

Report of the SAGE Polio Working Group Meeting 7-8 September 2015

The SAGE Polio Working Group met on 7-8 September 2015 in Geneva, Switzerland. This report summarises the group's discussions, conclusions and recommendations.

Background

The Global Polio Eradication Initiative (GPEI) is making strong progress towards polio eradication. In 2015¹, there have been just 39 cases of wild poliovirus (WPV) to date. At this time in 2014, there had been four times as many WPV cases – 169 in total. Since September 2014, WPV has affected only two countries – Pakistan and Afghanistan. The entire African continent has not detected a case of WPV since 11 August 2014. Nigeria, until recently a polio endemic country, has not had a case of WPV since July 2014.

This significant progress has created momentum towards achieving the program's objectives and has increased public and donor confidence in GPEI's ability to fully implement The Polio Eradication and Endgame Strategic Plan 2013-18. To optimize program accountability and ensure success, in June 2015 the Strategy Committee of the GPEI conducted a "midterm review" of the GPEI's progress in implementing the Strategic Plan. The review identified specific priority strategic adjustments that emphasized enhancing surveillance for poliovirus, reaching missed children, preparedness and capacity for outbreak response, and acceleration of activities to implement facility containment of type 2 poliovirus prior to the global withdrawal of type 2 OPV (OPV2). GPEI has taken steps and made investments to implement the strategic adjustments identified by the Mid-term Review.

Context for the withdrawal of type 2 OPV

The last case of type 2 wild poliovirus (WPV2) occurred sixteen years ago, in 1999. Despite this, widespread use of type 2 oral polio vaccine (OPV2) has continued, as a component of trivalent oral polio vaccine (tOPV). Since 1999, this continued use of OPV2 has caused an estimated 100-200 cases of Vaccine Associated Paralytic Poliomyelitis (VAPP) globally per year, accounting for 1600-3200 cases of paralysis between 2000 and 2015¹. Over the same period OPV2 has also caused 684 known cases of type 2

¹ As of 9 September 2015

circulating vaccine-derived poliovirus (cVDPV2), which occurs when type 2 containing OPV is used in populations with suboptimal coverage, allowing the vaccine virus to be transmitted from one susceptible individual to another, progressively acquiring through mutation the transmissibility and neurovirulence characteristics of wild polioviruses.

A major objective of the Polio Eradication and Endgame Strategic Plan 2013-18 is the globally synchronized withdrawal of OPV2 by switching from trivalent OPV to bivalent OPV (bOPV). Withdrawing OPV2 is a crucial step towards the global eradication of poliovirus. The process of doing so will also provide an opportunity to learn from experience prior to the full withdrawal of all OPVs, which will be possible when wild poliovirus types 1 and 3 have also been certified as eradicated.

Being able to switch from tOPV to bOPV requires extensive preparatory measures to be taken, which have been set out as readiness criteria for the switch². These apply globally, and are:

- 1) introduction of at least one dose of inactivated poliovirus vaccine into routine immunisation;
- 2) access to a bivalent oral polio vaccine that is licensed for routine immunization;
- 3) implementation of surveillance and response protocols for type 2 poliovirus (including constitution of a stockpile of monovalent oral polio vaccine type 2);
- 4) completion of phase 1 poliovirus containment activities, with appropriate handling of residual type 2 materials; and
- 5) verification of global eradication of wild poliovirus type 2.

The trigger for setting a definitive date for the withdrawal of OPV2 was set as the absence of all persistent cVDPV2 for at least six months, in addition to attainment of the readiness criteria.

The date for the tOPV-bOPV switch: April 2016

In April 2015, SAGE concluded that progress towards elimination of persistent cVDPV2 was on track, and recommended that all countries and GPEI should plan firmly for April 2016 as the designated date for withdrawal of OPV2. SAGE specified that it would consider delaying OPV2

² Sixty-Seventh World Health Assembly (2014); Report by the Secretariat on Poliomyelitis: intensification of the global eradication initiative:
http://apps.who.int/gb/ebwha/pdf_files/WHA67/A67_38-en.pdf

withdrawal only if the Working Group reports in October 2015 that the assessed risk of persistent cVDPV2 transmission is high³.

In May 2015, the World Health Assembly commended the progress across Africa and the success of the program in halting three large multi-country outbreaks in the Middle East, Horn of Africa and Central Africa. Member States expressed their full support for the program, adopted a resolution to stop polio, and committed to meeting preparedness criteria for the phased withdrawal of oral polio vaccines starting with the withdrawal of OPV2 in April 2016⁴.

The SAGE and the SAGE Polio Working Group (WG) have provided extensive input into the planning of the tOPV-bOPV switch, and have regularly monitored its preparations through teleconferences and meetings.

At its meeting of 7-8 September 2015, the WG reviewed the current epidemiology of cVDPV2 and assessed all readiness criteria. As is set out below, the WG unanimously concluded that the withdrawal of OPV2 with the switch from tOPV to bOPV should go ahead as planned in April 2016, and makes this recommendation to the SAGE.

Current Epidemiology of Type 2 vaccine-derived poliovirus (VDPV2)

VDPV2 circulation: summary table

Virus type	Definition	Status
VDPV2	OPV type 2 virus strains with ≥ 6 NT changes	In 2014-15, 15 countries have detected 46 emergences; only 4 became cVDPV
cVDPV2	VDPV2 isolates for which there is evidence of person-to-person transmission in the community	12 events in 2010-15 2 events in 2014-15 (South Sudan and Guinea).
Persistent	cVDPV2 strains	Pakistan:

³ World Health Organization (2015). Meeting of the Strategic Advisory Group of Experts on immunization, April 2015: conclusions and recommendations. World Epidemiological Record. No. 22, 2015, 90, 261–280

⁴ Sixty-Eighth World Health Assembly Resolution (2015); Agenda item 15.2 on Poliomyelitis: http://apps.who.int/gb/ebwha/pdf_files/WHA65/A65_R5-en.pdf

VDPV2	that continue to circulate for \geq six months following detection	<ul style="list-style-type: none"> - Eliminated two longstanding lineages that circulated until June 2014 - New emergence of cVDPV2 in July 2014, last detected in March 2015
		<p>Nigeria:</p> <ul style="list-style-type: none"> - Eliminated two longstanding lineages that circulated until March 2015 - New emergence of cVDPV2 in August 2014, last detected in May 2015

Persistent cVDPV2: The longstanding and highly mutated persistent cVDPV2 strains that circulated widely in northern Nigeria and in parts of Pakistan for multiple years have not been detected in AFP cases or environmental samples since March 2015 in Nigeria and since June 2014 in Pakistan. Both countries appear to have successfully eliminated these multiple lineages of persistent cVDPV2 strains which had established longstanding circulation.

There have been, however, two new instances of cVDPV2 emergence that became persistent within the last year – one in Nigeria and one in Pakistan. These new strains emerged in specific pockets with remaining program gaps (Zaria LGA in Kaduna, Nigeria and Gadap Town in Karachi, Pakistan). The first detection of the strain in Pakistan was in an environmental sample in July 2014. A full outbreak response was mounted, and this strain has not been detected since March 2015 in AFP cases or environmental samples. Although VDPV2 has been detected in three children with AFP in 2015 in Pakistan, these have not shown evidence of circulation and no cVDPV2 case has been detected in Pakistan in 2015. The Nigeria emergence was first detected in an environmental sample in August 2014 and the only case to date was reported in May 2015 from the Federal Capital Territory. A full outbreak response was mounted and the cVDPV2 strain has not been detected since.

VDPV2: In 2014-15, 15 countries have detected 46 separate emergences of VDPV2 in AFP and environmental surveillance⁵. Most of these

⁵ As of 9 September 2015

emergences did not become circulating VDPVs (cVDPV2). Only two emergences (in South Sudan and Guinea) evolved into cVDPV2, and two emergences (one in Pakistan and one in Nigeria, as noted above) became persistent cVDPV2.

cVDPV2: Between 2010 and 2015, there were 12 outbreaks of cVDPV2⁶ in countries other than Nigeria and Pakistan. Of these, 92% (11/12) were stopped after four SIAs, in less than six months.

The GPEI is currently managing two outbreaks of cVDPV2, one in South Sudan and another in Guinea. In South Sudan, VDPV2 strains linked to isolates from cases detected in September 2014 have not been detected since then and their circulation has likely stopped following the outbreak response. However, a new VDPV2 strain was isolated from a case with onset in June 2015. Given the extent of nucleotide changes and the setting of conflict in South Sudan, a full cVDPV2 outbreak response is being implemented.

The outbreak in Guinea was confirmed this month (September 2015) with the detection of cVDPV2 in a case investigated in Mali. The isolate is genetically linked to a case in Guinea, with onset on 30 August 2014. The GPEI is implementing a full outbreak response in Guinea and adjoining Mali. Surveillance in Guinea had been diminished as a result of the Ebola outbreak – most notably, stool samples could not be shipped out of the country for testing. Testing of samples from Guinea has commenced in June 2015. The infrastructure established to deal with the Ebola outbreak is now being used to support the response to this cVDPV2 outbreak.

Strategies to mitigate the risk of emergence and stop the circulation of Type 2 vaccine-derived poliovirus (VDPV2)

Updated definition for VDPV and program guidelines for responding to VDPV2

VDPV2 are considered in three categories:

- Vaccine-derived poliovirus (VDPV) is defined as an “OPV virus strain that is > 1% divergent (or ≥ 10 nt changes) for types 1 and 3 or $\geq 0.6\%$ divergent (≥ 6 NT changes) for type 2 from the corresponding OPV strain in the VP1 genomic region”.

⁶ Excluding two emergences in Nigeria and Pakistan which became persistent cVDPV

- Circulating VDPVs (cVDPVs) are broadly defined as “VDPV isolates for which there is evidence of person-to-person transmission in the community”, and are more precisely defined below.
- Persistent cVDPVs are defined as “cVDPVs that continue to circulate for more than six months following detection”⁷. Persistent cVDPVs therefore represent failures in the program to contain the cVDPV outbreak within 6 months of detection.

In July 2015, GPEI revised the definition of cVDPVs, enhancing the sensitivity of the definition of cVDPV. Under the new guidelines cVDPV is defined as:

- Genetically linked VDPVs, isolated:
 - i) *from at least two individuals – not necessarily acute flaccid paralysis (AFP) cases – who are not household contacts,*
 - ii) *from one individual and one or more environmental surveillance (ES) samples, or*
 - iii) *from two or more ES samples if they were collected at more than one distinct ES collection site (no overlapping of catchment areas), or from one site if collection was more than two months apart¹*
- or
- *a single VDPV isolate, with genetic features indicating prolonged circulation (i.e. a number of nucleotide changes from parent Sabin strains suggesting ≥ 1.5 yrs of circulation or 15 nt changes).*

The program has developed updated guidelines for immediately responding to VDPV2 between August 2015 and OPV2 withdrawal in countries using OPV. In summary, the guidelines emphasize that 1) the response to VDPV2 detection should not wait for classification of the strain as cVDPV2 or iVDPV2; 2) a rapid local response should be implemented to prevent further circulation; 3) immediately 3 mop up rounds with tOPV should be planned and implemented; 4) the first round should commence within 14 days of notification of the VDPV2; 5) the size and geographic scope should be based on risk of spread and estimated duration of circulation; 6) 3 rounds

⁷ Global Polio Eradication Initiative (2015). Reporting and classification of vaccine-derived polioviruses:
http://www.polioeradication.org/Portals/0/Document/Resources/VDPV_ReportingClassification.pdf

with tOPV should be completed even if the circulation of VDPV is not confirmed.

If the VDPV2 is confirmed as cVDPV, the scope of mopping up SIAs should be further expanded. All areas at risk should be covered in line with the GPEI Standard Operating Procedures for polio outbreak response. A minimum of 2 million children should be covered and tOPV SIAs should continue until 3 rounds have been implemented following the most recent cVDPV2 isolate. The WG also expanded that where 2 million children did not exist within a reasonable radius, all children, or children of 2 million total population could be targeted. The use of IPV should be considered, per existing guidelines.

To mitigate the risk of emergence of new VDPV2 in advance of the OPV2 withdrawal, a further intensified schedule of tOPV SIAs planned between September 2015 and March 2016 was presented to the WG.

WG comments on epidemiology of VDPV2

Persistent cVDPV2: The WG appreciated the strong progress that has been made in both Nigeria and Pakistan, toward improvement of surveillance and quality of immunization campaigns. The overall type 2 population immunity has improved substantially in both countries following increases in quality and frequency of tOPV campaigns supplemented by IPV. The group concluded that both countries appear to have successfully interrupted the transmission of the highly mutated cVDPV2 strains that had established prolonged widespread circulation. The new persistent strains had emerged recently in specific pockets in Kaduna and Karachi with residual gaps in immunization coverage. The group assessed that transmission of these recent persistent cVDPV2 strains has probably been stopped as a result of intensified programme activities.

The WG reviewed the planned Supplementary Immunisation Activity (SIA) schedules of both Nigeria and Pakistan between September 2015 and April 2016. The WG was satisfied that Nigeria's schedule includes sufficient tOPV to appropriately reduce the risk of further cVDPV2 emergence. However, the WG judged that Pakistan's planned schedule was not sufficient in this regard. The WG strongly recommended that Pakistan review its planned tOPV SIA schedule, in close coordination with its TAG, to ensure that the vaccine mix and geographic scope of SIAs will provide sufficient population immunity against emergence of VDPV2 before the switch, as well as for interruption of wild poliovirus transmission. The WG welcomed the

commitment of the Pakistan program to undertake such a review immediately.

VDPV2 emergence: The WG appreciated and endorsed the new definitions for VDPVs and updated guidelines for responding to VDPV2. The group also endorsed the intensified global schedule of SIAs planned to prevent the emergence of new VDPVs around the time of OPV2 withdrawal. Noting the guidelines and plans, the group emphasized the importance of ensuring sufficient supplies of tOPV.

The Working Group noted, however, that the definitive approach to stopping VDPV2 emergences is the coordinated withdrawal of OPV2. Until that time, the risk of VDPV2 emergence and circulation will remain due to insufficient coverage resulting in inadequate population immunity to type 2, particularly in settings of complex emergencies and conflicts where immunization programs are severely disrupted.

Stopping cVDPV2 transmission: The Working Group assessed the risk of continued cVDPV2 transmission at the time of the switch as low because:

- All persistent cVDPV2 transmission has probably been stopped;
- The GPEI has demonstrated its ability to rapidly stop cVDPV2 outbreaks, and has further intensified its approach with new definitions for cVDPV2 and outbreak response guidelines from August 2015.

The Working Group therefore assessed that the remaining risk of cVDPV2 transmission should not stop the tOPV-bOPV switch from proceeding as planned in April 2016.

The Working Group re-emphasised, however, the need for the current cVDPV2 outbreak in Guinea/, and the VDPV2 outbreak in South Sudan to be stopped rapidly, and welcomed the GPEI's work to allocate additional resources to doing so. The group acknowledged that the outbreak response guidelines set a target of stopping such outbreaks within 120 days. It is important that this is achieved. The Working Group also reiterated that, although the intensified tOPV SIA schedule will substantially reduce the probability of VDPV2 emergence, the risk of one or more cVDPV2 outbreaks occurring close to the time of the switch will remain regardless of the date of the switch.

Status of readiness criteria

The WG reviewed the progress of the five readiness criteria:

- **Introduction of at least one dose of inactivated poliovirus vaccine**

As of September 2015, 105 countries have introduced IPV in their routine immunization program. A global shortage in IPV supply has forced some delays for other countries. However, almost all 126 OPV-using countries (including all Tier 1 and 2 countries) are forecast to introduce IPV prior to the switch. The only exceptions are Indonesia, and 10 other Tier 3 and 4 countries, which intend to introduce IPV after April 2016⁸.

- **Access to a bivalent oral polio vaccine that is licensed for routine immunization**

There are 149 countries and 7 territories currently using OPV (156 total), which need to approve bOPV for use in their routine schedule by the switch date. To date, 55 countries are using bOPV in campaigns and approval for routine use is not anticipated to be an issue. The approval process is on track for completion in time for 93 countries that have not used bOPV yet. The countries in the latter group either accept WHO prequalified products, plan to go to an all-IPV schedule or accept WHO prequalification as a temporary licensure measure while the national licensure/registration process is ongoing. The remaining eight countries do not yet have appropriate regulatory pathways in place for expediting the bOPV licensure. This is particularly an issue in some OPV-producing countries that supply for domestic needs and which request in-country clinical trials for bOPV licensure. For these countries, a transitional contingency involving expedited licensure with WHO support or interim use of imported bOPV is being pursued as part of their switch readiness plan.

WHO HQ, in collaboration with regional offices and partners, is conducting an intensive program of work with prequalified bOPV manufacturers and national OPV suppliers to coordinate support to

⁸ Tier 1: WPV endemic countries OR countries that have reported a cVDPV2 since 2000; Tier 2: Countries who have reported a cVDPV1/cVDPV3 since 2000 OR large/medium sized countries with DTP3 coverage <80% in 2011, 2012, 2013 as per WHO-UNICEF; Tier 3: Large/medium countries adjacent to Tier 1 countries that reported WPV since 2003 OR countries bordering with the current cVDPV2 outbreaks, if not already included in tier 1 and 2, OR countries that have experienced a WPV Importation since 2011; Tier 4: All other OPV only using countries

countries identified at risk and to monitor the approval of bOPV for use in routine immunization before March 2016.

The WG concluded that bOPV approval for use is on track to date. However, the WG emphasised the importance of ensuring that this work is completed in due time as it is absolutely vital that all countries are ready to use bOPV in routine immunisation at the time of the switch.

- **Detection and response protocols for type 2 poliovirus, including constitution of a stockpile of monovalent oral polio vaccine type 2**

Surveillance: The GPEI has established a surveillance strengthening plan in the high-risk countries of Central and West Africa, including Central African Republic, Gabon, Niger, Mali, Liberia, Guinea, and Sierra Leone. The plan includes capacity building, refresher trainings, strengthening of active surveillance, expansion of environmental surveillance, and programme reviews. In addition, the GPEI has developed specific plans to manage surveillance in difficult-to-access areas (e.g. South Sudan, Somalia, Nigeria, Lake Chad, Afghanistan, Middle East) including engaging NGOs, increasing field presence, conducting contact sampling and stool surveys, focusing on high risk-mobile populations (e.g. internally displaced persons/IDPs, Nomads), and growing the networks of community informants.

- **Outbreak detection and response protocol:** The outbreak detection and response protocol was endorsed by SAGE in October 2014. An update with further refinements to this protocol is now being finalized. The WG reviewed the updates and provided input.

The updated protocol reflects the change in definition of cVDPV2 described above, and also reflects new scientific evidence on the VDPV2 emergence risk after the switch, on waning mucosal immunity, on the role of IPV, and on the effectiveness of the Short Interval Additional Dose Strategy. The major proposed changes are:

- 1) a new definition of VDPV2 outbreaks, aligned with the new VDPV2 definition;
- 2) wider use of IPV in outbreak response;
- 3) expansion of the scope of the immunization response.

The WG endorsed the updates with the following specific guidance:

- 1) The definitions and response for confirmed, probable and possible type 2 virus circulation should be segmented between vaccine-derived poliovirus, wild poliovirus, and Sabin viruses.
- 2) IPV-only response should be considered in selected cases, as below:
 - a. Initial response following detection of confirmed cVDPV in zone 3 (areas with low transmission risks) in phase 1 (<1 year after the switch) and for all geographic zones with probable VDPV2 transmission in all phases⁹.
 - b. Initial response following detection of probable WPV transmission (i.e. detection of WPV in ES) in the absence of evidence of replication in human population (e.g. likely poliovirus release from a facility) for all geographic zones¹⁰ and phases.
 - c. Protection of household and immediate community/work contacts for detection of a WPV2 AFP case with known exposure to poliovirus in a facility (e.g. from laboratory exposure) or for detection of new iVDPV2 cases.

The WG recognizes that the development of outbreak response guidelines is an iterative process; it requested the program to review and revise the guidelines after one year of the switch. The WG also suggested highlighting that countries exclusively using IPV prior to the switch will have a different risk pattern than countries that have used tOPV.

The WG also reviewed the results from a regulatory fractional intradermal (ID) IPV study recently conducted among adults in Cuba, comparing immune response rates following a booster dose of ID fractional IPV versus IM full dose IPV. The differences in immune response rates between the study groups met the non-inferiority criteria of <10% at day 7, which was maintained at days 28 and 56

⁹ Time since OPV2 cessation: Phase 1: within 1yr; Phase 2: 2-3 yrs; Phase 3: 4+ yrs

¹⁰ Zone 1 (high risk): Clear history of sustained WPV or reported cVDPV2 since 2000; OR affected community with other risks for low immunity or high mobility links to susceptible communities; Zone 2 (high-medium risk): Consistently low DTP3 coverage <80% in the previous 3 years; OR history of imported WPV or any cVDPV in the previous 3 years; OR with DTP3 coverage <90% and adjacent to affected area; Zone 3 (low risk): DTP3 coverage consistently >80%; affected community with few risk factors for sustained transmission

after booster dose. The WG welcomed the progress of the development of ID IPV as this would mitigate the IPV supply shortage for outbreak response. It also encouraged the GPEI to accelerate the development and introduction of ID IPV devices as ID administration with needle and syringe required highly trained health workers.

mOPV2 stockpile: A global stockpile of mOPV2 is being established and will be maintained after the switch, for potential use in responding to type 2 polio outbreaks following withdrawal of type 2 OPV. The operational framework for the mOPV2 stockpile was approved by the SAGE in October 2014. Since then, the framework has been updated according to the new VDPV2 classification, and the new approach for type 2 outbreak response. A stockpile of 50 million doses of mOPV2 in finished product has been purchased and will be available for deployment by March 2016. An additional 50 million doses to be available by July 2016 are currently under negotiation. GPEI will identify countries that decide to build a national mOPV2 stockpile and ensure the authorities are fully aware of commitments under WHA 68.3 related to storage under appropriate containment and use of mOPV2 only after authorization by the Director General of WHO. The WG welcomed this progress and requested WHO to finalize the stockpile release criteria and establish the expert group that will advise the Director General of WHO on release of mOPV2 in response to type 2 poliovirus detection.

The WG noted that the programme has reserved more than 4 million doses of IPV for use in response to a cVDPV2 detection after the switch.

- **Verification of global eradication of wild poliovirus type 2**
After the WG's meeting, on 20-21 September 2015, the Global Certificate Commission (GCC) met to review evidence submitted to WHO and Regional Certification Commissions (RCCs). It concluded that WPV2 has been eradicated globally. Its report will be made available to SAGE at its meeting of 20-22 October 2015. (The recommendation of the SAGE WG – that the tOPV-bOPV switch should go ahead as planned in April 2016 – was based on the assumption that the GCC would declare that indigenous WPV2 has been eradicated).

- **Completion of phase 1 poliovirus containment activities, with appropriate handling of residual type 2 materials¹¹**

To date, inventory of facilities storing or handling WPV has been completed in all countries in AMRO, EURO, SEARO and WPRO, the four regions that have been certified as polio free. However, only 15 of 47 countries in AFRO and 18 of 21 countries in EMRO have completed this inventory. The WG emphasized the importance of these remaining countries urgently completing their inventory. Also, all countries in every region should update national inventories of poliovirus facilities and confirm the number of facilities holding WPV2 and type 2 Sabin material on time for completion of Phase I.

Poliovirus essential facilities are those which serve critical functions, including IPV and Sabin-IPV production, storage of OPV stockpiles, vaccine quality assurance, diagnostic reagent production, virus diagnostic and reference functions, and/or crucial research. As such, these facilities are nominated and certified by governments¹². Although the number of designated 'Poliovirus- Essential Facilities' that will hold or handle type 2 poliovirus materials is expected to be less than 50, and in a limited number of countries, the GPEI anticipates challenges in implementation of full containment in phase II¹³. A national regulatory framework for containment needs to be established in countries that decide to host poliovirus-essential facilities; in parallel, national authorities for ensuring facility containment will need to be designated, and international expertise needs to be brought together to help oversee and guide the implementation of containment in essential facilities. Interim risk management measures are therefore being established during this period until full containment is implemented. The SAGE has previously endorsed the principles of the scheme to certify appropriate containment in poliovirus-essential facilities. The scheme will be reviewed and endorsed by the Global Commission for Certification of Polio Eradication in September 2015. The WG stated that the implementation of GAP III must be

¹¹ Phase I refers to: Preparation for containment of poliovirus type 2, including national laboratory inventory, destroying un-needed type 2 materials, transferring needed type 2 materials to essential poliovirus facilities, informing governments about upcoming need for poliovirus containment, and certifying designated essential poliovirus facilities for containment

¹² WHO Global Action Plan to minimize poliovirus facility-associated risk (GAPIII):

http://www.polioeradication.org/Portals/0/Document/Resources/PostEradication/GAPIII_2014.pdf

¹³ This phase comprises two parts: the first (Phase IIa) addresses the containment of WPV2, and the second (Phase IIb) the containment of OPV2/Sabin2 polioviruses in certified essential facilities. Phase IIa begins at the time of global readiness for OPV2 withdrawal, and ends after all six WHO regions have certified WPV eradication

adequately resourced at all levels from WHO HQ to the regions and countries.

Rationale for proceeding with tOPV-bOPV switch in April 2016

The SAGE Polio Working Group unanimously recommends to SAGE that the tOPV-bOPV switch proceed, as planned, in April 2016.

Evidence shows that national efforts with support from GPEI have eliminated several persistent cVDVP2 outbreaks in Nigeria and Pakistan, and the more recently identified persistent cVDPV2 outbreaks have probably stopped. GPEI has developed robust strategies and plans to prevent VDPV2 emergence. The program has also demonstrated the ability to rapidly stop cVDPV2 outbreaks.

There has been strong progress towards the achievement of readiness criteria. Although these have not yet all been met in full, the WG assesses that there are no critical gaps, and that the gaps that do exist are clear to the GPEI and are being addressed and/or mitigated.

The WG judges that it is appropriate to proceed despite the readiness criteria not being met in full. The tOPV-bOPV switch can never be risk-free, and determining whether or not to proceed requires a balanced judgement of risk.

One key risk applies regardless of whether the switch proceeds in April 2016 or is delayed:

- VDPV or cVDPV outbreaks: The GPEI may not be able to stop a new outbreak just before the date of the switch, although the tOPV SIAs planned between now and April 2016 should significantly help to prevent outbreaks before and after the switch. The post-switch outbreak response protocol covers the management of any outbreaks that occur. Because VDPV emergence will continue until OPV2 use is stopped, this risk will likely not be reduced by delaying the switch rather than by proceeding with it as planned.

One potential risk of proceeding in April 2016 is:

- Full containment measures are currently behind schedule. Delaying the switch would allow an additional year to make progress. The WG, however, is of the opinion that facility-associated risks of

poliovirus transmission can be reduced substantially with full implementation of Phase I of GAP III, including destruction of WPV2 by end 2015 and other residual type 2 materials by July 2016.

The main additional risks of the alternative – delaying the switch to April 2017 – are:

- Historical experience suggests that delaying the switch by a year will result in an additional 100-200 children being paralysed by VAPP, and a smaller additional number of children being paralysed by new cVDPV2 outbreaks. Continuing use of the type 2 component of OPV is hard to justify since there have been no WPV2 cases naturally occurring since 1999.
- The GPEI currently has an unprecedented level of capacity, which will begin to diminish by April 2017. In particular, the current surveillance and outbreak capacity in Africa has been heightened as part of the intensive program to stop WPV transmission, but cannot be maintained indefinitely. Thus the program's ability to detect and stop pre- and post-switch cVDPV2 outbreaks would be reduced.
- The conditions in which the GPEI is currently operating could deteriorate, making stopping pre-switch cVDPV outbreaks more difficult. This is particularly relevant in Nigeria and Pakistan, where a period of relatively stable operating conditions has enabled the GPEI to stop several strains of persistent cVDPV2 recently. Immunization programs continue to be disrupted in several regions, particularly affecting countries in the Middle East, Horn of Africa and Central Africa and in Ukraine, increasing the risk of emergence and circulation of VDPV2.
- Based on the clear advice of SAGE, countries are well-prepared for the April 2016 switch. Preparation has required significant financial and political investment. If the switch was now delayed, the delayed switch date would have less credibility and therefore readiness for it may well be reduced. There is also the risk of program losing credibility with countries, its donors and other stakeholders.

The Working Group assessed that the risks of delaying the switch significantly outweigh the risks of proceeding with it as planned. However, it must be reinforced that:

- The tOPV-bOPV switch can never be risk-free, and the risks outlined above must be carefully managed
- In particular, stopping current cVDPV2 outbreaks, implementing the intensified tOPV SIA schedule and the acceleration of containment measures are vital, as detailed below.

Recommendations for additional risk-reducing measures

In conclusion, the WG recommends proceeding with the tOPV-bOPV switch in April 2016.

Three particular areas of risk have been highlighted in this report, and are repeated here in summary:

Pakistan SIA schedule: The WG was not satisfied that Pakistan's planned Supplementary Immunisation Activity (SIA) schedule between September 2015 and April 2016 includes sufficient tOPV to appropriately reduce the risk of further cVDPV2 emergence. The WG strongly recommends that Pakistan review its planned schedule, in close coordination with its TAG, to ensure that the vaccine mix and geographic scope of SIAs will provide sufficient population immunity against VDPV2 before the switch. The WG welcomed the intention of the Pakistan program to undertake such a review immediately.

Current outbreaks: The WG recommends that the GPEI ensures that a full outbreak response is mounted to interrupt the new cVDPV2 outbreak in Guinea, and the current cVDPV2 outbreak in South Sudan, within the period of 120 days that the Polio Eradication and Endgame Strategic Plan specifies.

Containment: The primary purpose of implementing GAPIII is to reduce the risk of release and subsequent circulation of poliovirus from facilities that store or handle poliovirus. The WG recommended that the GPEI now:

- accelerate the implementation of phase I of GAPIII, including: a) all countries complete phase I, and b) focal points in all regions closely monitor country level activities and ensure that each country completes and updates its inventories of facilities that hold or handle polioviruses, have destroyed or commits to destroying WPV2 by end 2015 and any other type 2 materials including Sabin poliovirus by July 2016;
- develop a targeted advocacy plan to engage countries that have not responded or will be late in completing phase I;
- develop an intensified communications plan to ensure that countries and key stakeholders and actors take necessary actions taking into consideration the recent WHA resolution and the confirmation by SAGE of April 2016 as the date for OPV2 withdrawal – a global

landmark. The communication should also guide actions by research and academic facilities that store clinical samples that may be potentially contaminated with WPV or Sabin 2 poliovirus;

- identify any remaining risk of delay in phase I, and rapidly develop an interim risk management plan to address them; and
- develop a separate advocacy plan for countries that plan to host poliovirus-essential facilities to ensure establishment of national regulations and authorities to assure compliance with regulations on containment.

Given the global impact and reach of the decisions made, as well as the fluidity of the programmatic and epidemiological situation, the WG agreed to meet in January 2016 to review the progress of implementation of the aforementioned recommendations.