

SAGE Polio Working Group

3 March 2016

Conference Call Notes

INTRODUCTION

A SAGE Polio Working Group (WG) teleconference was held on 3 March 2016 to discuss follow-up items from its January 2016 meeting. The call was attended by the following WG members: Yagob Al-Mazrou (Chair), Peter Figueroa, Walter Orenstein, Walter Dowdle, T Jacob John, Elizabeth Miller, Kimberly Thompson, Hyam Bashour and Antoine Kabore. Francis Nkrumah, Zulfiqar Bhutta and Nick Grassly were unable to attend. This note presents a summary of the presentations, key discussion points, decisions and recommendations from the call.

OBJECTIVES

The objectives of the meeting were to:

1. Review the current epidemiology of circulating vaccine derived poliovirus (VDPV) type 2 (**Information**)
2. Review the preparations for OPV2 withdrawal (**Information**)
3. Discussion on reporting type 2 case detection under IHR (**Endorsement**)
4. Use of fractional ID IPV for campaign and routine immunization (**Endorsement**)

PRESENTATIONS, DISCUSSIONS AND CONCLUSIONS

TOPIC 1
Review the current epidemiology of cVDPV type 2
<p>The WG reviewed the current status of cVDPV type 2. In 2015, cVDPV type 2 cases were reported in Nigeria, Guinea, and Myanmar. Nigeria conducted multiple tOPV SIAs in 2015, which appear to have stopped the transmission of cVDPV2s there. The outbreak response in Myanmar is on track; with no cVDPV type 2 cases after 5 October 2015, four tOPV SIAs completed as of March 2016, and a fifth SNID currently under consideration. With high quality tOPV SIAs and high routine immunization coverage, the probability of outbreak continuation in Myanmar beyond switch or geographic expansion seems low. Guinea experienced several challenges in responding to the cVDPV2 outbreak, including competing national priorities due to Ebola that led to decreased quality of polio SIAs and surveillance. To date Guinea has reported 8 confirmed cases of a newly emerged cVDPV2 with onset between 30 August 2014 and 14 December 2015, in Kankan Region, in eastern Guinea. In response, an emergency outbreak plan has been implemented with support from GPEI, including: Outbreak Assessment with focus on surveillance with active case searching in Guinea and neighbouring Ebola-affected countries. Guinea has conducted and is planning tOPV NIDs to stop transmission, but some risk of continuation of circulation of cVDPV2 beyond the switch exists for Guinea, with possibility of spread to neighbouring areas.</p> <p>In addition, a VDPV2 case was recently reported from Democratic Republic Congo with 16 nt changes with onset on 13 January 2016. The investigation is ongoing. Urgent measures are underway to ensure three SIAs are implemented prior to switch. If this outbreak continues beyond the switch, the program will use mOPV2 for the outbreak response rounds after the switch. The DRC may move its national switch date to the end of the switch window, but this outbreak will not delay the global switch from tOPV-bOPV that will occur during April 15-30.</p> <p>WG comments</p> <ul style="list-style-type: none">• Agreed that outbreak in Myanmar is unlikely to pose any threat to the global switch.• Expressed concern about the situations in Guinea and DRC, and encouraged the WHO to accelerate the implementation of response in these countries, including delaying the switch towards the end of two weeks switch period.

- Expressed concern that Pakistan still appears to present a risk for cVPDV type 2 cases after the switch due to the relatively low number of tOPV SIAs conducted there in the run up to the switch.

TOPIC 2

Global preparations for OPV2 withdrawal

The WG reviewed the different aspects of preparations for the OPV2 withdrawal.

IPV introduction and supply

To date, 92 countries introduced IPV since January 2013, including all 17 tier 1 countries and 14/19 tier 2 countries. Due to the IPV supply shortage, 20 low-risk countries and one self-procuring country (Indonesia) will introduce IPV after the switch.

As of early February 2016, Bilthoven Biologicals, one of the two IPV suppliers to the GPEI, informed UNICEF SD and PAHO RF that they are facing production problems and will need to reduce again the amount of IPV they are able to provide.

- For UNICEF SD: Overall reduction of 1m doses in 2016, and a delay in provision of 6m doses (Only 4.6m out of the planned 10.6m will be delivered before the switch).
- For PAHO RF: Overall reduction of 2.8m doses in 2016, with most being provided only as of Q3 (post switch). In addition, PAHO still has pending orders from 2015 totalling 1.4 million doses which will hopefully be delivered by May 2016.

As a result, seven low risk countries (tier 3 and 4) will not be able to introduce IPV before the first quarter of 2017. In addition, some shipments of IPV to countries that have already introduced in their programme will need to be delayed:

- by 1-3 months for 10 Tier 2 (higher risk) countries, with limited risk of disruption of their programme
- by 2-6 months for 12 low risk countries (tier 3 and 4), with a high risk that these countries will face stock outs

IPV supply shortage is likely to continue over 2016-18; it may be limited further for the 5-dose and 1-dose presentation from Bilthoven Biologicals.

Given the unreliability of the IPV manufacturers to meet supply projections to date, the GPEI has already started working on further contingency plans.

Regulatory approval of bOPV for routine use

To date, 134/144 countries approved the use of bOPV for routine (including all countries SEARO and AFRO). The program is closely following up with the remaining 10 countries, and no issues are expected.

Environmental surveillance

The global plan to expand environmental surveillance is on track in the majority of countries, with the expansion in DRC being implemented by April 2016, and Mali by July 2016. Unfortunately, Yemen and Somalia will not be able to implement the plan due to unstable security conditions in country.

Containment

The implementation of GAP III phase I shows substantial progress for most regions, with recent completion of phase I in WPRO with all reports received. Unfortunately, no reports have been received yet from PAHO.

Country preparation

All tier 1, 2, and 3 countries have developed their switch plans. Distribution of financial support to selected (67) countries is on track; 16/17 Tier 1, 17/19 Tier 2 countries have received financial support. 24 countries were identified for technical assistance to support monitoring activities during the validation of the switch.

WG comments

- WG noted the update and encouraged WHO to continue to monitor the IPV supply situation and

explore different options to mitigate the IPV supply shortage

TOPIC 3

Discussion on reporting type 2 case detection under IHR

Under the International Health Regulations (IHR) (2005), a notifiable case of poliomyelitis due to wild-type poliovirus is defined as “a suspected case with isolation of wild poliovirus in stool specimens collected from the suspected case or from a close contact of the suspected case.” This definition does not include VDPV nor virus isolation from the environmental samples, so WHO added the VDPV and Virus detected from non-human sources (e.g. environmental samples) to the WHO surveillance case definition for notification under the IHR on the grounds that such events are “unusual or unexpected and may have serious public health impact.”

After OPV2 withdrawal, it is critical to ensure post-switch that all type 2 polioviruses are notified, including Sabin 2, in addition to VDPV and WPV. WHO proposed that type 2 Sabin virus be added to the WHO surveillance case definition as a notifiable event in addition to WPV and VDPV after 1 August 2016.

WG comments

- WG endorsed the proposal to amend and broaden the WHO surveillance case definition to include type 2 Sabin in addition to wild and vaccine-derived PV
- WG recommended that WHO communicate (after the switch and prior to 1 August) the need for Member States to report Sabin type 2

TOPIC 4

Use of fractional ID IPV

Due to the IPV supply shortage, the WG considered an option of use of fractional intradermal (ID) IPV for both outbreak and routine immunization use.

SAGE previously reviewed the evidence regarding the use of ID and recommended to accelerate the development of an ID IPV option (April 2012). SAGE WG revisited it again in September 2015, welcoming the progress of the development of ID IPV and encouraged the GPEI to accelerate the development and introduction of ID IPV devices.

Recent studies from Bangladesh¹ and Cuba² demonstrated that the immunogenicity of two fractional doses of IPV is superior to one full dose at the ages given in the studies. In Cuba, two fractional (1/5) doses of ID IPV given at 4 and 8 month induced 98% seroconversion rate against type 2, which is much higher than one full dose IM IPV given at 4 month (63%). Likewise, in Bangladesh, two fractional doses of ID IPV given at 6 and 14 weeks in Bangladesh induced 81% seroconversion against type 2 vs. 39% among those with one full dose IM IPV at 6 weeks. In both studies, two fractional doses induced substantially higher antibody titers against type 2 than one full dose. The use of fractional ID IPV is dose-sparing, with the 2 fractional doses using 2/5 of the full dose (i.e., 60% dose-sparing), although it requires an additional injection and the associated injection supplies and trained personnel.

Also, a recent Cuba study indicated that one ID IPV dose was as effective as an intramuscular (IM) IPV to boost the immunity among OPV-immunized adults (with the non-inferiority criteria of <10% at days 7, 28, and 56)³.

Based on these data and the ongoing IPV shortage, the recent WHO position paper on polio vaccine (to be published in March 2016) states:

¹ Anand A et al. Early priming with inactivated poliovirus vaccine (IPV) and intradermal fractional dose IPV administered by a microneedle device: A randomized controlled trial. *Vaccine*. 2015 Nov 27;33(48):6816-22

² Resik S et al. Priming after a Fractional Dose of Inactivated Poliovirus Vaccine. *N Engl J Med* 2013;368:416-24.

³ Resik S et al. (unpublished data)

In the context of an IPV shortage, countries could consider instituting a 2-dose fractional dose schedule which could ensure that all eligible infants receive IPV, is dose-sparing and results in better immunogenicity than a single full dose of IPV. To ensure early protection a schedule of fractional doses administered at 6 and 14 weeks may be considered. The two fractional doses should be separated by a minimum interval of 4 weeks. Fractional-dose IPV may be particularly appropriate for outbreak response if supplies are limited.

Recently, the India Expert Advisory Group (IEAG) recommended that 7 states in India will introduce a schedule of two fractional doses of IPV (before or shortly after the switch) at 6 and 14 weeks.

There are a few other studies available/ongoing/planned in Pakistan, Sri Lanka and Cuba

- **Cuba:** Use of different ID IPV devices indicated Pharmajet needle-free jet injector can similar immunity to BCG needle⁴ (study completed)
- **Pakistan:** Use of needle adapters for facilitating intradermal administration (with Star syringe, West needle adapters vs. BCG needle) (study ongoing)
- **Sri Lanka:** Boosting of mucosal immunity 10-12 year olds with fractional-dose IPV (in ethical review)

WG comments

- Confirmed that the proposed schedule of two fractional IPV doses can induce equal or better immunity than current one full-dose schedule
- Endorse the proposed strategy to use fractional ID IPV in campaigns and routine schedule to pro-actively address IPV supply shortage:
 - The program should use one fractional dose in outbreak response; it provides good seroconversion in naïve infants and protects them from paralysis, and it boosts humoral (and likely boosts mucosal) immunity in older previously OPV-vaccinated children
 - Selected countries or states within a large country (e.g. those with strong routine immunization system) may also consider two fractional doses in the routine schedule (e.g. at 6 and 14 weeks for early protection)
- Encourage that countries introducing two fractional ID IPV into their routine schedule assess the operational feasibility and challenges

⁴ S. Resik et al. Immune responses after fractional doses of inactivated poliovirus vaccine using newly developed intradermal jet injectors: a randomized controlled trial in Cuba. *Vaccine*. 2015 Jan 3;33(2):307-13