16th WHO/UNICEF Consultation with OPV/IPV Manufacturers and National Authorities for Containment

26 October 2017

Geneva, Switzerland

Note for the Record

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16th WHO/UNICEF Consultation with OPV/IPV Manufacturers
and National Authorities for Containment
26 October 2017, Geneva, Switzerland
Executive Board Room, WHO/HQ,

Rapporteurs:
Dr Carolyn Sein
Dr Harpal Singh

Thursday 26 October 2017		**Chair: Michel Zaffran**
08:30	Registration	
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SESSION 2: Interrupting poliovirus transmission		
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10:00	IPV implementation update and mitigating actions at global level to address the supply shortage	Alejandro Ramirez Gonzalez
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Overview

A world without polio will face unique challenges to ensure that it remains polio free. The containment of polioviruses (considered 'the other half of eradication'), future immunization policy in the post eradication era, high-quality surveillance and outbreak response, within an effective post-eradication infrastructure are some of these critical post-eradication actions.

The 16th WHO/UNICEF consultation with OPV/IPV manufacturers and National Authorities for Containment (NACs) took place on 26 October 2017 in Geneva. This was the first time the consultation was attended by the NACs who will be responsible for national level oversight and implementation of the Global Action Plan III (GAP III) for containment certification.

The key objective of the consultation was to strengthen collaboration between stakeholders. The consultation outlined the status and needs of the polio eradication programme with implications for OPV and IPV demand and supply; provided an update on research, product development (including Sabin IPV) and future immunization policy; and emphasized the importance and necessity of ensuring containment as the programme moves towards the post-eradication era. The key outcome of the consultation was the alignment of interests and improved coordination of activities between stakeholders.

Containment and the role of the NACs featured significantly in this consultation given their increasing importance as progress is made towards eradication. The statutory requirement to meet containment prerequisites for the certification of eradication was emphasized. This includes implementation of GAPIII, ensuring primary, secondary and tertiary safeguards, and establishing a national oversight infrastructure.

Session 1: Introduction

Update on Polio Eradication and Endgame Strategy

Michel Zaffran (Director, Polio Eradication, WHO)

An overview of the Polio Eradication programme was provided, with an emphasis on the status, progress and challenges in the remaining endemic countries: Nigeria, Afghanistan and Pakistan. As of 24 October 2017, 6 cases of type 1 wild poliovirus (WPV1) have been reported in the past 6 months (12 cases for the same period in 2016): the last cases of WPV1 were reported in September 2017 in Afghanistan and August 2017 in Pakistan. The last virus in Nigeria was detected in a health y child in September 2016. There is also ongoing transmission of circulating vaccine derived poliovirus (cVDPV) with 47 cases reported in Syria and 5 cases in 2 outbreaks in the Democratic Republic of the Congo as of 24 October 2017. The Global Polio Eradication programme remains guided by the *Polio Eradication and Endgame Strategic Plan (PEESP) 2013 – 2018*[1].

The withdrawal of bOPV is expected to occur as soon as possible after certification of WPV eradication by the Global Commission for the Certification of the Eradication of Poliomyelitis (GCC). An estimated 18 months of planning is required for the withdrawal of bOPV. The Strategic Advisory Group of Experts - Polio working group has started discussion on the readiness criteria for eventual bOPV withdrawal.

35 countries are currently affected by the global shortage of IPV either through delayed introductions or resupply. Key strategies to overcome this have included the allocation of IPV to highest risk countries (e.g., at risk of cVDPV2), introduction of fractional IPV use in several countries in the WHO region of the Americas and the South East Asia region and it is expected that new manufacturers coming on line in 2019 -2020 will further contribute to addressing the shortage. Mainstreaming of polio-essential functions to sustain global eradication is the focus of the Post-Certification Strategy and is in line with objective 4 (transition planning) of the PEESP 2013 – 2018.

The programme's priorities for the next 6 months include: 1) interrupting WPV and cVDPV transmission in affected countries; 2) ensuring high quality surveillance in endemic and access compromised areas; 3) financial planning to extend through 2020; 4) acceleration of

[1] Polio Eradication and Endgame Strategic Plan (PEESP) 2013- 2018. Available at: http://polioeradication.org/wp-content/uploads/2016/07/PEESP_EN_US-1.pdf

containment certification; and 5) engagement of non-polio progammes in the implementation of post-certifications strategy.

Session 2: Interrupting Poliovirus Transmission

OPV Requirements Forecast-Placeholder Calendar

SIAs for 2018 up to OPV Cessation

Arshad Quddus (Team Lead, Polio Eradication, WHO)

The GPEI is implementing an intense SIA calendar in 2017, with an estimated requirement for 1.6 billion doses of bOPV. SIAs are conducted to interrupt the circulation of WPV1 circulation in Afghanistan and Pakistan, and boost population immunity in high-risk countries. The process, assumption and input for the development of the 2018-2021 SIA calendar was outlined. The GPEI reviews and updates the SIA calendars on a 6 monthly basis, taking into consideration the need for any additional SIAs. Assuming interruption of WPV circulation in Q2 of 2018, the estimated requirement for bOPV in 2018 is 1.4 billion doses, decreasing to 818M by 2021.

IPV and OPV Supply: Current Status and Looking Forward

Monica Pereira (Specialist, Revolving Fund Management, PAHO) and

Ann Ottosen (Lead, Polio Supply, UNICEF Supply Division/SD)

The PAHO Revolving Fund faces ongoing challenges in IPV supply due to constraints in global IPV supply. Although the TAG for PAHO in 2014 recommended a 2 dose IPV schedule, only 1 dose was introduced. Subsequently the TAG held extraordinary meetings in 2016 and 2017, with the outcome that fractional dose IPV (fIPV) will be used in lieu of full dose IPV until the situation improves.

It is estimated that 5.1 million IPV doses will be supplied through the PAHO Revolving Fund in 2017 which falls short of the 8M IPV doses requested. To date however, only 2.4M doses have been delivered resulting in 31 countries facing potential stock-outs. Specific mitigation strategies were implemented including preparation for fIPV introduction in 8 countries, and procurement of pre-filled IPV syringes for an interim period until IPV supply improves. In contrast bOPV supply is sufficient. The 2017 demand for 24.7 million bOPV doses is on track to be met by three manufacturers, and the 2018 demand for 26 million doses is also expected to be met.

UNICEF SD provided an update on IPV supply highlighting that availablity was <50% of the awarded supply of +400 million doses for 2014-2018 contracts. Mitigation strategies were implemented including a risk based assessment prioritizing IPV allocation to countries with

higher risk of VDPV2 events or outbreaks (Tier 1 and 2). Consequently lower risk (Tier 3 and 4) countries are facing IPV shortages, with 18 countries yet to introduce IPV and 17 countries having supplies interrupted after introduction and facing stock-outs.

Improvements in IPV supply for routine immunization are anticipated in 2018, however quantities will be insufficient for vaccinating the cohorts which were not offered IPV since the withdrawal of type 2 containing OPV in April 2016; for this, IPV will be allocated on a risk assessment basis from 2019 onwards for countries requiring a full dose, whereas fractional doses can be offered sooner. In addition, a reserve stock of 2 million IPV doses will be set side in 2018 for outbreak response. The IPV tender for 2019-2022 supply closed on 15th September 2017 with awards antipated by the end of the year.

Supply of bOPV for 2017 is around 1.3 billion doses, and bOPV is overall expected to meet projected demand until 2019, with additional awards for 2020 and beyond anticipated in April 2018 as more information becomes available. UNICEF emphasized the importance of close coordination between program partners and suppliers and the need to factor in production lead times around policy decisions and changes in SIA calendar, as the OPV supply and demand moves forward towards eradication and cessation.

IPV Implementation Update and Mitigating Actions at Global Level to Address the Supply Shortage

Alejandro Ramirez Gonzalez (Technical Officer, EPI, WHO)

WHO provided an overview on the status of IPV implementation. Due to constraints in IPV supply 18% of the global birth cohort have either not been able to introduce IPV or face IPV stock-outs. Consequently India and Sri Lanka (19% global birth cohort) have implemented fIPV in routine immunization in a 6, 14 week schedule, and other countries will follow inclduing Nepal, Bangladesh, and 15 countries in PAHO. Other mitigating strategies which have been implemented inlcude multi-dose vial policy; priortization of IPV allocation to countries with highest risk of VDPV2 event or outbreak (Tier 1 and 2); grading risk in lower-risk (Tier 3 and 4) countries; ongoing timely communications to countries; and incorporation of technical guidance from the Strategic Advisory Group of Experts on Immunization (SAGE) and the Polio Oversight Board (POB).

In October 2017, the SAGE recommended countries affected by supply constraints implement catch-up campagins as soon as IPV becomes available. The global birth cohort requiring catch-up IPV dose is estimated to total 27 million children; full dose of IPV for catch up will be availablein

2019, however supply for 2 fIPV doses can be made available at the time of routine immunization introduction.

http://polioeradication.orgworld/containment/containment-resources/

Session 3: Biocontainment

GAPIII implementation: progress and obstacles

Nicoletta Previsani (Technical Officer, Polio Eradication, WHO)

There is an increasing importance of containment as progress is made towards eradication and is a criticial component to maintain eradication. As of 21 October 2017, 28 countries have plans to designate 91 poliovirus-essential facilities (PEFs) with 18 of these countries already having establish their National Authorities for Containment (NACs). The WHO Global Action Plan (GAPIII)[2] which was endorsed by the WHO Strategic Advisory Group of Experts (SAGE) on Immunization in October 2014[3] and the World Health Assembly resolution WHA68.3[4] in May 2015, the GAPIII Containment Certification Scheme (CCS)[5] which was endorsed by the SAGE on Immunization in October 2016[6] and the Technical Report Series (TRS) 926 Guidelines for the safe production and quality control of poliomyelitis vaccine currently undergoing revision are the reference documents for containment.

There are several oversight bodies whose decision can impact containment. These include the Containment Advisory Group (CAG), Global Certification Comission (GCC), Expert Committee on Biological Standardization (ECBS), and SAGE. The global oversight body for containment is the GCC which initially in 1997[7] and again in 2017[8] stressed the importance of implementation of

[2] Global Plan of Action for Poliovirus Containment (GAPIII). Available at: ttp://polioeradication.org/polio-today/preparing-for-a-polio-free-world/containment/containment-resources/

[3] WHO. Meeting of the Strategic Advisory Group of Experts on Immunization, October 2014 – conclusions and recommendations. Wkly Epidemiol Rec. 2014;89:572-3. Available at: http://www.who.int/wer/2014/wer8950.pdf?ua=1

[4] WHO. Resolution WHA68.3. Poliomyelitis. In: Sixty-eighth World Health Assembly, Geneva, 18–26 May 2015. Geneva: WHO; 2015. Available at: http://apps.who.int/gb/ebwha/pdf_files/WHA68-REC1/A68_R1_REC1-en.pdf#page=27

[5] GAPIII- Containment Certification Scheme (CCS) . Available at: http://polioeradication.org/polio-today/preparing-for-a-polio-free-world/containment/containment-resources/

[6] WHO. Meeting of the Strategic Advisory Group of Experts on immunization, October 2016 – conclusions and recommendations. Wkly Epidemiol Rec. 2016;91:567-9. Available at: http://apps.who.int/iris/bitstream/10665/251810/1/WER9148.pdf?ua=1

[7] 2nd meeting of the Global Commission for the Certification of the Eradication of Poliomyelitis, 1 May 1997, Geneva, Switzerland. Available at: http://polioeradication.org/wp-content/uploads/2016/07/9Report.pdf

containment as a prerequisite for global certification. To meet this, certification activities of facilities as described in the CCS must be initiated urgently by the NAC who will work in consultation with the GCC-Containment Working Group (CWG), the body delegated by GCC to perform the day-to-day certification functions. The CAG met for the first time in June 2017 and several of the recommendations made by the CAG[9] will form the basis for the revision of GAPIII.

In terms of next steps, countries that have yet to nominate the NACs should urgently do so, there is also an ongoing need to work with national authorities to reduce the number of PEFs, submission of the 1st certificate of participation (CP) is expected and the 2nd meeting of the CAG which is expected at the end of November 2017.

Revised WHO TRS for safe production and quality control of Polio Vaccines

Insoo Shin (Scientist, Essential Medicines and Health Products, WHO)

The Consitution requires WHO to develop, establish and promote international standards with respect to biological and pharmaceutical products and this has been done continuously for more than 60 years[10]. These norms and standards called Technical Reports Series (TRS)[11] are established by the Expert Committee (EC) in this case the WHO Expert Committee on Biological Standardization (ECBS). The ECBS just like other EC are advisory bodies to the Director-General of WHO and are estabslihed Established by World Health Assembly or Executive Board.

The need for the revision of TRS 926, Annex 2, first published in 2004 (a year after the publication of GAPII) was identified in 2015 by the ECBS following the publication of GAPIII. The working group on the revision of this guidelines submitted technical issues for clarification of the CAG at their 1st and 2nd meeting. The resulting draft document plans to be available for public consultation in the December 2017 through January 2018, this will be followed by an informal consultation in the 1st half of 2018 and a second round of public consultation in the 3rd Q of 2018 before submission to ECBS in October 2018.

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[8] 16th meeting on the Global Commission for the Certification of the Eradication of Polio, 4-5 July 2017, Paris, France. Available at: http://polioeradication.org/wp-content/uploads/2017/09/GCC-16th-meeting-report-0405072017.pdf

[9] Report of the First Meeting of the Containment Advisory Group. Available at: http://polioeradication.org/wp-content/uploads/2017/08/CAG1-Report-30082017.pdf

[10] WHO Regulatory Standards for Vaccines and Biologicals http://www.who.int/biologicals/en/

[11] WHO Technical Report Series
http://apps.who.int/medicinedocs/en/cl/CL3.2.1.4.34.1/clmd,50.html

The GAPIII focuses on biorisk management (biosafety and biosecurity) but is not entirely production-specific. The TRS is more specific to the biosafety aspects of Poliomyelitits vaccines, and attempts to reconciles GMP and biosafety requirements. Therefore, ensuring the alignment of these 2 documents is crucial.

A WHO collaborative study to establish international standards (IS) for bOPV and mOPV for use in potency assays of Oral Polio Vaccines has been completed and the IS were endorsed by ECBS in 2017. IS for bOPV 1+3, mOPV1, 2 and 3 have been estabslihed. These standards can also be used with new emerging Polio vaccines based on safer strains (nOPV) and Sabin IPV [12].

Containment certification scheme: challenges and way forward

Arlene King [Chair, GCC Containment Working Group (CWG) and Regional Commission for the Certification of the Eradication of Poliomyelitis (RCC) for the Americas, and Member, RCC – African Region]

The GCC acts as the global oversight body for containment and confirms global poliovirus containment. At its 15th meeting in December 2016, the GCC fully endorsed the proposed oversight structure for containment, including the establishment of a GCC-CWG to be led by a GCC member[13]. The GCC also agreed to delegate day-to-day operational level containment certification activity to the CWG and this will include review of application submitted by the NACs and ensure only eligibile facilities enroll in the CCS, endorse or reject the issuance of the various containment certificates. The CWG will report to the GCC and its aim is to provide the required level of assurance that GAPIII requirements are appropriately identified, implemented and monitored, following the CCS. The GCC-CWG was established in early 2017 and will begin functioning as soon as the NACs submit applications for containment certification as described in the CCS. The functioning mechanism of the CWG are defined in their terms of reference[14] and is in line with the CCS.

[12] National Institute for Biological Standards and Control (NIBSC). Report on the WHO Collaborative study to establish International Standards for potency assays of Oral Polio Vaccine. Available at: http://www.who.int/biologicals/expert_committee/BS2313_OPV_Study_2017F.pdf?ua=1

[13] 16th meeting on the Global Commission for the Certification of the Eradication of Polio, 4-5 July 2017, Paris, France. Available at: http://polioeradication.org/wp-content/uploads/2017/09/GCC-16th-meeting-report-0405072017.pdf

[14] Global Certification Commission Containment Working Group (GCC-CWG), Terms of Reference. Available at: http://polioeradication.org/wp-content/uploads/2016/10/TOR_GCC-CWG.pdf

Communication channels between the NAC and the CWG for the submission of applications and discussion have been established and are operational. Submission of applications to the CWG can be made via containmentcertification@workspace.who.int. In most situations, the CWG will expect to communicate with only the NAC. However, the CCS does provide provision for PEFs to appeal to the CWG in cases of dispute but will have to keep the NAC fully-informed throughout the process.

It is crucial that the NACs begin country level discussions with the potential PEFs in the country and urgently initiate the CCS application process. PEFs are expected to have a Certificate of Containment (CC) as described in the CCS, indicating full compliance with GAPIII at the time of global certification of eradication. This was among the several important decision made by the GCC at the Special Meeting of the GCC on Containment, 23 – 25 October 2017. Countries that have yet to nominate their NAC, should accelrate the appointment of a competent NAC. The NAC is the national oversight body responsible for GAPIII containment certification. NACs are nominated by the ministry of health or other designated national authorities.

In order to support the NACs in roll-out and implementation of the CCS process, WHO has developed numerous templates and forms that are available at:
http://polioeradication.org/polio-today/preparing-for-a-polio-free-world/containment/containment-resources/

New Polio strains development and containment requirements

Kostya Chumakov (FDA Center for Biologics Evaluation and Research)

The development of newer poliovirus strains that are reportedly hyper attenuated, genetically stable and less pathogenic poliovirus strains may actually require a lower level of containment compared to GAPIII in the production and control of IPV. Similarly, the development of genetically more stable OPV, including the new monovalent OPV2, is a priority for the Global Polio Eradication Initiative (GPEI), both for the polio endgame and the post-OPV cessation era due to its ability to reduce the number of VDPVs. To continue to encourage newer safer technologies or newer strains for the production and control of polio vaccines and to determine the appropriate containment requirements for the handling these new strains (e.g. S-19 Sabin 2 containing Sabin 2 capsid sequence; nOPV2 strains), the CAG at its first meeting recommended the creation of CAG Expert Support Group (CAG-ESG) to review the available scientific evidence

and to consider containment requirements for the new strains and propose potential solutions to the CAG and other groups if necessary, for review and approval[15].

The main determinant of the attenuation of poliovirus lies in its internal ribosome entry site (IRES) so that the more stable the IRES is the more avirulent is the strain. Numerous methods have been developed by research groups around the world to make this virus more stable. The rational design of the poliovirus genome can be exploited to make it more avirulent to be used in production and control of IPV, may have lower containment requirements and may even become part of the new generation live OPV vaccine[16].

[15] Report of the First Meeting of the Containment Advisory Group. Available at: http://polioeradication.org/wp-content/uploads/2017/08/CAG1-Report-30082017.pdf

[16] A list of selected references on novel poliovirus strains:

- Sanders BP, de los Rios Oakes I, van Hoek V, Bockstal V, Kamphuis T, Uil TG, et al. Cold-Adapted Viral Attenuation (CAVA): Highly Temperature Sensitive Polioviruses as Novel Vaccine Strains for a Next Generation Inactivated Poliovirus Vaccine. PLoS Pathog 12(3): e1005483 (2016).
- Knowlson S, Burlison J, Giles E, Fox H, Macadam AJ, Minor PD. New Strains Intended for the Production of Inactivated Polio Vaccine at Low-Containment After Eradication. PLoS Pathog 11(12): e1005316 (2015).
- Ahd Hamidi, Wilfried AM Bakker. Innovative IPV from attenuated Sabin poliovirus or newly designed alternative seed strains. Pharmaceutical Patent Analyst 1 (5), 589-599 (2012).
- Verdijk P, Rots N Y, Bakker WAM. Clinical development of a novel inactivated poliomyelitis vaccine based on attenuated Sabin poliovirus strains. Expert Review of Vaccines 10:5, 635-644 (2011).
- Lauring AS, Jones JO, Andino R. Rationalizing the development of live attenuated virus vaccines. Nat. Biotechnol.28(6), 573–579 (2010).
- Burns CC, Campagnoli R, Shaw J, Vincent A, Jorba J, Kew O. Genetic inactivation of poliovirus infectivity by increasing the frequencies of CpG and UpA dinucleotides within and across synonymous capsid region codons. J. Virol. 83(19), 9957–9969 (2009).
- Coleman JR, Papamichail D, Skiena S, Futcher B, Wimmer E, Mueller S. Virus attenuation by genome-scale changes in codon pair bias. Science 320(5884), 1784–1787 (2008).
- Vignuzzi M, Wendt E, Andino R. Engineering attenuated virus vaccines by controlling replication fidelity. Nat. Med. 14(2), 154–161 (2008).
- Toyoda H, Yin J, Mueller S, Wimmer E, Cello J. Oncolytic treatment and cure of neuroblastoma by a novel attenuated poliovirus in a novel poliovirus-susceptible animal model. Cancer Res. 67(6), 2857–2864 (2007).
- Burns CC, Shaw J, Campagnoli R et al. Modulation of poliovirus replicative fitness in HeLa cells by deoptimization of synonymous codon usage in the capsid region. J. Virol. 80(7), 3259–3272 (2006).
- Macadam AJ, Ferguson G, Stone DM et al. Rational design of genetically stable, live attenuated poliovirus vaccines of all three serotypes: relevance to poliomyelitis eradication. J. Virol. 80(17), 8653–8663 (2006).

Two novel live attenuated serotype-2 OPV, derived from a modified Sabin 2 infectious cDNA clone (nOPV2 candidates) have completed Phase I of clinical trials. The two nOPV2 candidates are designed to improve genetic stability and decrease the risk of loss of attenuation relative to the parental Sabin 2 strain in that there was reduced replication in vaccine recipients and reduced shedding of the virus. Other evaluations are still to be performed such as an evaluation of genetic stability of the candidate strains by transgenic mouse neurovirulence test and deep sequencing as well as an evaluation of its efficacy to boost an immune response.

The determination of the level of contaiment of newer strains must be based on a robust risk assessment taking into consideration the biological properties of the strain (virulence, transmissibility, genetic stability, stability in environment, etc.) and intended use of the strain and handling procedures. The handling of newer strains should also be taken in the context of

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- De Jesus N, Franco D, Paul A, Wimmer E, Cello J. Mutation of a single conserved nucleotide between the cloverleaf and internal ribosome entry site attenuates poliovirus neurovirulence. J. Virol. 79(22), 14235–14243 (2005).
- Gromeier M, Alexander L, Wimmer E. Internal ribosomal entry site substitution eliminates neurovirulence in intergeneric poliovirus recombinants. Proc Natl Acad Sci U S A. 1996 Mar 19;93(6):2370-5.
- Burns CC, Shaw J, Campagnoli R, Jorba J, Vincent A, Quay J, Kew O. Modulation of poliovirus replicative fitness in HeLa cells by deoptimization of synonymous codon usage in the capsid region. J Virol. 2006 Apr;80(7):3259-72.
- Coleman JR, Papamichail D, Skiena S, Futcher B, Wimmer E, Mueller S. Virus attenuation by genome-scale changes in codon pair bias. Science. 2008 Jun 27;320(5884):1784-7. doi: 10.1126/science.1155761.
- Toyoda H, Franco D, Fujita K, Paul AV, Wimmer E. Replication of poliovirus requires binding of the poly(rC) binding protein to the cloverleaf as well as to the adjacent C-rich spacer sequence between the cloverleaf and the internal ribosomal entry site. J Virol. 2007 Sep;81(18):10017-28
- Pfeiffer JK, Kirkegaard K. A single mutation in poliovirus RNA-dependent RNA polymerase confers resistance to mutagenic nucleotide analogs via increased fidelity. Proc Natl Acad Sci U S A. 2003 Jun 10;100(12):7289-94. Epub 2003 May 16.
- Vignuzzi M, Wendt E, Andino R. Engineering attenuated virus vaccines by controlling replication fidelity. Nat Med. 2008 Feb;14(2):154-61. doi: 10.1038/nm1726.
- Macadam AJ, Ferguson G, Stone DM, Meredith J, Almond JW, Minor PD. Live-attenuated strains of improved genetic stability. Dev Biol (Basel). 2001;105:179-87.
- Rowe A, Burlison J, Macadam AJ, Minor PD. Functional formation of domain V of the poliovirus noncoding region: significance of unpaired bases. Virology. 2001 Oct 10;289(1):45-53.
- Arita M, Iwai M, Wakita T, Shimizu H. Development of a poliovirus neutralization test with poliovirus pseudovirus for measurement of neutralizing antibody titer in human serum. Clin Vaccine Immunol. 2011 Nov;18(11):1889-94. doi: 10.1128/CVI.05225-11.

the reference documents such as GAPIII, TRS 926, Annex 2 for safe production and quality control of Polio Vaccines, national biosafety and biosecurity regulations and the outcome findinga from the CAG-ESG which should be expected by mid-2018.

Session 4: Research, Policy and Product Development for the Future

Future Immunization Policy

Roland Sutter (Coordinator, Polio Eradication, WHO)

The 5 key recommendations on future routine immunization made by the SAGE working group (WG) in April 2016 were reiterated: 1) immunogenicity target of >90% seroconversion and robust antibody titers against all 3 serotypes; 2) schedule of at least 2 IPV doses with the first dose administered at ≥14 weeks (3.5 mo) at DTP2/DTP3 contact; 3) minimum interval of 5.5 mo between IPV doses with the second dose adminsitered at 9 mo measles contact; 4) ideally the administration of full dose IPV, however that fractional dose would also be acceptable; and lastly that 5) opportunity for catch-up for missed cohorts should occur as soon as IPV supply becomes avaialble.

It was emphasized that countries hosting Polio Essential Facilities (PEFs) (53% of global birth cohort) are required to implement secondary safeguards to ensure high population immunity against polio. The IPV doses and coverage for secondary safeguard as stipulated by the Global Action Plan (GAP) III were endorsed by the World Health Assembly in 2016. The timeline for the certification of polio eradication was outlined; validation and declaration of the eradication of WPV will be made by the Global Certification Commission at least 3 years after the last detection of WPV.

Sinovac sIPV Project Update

Yijing Wang (Sinovac, China)

Sinovac provided an update on the development and progress of their sIPV project. The timeframe of the project was presented, commencing with technology transfer initiation in 2014 to antipicated completion of Phase III clinical trials in 2019, and product license and WHO PQ anticipated in 2019 and 2020, repsectively. The study design for Phase I, II and III clinical trials and subsequent results were shared. Sinovac highlighted their commitment to meet GAP III requirements and detailed specific measures which had been implemented including approach to hardware (physical containment) and software (procedures and managements systems).

Sabin-IPV Development in
Beijing Bio-Institute Biological Products Co. Ltd - CNBG

Wang Hui (CNBG)

BBIBP provided an update on the development and progress of their sIPV project. The timeline was detailed, commencing with process development initiated in 2007; completion of pre-clinical studies in 2014; completion of Phase III clinical trials in Q1 2017; and drug registration submission in Q3 2017. Product license and GMP certificate were obtained in September 2017.

The process for establishing quality control, product profile, and upstream and downstream processes were outlined. The study design for Phase I, II, and III clinical trials and subsequent results were shared. In addition BBIBP has provided samples to the Centers for Disease Control as part of a cross neutralization study. BBIBP highlighted their commitment to meet GAP III containment requirements, and are currently building a new GAP III compliant facility which is expected to be completed by 2020 with an expected production capacity of 20-25 million doses.

New Quality Control Tests for Measuring
Potency and Consistency of sIPV

Kostya Chumakov (FDA Center for Biologics Evaluation and Research)

The rationale and need to establish international harmonization of sIPV testing was highlighted, specficially, the development of a single potency assay and validation of reference reagents. In addition, the importance and ability to ensure genetic stability of sIPV strains and consistency in the manufacturing process as a work in progress was emphasized. PATH and BMGF are supporting a collaboration by the Lankenau Institute for Medical Research and NIBSC to develop a universal ELISA test to measure D antigen content using human clonal antibodies. Available results and next steps in the project including further optmiztion, validation, use to calibrate sIPV reference, were detailed.

The advanatages and limitations of the 3 tests currently used to ensure sIPV is produced from Sabin stocks (neurovirulence assay, MAPREC and deep sequencing), were detailed. It was highlighted among these tests, deep sequencing technology with whole genome profiling likely the best way to monitor consistency with results demonstrating that identified patterns of mutations in vacicnes which were unique to each manufacturer.

Closing remarks

Roland Sutter (Coordinator, Research, Policy and Containment, Polio Eradication, WHO)

The attendees of the consultation were thanked for their participation and continuing contribution towards the global comittment of polio eradication and sustaining a polio-free world. The ongoing close collaboration between vaccine manufacturers, NACs, GCC-CWG, UNICEF and WHO leading into the post-eradication era was emphasized, particularly given the increasing importance of containment in ongoing constraints in global IPV supply and the changes in future immunization policy in the post eradication era.