mediterranean Region. This meeting was held from 17 to 20 September in Sharm El Sheikh and was attended by the national EPI managers and the chairmen of the NITAGs in the 23 EMR member states, as well as by several partners.

So far, 10 EMR countries have introduced at least one dose of IPV into their national routine immunization schedule, and one country is in the process of doing it. The remaining 12 countries include the 7 GAVI-eligible EMR countries (Afghanistan, Djibouti, Pakistan, Somalia, Sudan, South Sudan and Yemen) and 5 low-middle income countries (Egypt, Iran, Iraq, Morocco & Tunisia).

The tOPV-bOPV switch session was conducted first in plenary, with all countries, and several issues were raised, mainly concerns about the IPV price. Different prices were raised for the full IM IPV: 1) currently prices paid by some countries in the Region (self procuring MIC and HIC) are around 3.2 to 3.5 USD 2) UNICEF price currently around 2.5 USD and 3) participants were informed about the new SII offer to UNICEF of 1.5 USD. SII initiative was well received from the country representatives and they consider it as a positive sign towards lower prices in the future (competition between producers), but still this is considered by MIC as beyond their current financial capacities as most of them are still struggling to introduce new vaccines like PCV (and even Hib) despite the practitioners and public pressure and the availability of strong evidence of high disease burden related to these new vaccines.

Participants raised as well concerns about bOPV and IPV global production capacity, the best timing for the IPV dose (with DPT1 to provide better protection against VAPP, or with DPT3), IPV and maternal antibodies, OPV birth dose and the new proposed strategy, OPV/IPV sequential versus simultaneous administration, IPV as additional dose or replacing one of the OPV doses, the lack of trained human resources in poor health system countries and the need to reach high coverage with the required additional injectable vaccine (IPV), the expected impact on the cold chain of the additional IPV dose, etc). Participants from some GCC countries reported that their countries are currently considering adding a second IPV dose to their routine immunization schedule, and that this issue is one of the agenda items of the 2nd GCC States Symposium on New trends in Vaccination that will be held in Dubai from 9 to 10 October 2012.

In summary from the plenary session, participants agreed on the importance for each country to start preparing for registering the bOPV as well as mOPV1 & mOPV2 as soon as possible. They raised several concerns in particular about the cost of IPV. They requested SAGE to be more explicit about the recommended IPV dose to be an additional one or to replace one OPV dose, as well as the best recommended administration time.

Considering the fact that countries that have already introduced at least one IPV dose into their routine immunization schedule won't have much concerns about the proposed tOPV=bOPV switch except for the bOPV, mOPV1 & mOPV3 registration; the meeting organizers decided to have a special group work with the remaining 12 countries that did not introduce yet any IPV into their routine EPI, to discuss their future plans as well as financial and programmatic capacities and expected constraints in relation to proposed switch strategy. The main outcomes from this group work (see detailed information attached) include:

1. Morocco and Tunisia are already planning to introduce at least one dose of IPV by end of 2014 and 2015 respectively. Egypt and Iran raised their national vaccine production as major constraint for both bOPV and IPV use. All remaining countries think that introducing one dose of IPV in the context of a global tOPV-bOPV switch might be possible and pending partners financial support (GAVI ++). Pakistan representatives were the only ones that believe that this won't most probably be possible for their

country mainly because of the expected financial impact, even if supported by GAVI, as well as the expected programmatic implications.

2. All countries, except Tunisia, and in particular the GAVI eligible countries, are more in favor for an IM IPV option, mainly because of the capacity of the field staff to deliver ID injections. Tunisian representatives mentioned that their country will definitely go for the ID IPV option for financial reasons. All participants were concerned about the possible impact of a non-correct ID injection of IPV on the expected immunologic response and requested SAGE to clarify that.
3. The main expected challenges mentioned by the participants relate to financial constraints for both the IPV vaccine price and the introduction cost (training, cold chain, etc), programmatic (another injectable vaccine for some already overloaded and poor delivery systems, increased number of injections during same session (IPV, Penta, etc), capacity of the field staff to deliver ID injections, capacity of the programme to reach as high coverage figures with an injectable vaccine as with OPV, in particular in some remote and difficult areas, etc) and logistic (cold chain issues). Participants highlighted their wish to see a low cost hexavalent vaccine option among WHO and partners priorities.