

19-20 January | 2015

11th Meeting of the SAGE Polio Working Group

Conclusions and recommendations

Note for the Record



**World Health
Organization**

DRAFT AS OF 3/8/16

Background

The 11th face-to-face meeting of the SAGE Polio Working Group (WG) was held during 19-20 January 2016 at the World Health Organization in Geneva, Switzerland.

The meeting was attended by the following WG members: Yagob Al-Mazrou (Chair), Peter Figueroa (Ex-chair), Elizabeth Miller (Ex-chair), Francis Nkrumah, Walter Orenstein, Antoine Kabore, Kimberly Thompson, Nicholas Grassly, Walter Dowdle, Hyam Bashour, T Jacob John and Zulfiqar Bhutta.

This note presents a summary of the main findings, conclusions and recommendations of the meeting.

Context and objectives of the Meeting

In October 2015, SAGE reaffirmed that the withdrawal of type 2 oral polio vaccine (OPV type 2) should proceed in April 2016, through a globally synchronized switch from trivalent to bivalent OPV (the tOPV-bOPV switch). This decision was based on an assessment that the public health risks associated with continued use of the type 2 component of trivalent oral polio vaccine (tOPV) outweigh the risks associated with withdrawing this component of the vaccine. SAGE also recommended risk mitigation measures, including implementing an aggressive schedule of Supplementary Immunization Activities (SIAs) with tOPV, strengthening response to outbreaks in Guinea and South Sudan, accelerating implementation of WHO Global Action Plan for containment (GAPIII), and prioritizing an adequate IPV supply to countries at higher risk of type 2 polio outbreaks.

The WG met on 19-20 January 2016 to: Follow up on the SAGE recommendations regarding OPV type 2 withdrawal; and ii) start discussions on future immunization policy after OPV type 2 withdrawal. The specific objectives of the meeting were:

1. To appraise the current epidemiology of cVDPV2
2. To examine the status of preparation for OPV type 2 withdrawal
3. To discuss the roadmap for SAGE discussions and recommendations on future polio immunization policy
4. To review the epidemiology of immunodeficiency-related vaccine-derived polioviruses (iVDPVs), progress on antiviral agents, and options for increasing sensitivity of surveillance for iVDPV.

Topic 1: Current cVDPV epidemiology

The WG reviewed progress towards interruption of wild poliovirus (WPV) and type 2 circulating Vaccine-Derived Poliovirus (cVDPV2). In the last six months, WPV cases have only occurred in Pakistan and Afghanistan, with no cases in the Middle East (last case 7 April 2014) or Africa (last case 11 Aug 2014). The number of WPV1 cases declined in both Pakistan (from 306 in 2014 to 52 in 2015) and Afghanistan (from 28 to 19 respectively). No WPV3 has been detected globally for over three years.

In Afghanistan, two epidemiological blocks can be distinguished: the Southern Region (Helmand and Kandahar) and the Eastern Region (Nangarhar and Kunar). Security issues continue to limit access, particularly in the Eastern Region. Repeated cross-border transmission with Pakistan is affecting the Eastern Region. The program has designated 47 high-risk districts in which efforts to address access and campaign quality issues are being focused, and plans to conduct targeted SIAs combining both OPV and Inactivated Polio Vaccine (IPV) in 28 highest-risk districts.

In Pakistan, the number of children in inaccessible areas has been reduced from more than 600,000 in 2013 to 16,000 in 2015. The programme is prioritizing efforts to access the remaining unreached children, and maximizing immunity through a series of strategies including OPV SIAs, using IPV in specific areas, setting-up health camps, and expanding Continuous Community Protected Vaccination¹ (CCPV).

¹ In CCPV, full-time volunteers are appointed from local areas and they work throughout the month. These volunteers are typically assigned the task to cover small areas.

The program has also made progress in eliminating persistent cVDPV2. There have been no persistent cVDPVs since March 2015 in Pakistan and since May 2015 in Nigeria. However, there have been several VDPV emergences in 2015, including cVDPV2 outbreaks in Guinea and Myanmar, and cVDPV1 outbreaks in Ukraine, Laos and Madagascar. The program has launched extensive response activities to these outbreaks. The response in Guinea has faced challenges, including suboptimal quality of SIA campaigns, and needs to be further intensified to ensure that the outbreak is stopped before the tOPV-bOPV switch. Surveillance for poliovirus remains in abeyance in Liberia and Sierra Leone, the other two Ebola-affected countries adjacent to Guinea.

WG decisions/recommendations

- **WPV:** The WG noted the significant progress made in improving access and coverage, and decreasing the number of type 1 WPV cases in Pakistan and Afghanistan. The WG encouraged the program to further accelerate progress, especially in improving the monitoring of SIAs, strengthening surveillance and improving access in key areas (particularly Karachi, Peshawar, Khyber in Pakistan and the Eastern Region of Afghanistan), and reaching missed children including by addressing socio-cultural barriers.
- **VDPV2:** The WG acknowledged the progress made in eliminating persistent cVDPV2 in Pakistan and Nigeria (i.e. no case since May 2015), however the WG expressed its continuing concern about Pakistan. The WG judged that the response to the VDPV outbreak in Myanmar is adequate. However, the WG was concerned about the outbreak response in Guinea. The WG recommends that the program should further intensify the response to this outbreak. The WG also recommends that the program intensify programme surveillance (including expedited shipment of AFP samples, and establishment of environmental surveillance sites) in Guinea and its neighbouring and recently Ebola-affected countries of Sierra Leone and Liberia.
- **Rapid detection of VDPV2:** The WG recommends that the Global Polio Laboratory Network (GPLN) should continue to optimize diagnostic methods to rapidly detect poliovirus in AFP and environmental samples. Moreover, the GPLN, needs to be able to provide additional programmatically relevant information on any isolated type 2 polioviruses (i.e... whole genome sequencing and determination of recombination with class C enteroviruses) in an accelerated manner, to allow timely institution of appropriate response measures, particularly after the tOPV-bOPV switch.

Topic 2: Review the status of preparation for OPVOPV type 2 withdrawal

Type 2 cVDPV outbreak risk and response protocol

The WG reviewed a summary of a discussion held (on 18 January 2016) between representatives of the WG (Al-Mazrou, Figueroa, Grassly, Orenstein, Thompson) and three modelling groups (Kid Risk, Institute for Disease Modelling and Imperial College London) on cVDPV2 emergence risks and response strategy (see appendix 1). The WG also reviewed the updated type 2 outbreak protocol that had been revised since the September WG's previous meeting (see appendix 1).

Key changes made to the protocol since that time, in response to extensive internal and external review were: 1) adjustments to the scenarios in which IPV will be used; 2) adjusting the response activities for VDPVs, WPVs, and Sabin poliovirus by geographic zones; and 3) expanding the use of mOPV2 in response to a WPV2 AFP case or detection in environmental sampling (ES). The protocol emphasizes the primacy of rapid institution of control measures (an mOPV2 SIA within two weeks), recognizing that coverage of the initial rapid response may not be optimal. Even with sub-optimal coverage, mathematical models project substantial impact on reducing transmission, if done quickly and followed up by high-quality subsequent rounds. WHO Country Offices and UNICEF Supply Division have confirmed that deployment of mOPV2 within 2 weeks and IPV within 30 days after the decision of WHO DG to release stockpile is feasible, if adequate supplies of IPV are available.

There is a continuing IPV shortage globally, which will likely persist into 2017. For this reason, intradermal (ID) fractional-dose IPV should be used for outbreak response, preferably administered with an ID device rather than a needle and syringe. It is anticipated that the first ID IPV device will become available in June 2016, and the next in October/November 2016. There is an ongoing study in Pakistan to assess the immunogenicity (i.e. humoral immunity) of ID IPV and its usability in SIAs, with a similar study planned in the African region. Administering IPV in previously OPV-vaccinated children is boosting of mucosal immunity and providing

protection from paralysis for serotypes for which the IPV leads to seroconversion, which will contribute to decreasing the burden of poliovirus associated with the outbreak.

WG decisions/recommendations

- Based on the mathematical models considered, the program should expect at least 1-2 cVDPV type 2 outbreaks within the first 12 months following the switch, with Pakistan representing a high-risk area.
- It is important to fully sequence any newly detected type 2 VDPV strain rapidly, to identify whether or not an outbreak response is required iVDPV requiring a different set of response activities.
- The WG endorsed the revised protocol, including:
 - The use of IPV in the case of “confirmed” outbreaks in Zone 1-2 countries.
 - Minimum number of SIAs (4 or more SIAs)
 - Target age group (0-5 years unless epidemiology suggests older persons involved)
 - Minimum target population (2 million)
- Recognizing the continuing IPV shortage, the program should ensure the availability of ID devices to facilitate administration of fractional-dose ID IPV for outbreak response.
- WG concluded that sufficient number of tOPV campaigns with high coverage is the key to reduce the risk of type 2 VDPV emergence. In this regard, WG expressed concern over the SIAs calendar of Pakistan as there is only one tOPV nationwide vaccination round (March 2016) within six months before the OPV2 withdrawal (with two sub-national tOPV SIAs in October 2015 and February 2016 targeting about 50% of the target population aged less than five years).
- The program should be prepared for outbreaks, so that an outbreak response can be launched within two weeks of confirmation of a case. This requires preparation for rapid field investigation, strengthening surveillance, accelerating laboratory processing, and communication with countries and the scientific and public health community ahead of time.

Preparation for OPV type 2 withdrawal

The WG reviewed the progress towards OPV type 2 withdrawal, scheduled in the second half of April 2016. IPV introduction is on track in the highest priority countries. So far 149 countries already use IPV and all remaining 45 countries are planning to introduce IPV in 2016. There are 20 tier 3 and 4 countries and two tier 2 countries (Equatorial Guinea and Indonesia) that will introduce IPV after April 2016. By the end of 2015, more than 80% of the global birth cohort was living in countries in which IPV has been introduced in the routine immunization schedule. The use of bOPV has been approved by 123 of 151 OPV-using countries due to carry out the tOPV-bOPV switch, with the remaining 28 countries expected to approve bOPV use by April 2016. Switch plans have been developed by all tier 1-3 countries, with financial support provided to selected countries to ensure on-time implementation.

WG decisions/recommendations

- The WG acknowledged the strong and sustained progress toward addressing the readiness criteria for the tOPV-bOPV switch.
- The WG expressed concern that the IPV supply shortage will likely persist into 2017, and encouraged the program to closely monitor the supply and demand to ensure IPV availability in countries, and minimize stock-outs.
- The WG emphasized the importance of ensuring that the scientific and medical communities are aware of the switch and its rationale

Containment

The WG reviewed the status of GAP III implementation. Since the last WG meeting in October 2015, there has been significant progress, particularly: 1) communication to the scientific community on regions, countries and facilities; 2) targeted engagement with countries at risk of lagging behind (especially 95 countries which have not completed reporting on WPV2/VDPV2); and 3) intensified efforts for GAP III implementation. WHO is establishing a Containment Advisory Group (CAG) to provide further guidance on the handling of potentially-infected specimens, essential research projects, and interim risk reduction measures. WHO is strengthening its headquarters containment team and has conducted regional GAP III implementation and certification workshops in AFR, EUR, SEAR, EMR and WPR. (Additional AFR, AMR and EUR workshops are scheduled in May

2016). Phase I implementation continues to achieve destruction of WPV2 and cVDPV2 stocks in advance of the switch. , Member States are expected to report on disposition of OPV2/Sabin2 materials as of July 2016.

WG decisions/recommendations

- The WG emphasized the importance of polio facilities destroying WPV2 and cVDPV2 materials before the time of the tOPV-bOPV switch in April 2016, except those that plan to become poliovirus-essential facilities and expect to be officially designated as such by their respective national authority for containment.
- The program should urgently engage countries hosting non-poliovirus facilities that handle potentially infectious material, and support them in their efforts to complete the identification, destruction or containment of Sabin 2 materials

Topic 3: Future immunization policy

Global withdrawal of tOPV will take place in April 2016. With the planned interruption of WPV transmission during 2016, it is expected that the withdrawal of all OPV should take place around 2020. There are important questions to address about immunization policy beyond this time. National programs, manufacturers and donors need to start discussions and preparations. Remaining uncertainties that need to be addressed include: polio program timelines, the immunogenicity (humoral and mucosal) of one or two IPV doses under different schedules, projected vaccine supply, vaccine costs (and funding), and countries' willingness of countries to continue to pay for IPV and polio risk management measures.

The WG began discussion of this topic and identified topics for further discussions at future meetings. It is likely that vaccination against polio will need to continue into the 2020-2030 period. There will be a need for global level agreement on how long polio vaccination should continue, though countries may choose to diverge from this. Advice by SAGE will be needed on the criteria that countries should meet before stopping vaccination (e.g., meeting of surveillance performance standards, appropriate implementation of containment measures). More work is needed to define the number, schedule and formulation of IPV doses, and further analysis is needed of the vaccine supply situation and vaccine costs and affordability.

The WG reviewed the current IPV market dynamics. New suppliers are likely to enter the market around 2018-2020, likely alleviating the global demand shortages of IPV. Several suppliers are also working on hexavalent vaccine that includes IPV and whole-cell pertussis vaccine, but all manufacturers face significant challenges in terms of manufacturing logistics, capacity, and cost-of-goods.

WG decisions/recommendations

- To secure the long-term success of polio eradication, vaccination will likely need to continue after OPV withdrawal, possibly for at least 5-10 years, because of risks associated with iVDPVs, and containment facilities.
- The program should develop the criteria for countries and regions to stop poliovirus vaccination (e.g. surveillance capacity and sensitivity, , no evidence of iVDPVs).
- The program should continue to monitor the vaccine supply situation, including IPV availability and affordability.
- The WG proposes to develop a recommended high-level policy direction during 2016 and to finalize its recommendations for full SAGE consideration in 2017.

Topic 4: iVDPV epidemiology and management strategy

The WG reviewed an update on the current known epidemiology of iVDPV infections. Currently, there are 107 iVDPV patients in the WHO registry, who are or have excreted iVDPV. There has been a substantial increase in detected cases (with two divergent trends – an increase from middle-income countries and a decrease from high-income countries). In terms of geographical distribution, there is clustering in the Middle East – possibly due to co-sanguinity. There is substantial underreporting (particularly for iVDPV excretors without acute flaccid paralysis). Type 2 polioviruses are the predominant cause of iVDPV cases, causing >60%% of all cases. These iVDPVs might constitute a significant risk in triggering outbreaks among under-immunized populations post-OPV cessation. This risk appears to be concentrated in lower and upper middle-income countries (e.g. India, Nigeria, Indonesia, and Egypt).

The WG then reviewed the progress of the development of antivirals against poliovirus. Early clinical studies have found that Pocapavir (V-073) is safe and effective in clearing excretion, but the rate of emergence of resistance is considerable. Therefore, the Polio Antivirals Initiative (PAI) is now preparing to study the combination of Pocapavir and one more compound (V-7404).

WG decisions/recommendations

- The WG recognized that iVDPVs can pose a significant risk to maintaining global polio eradication. While iVDPV excretors are rare and the risk of transmission is low, any transmission could have significant consequences, especially after OPV withdrawal.
- The WG requested the WHO secretariat to develop options for enhancing surveillance sensitivity for detecting iVDPVs and discuss modelling of risk estimates during the next face-to-face meeting of the SAGE WG.

Summary and next steps for the SAGE Working Group

The 11th meeting of the SAGE WG reviewed the final stage of preparation for OPV type 2 withdrawal and started its discussions on future immunization policy. The WG also reviewed the epidemiology of iVDPV and the development of antiviral drugs and learned about published modelling results that explored iVDPV risks and the potential benefits of antiviral drugs.

The WG requested a follow-up conference call in February or March 2016, particularly to receive a further update on: i) the progress on interrupting the cVDPV2 outbreak in Guinea and Myanmar; and ii) IPV supply situations.

Conclusion: Risk of VDPV Emergence

- **Risk of emergence:** There is high probability that at least 1 cVDPV will emerge within 12 months of the switch. High quality tOPV SIAs before the switch (i.e. at least three times with at least 80% coverage) will reduce the risk of emergence significantly.
- **Timing of emergence:** The risk is greatest in the first year and declines thereafter. However, the consequences are greater, the longer the time between the switch and emergence. This presentation only focuses on the risks within 12 months of the switch.
- **Risk factors:** Low type 2 immunity is greatest risk factor. (Other risk factors include birth rate, population size and density, low RI coverage, failure to reach unvaccinated children in pre-switch SIAs, and other conditions associated with high levels of transmission, particularly fecal-oral route).
- **Geography:** The biggest risk exists in AFRO and some parts of EMRO, SEARO and WPRO. Pakistan remains a concern because Pakistan plans only one national tOPV campaign in 2016, prior to the switch in April.
- **Risk of aVDPV evolving to cVDPV:** Historically, most aVDPVs died out without program intervention in the context of relatively high vaccination rates during polio eradication. More aggressive response to aVDPV is needed, the longer the interval from the switch, occurrence in an area with prior cVDPV emergence, substantial genetic deviation from parent Sabin virus (nt deviations, recombination with class C enterovirus).

Conclusion: cVDPV2/WPV2 Response Strategy

- **Optimal number of SIA rounds:** 4 minimum, more may be needed in high R0 settings.
- **Speed of SIAs:** First SIA within 2 weeks of detection is beneficial even with suboptimal coverage. Reaching high coverage is critical in subsequent rounds (esp. populations in low RI coverage).
- **Interval of SIAs:** Short (2 weeks) interval is better if not compromising the coverage (program feasibility must be considered).
- **Target age group:** 0-5 years old. Unless there is evidence of circulation among older persons
- **Target population:** A minimum of 2 million children is adequate in most places if the program can achieve high coverage. Consider expanding the scope further if there is evidence of extensive circulation (higher nt changes) and the program can attain high coverage.
- **Use of tOPV:** Although the tOPV and mOPV2 have similar immunogenicity against type 2, use of tOPV in post-switch is not possible because all tOPV is removed from the field and destroyed. Simultaneous bOPV and mOPV2 might be considered in areas at risk for WPV1/3.

Conclusion: Role of IPV

- **Benefit of IPV:** IPV is useful in boosting intestinal immunity among OPV-primed children. Therefore, within first 12 months after the switch, the program should include IPV in the second SIA. Special attention should be paid to achieving high coverage. With time, IPV alone is less useful to prevent transmission, but will reduce paralytic disease.
- **Timing of IPV:** IPV should be used in the second SIA to assure adequate time for planning and high coverage without compromising the coverage and timing of OPV rounds. High OPV and IPV coverage are essential.
- **Target of population:** same as mOPV2 (2 million in core areas). If IPV supply is adequate, consider additional 2 million in the surrounding areas. Fractional doses of IPV can be used if ID devices are available.
- **Effectiveness of ring vs. transit strategy:** unable to fully assess at this time. A country should select the strategy based on in-depth investigation of epidemiology and expected coverage. International Health Regulations may require vaccination of travelers from/to infected areas.