

STANDARD
OPERATING
PROCEDURES

RESPONDING TO A POLIOVIRUS EVENT OR OUTBREAK

PART 2: Protocol for poliovirus type 2

V2.1 20 April 2016
V2.2 15 August 2016
V2.3 01 May 2017
V2.4 01 November 2017

EFFECTIVE 01 NOVEMBER 2017 UNTIL 30 APRIL 2018

Published by the World Health Organization (WHO) on behalf of the Global Polio Eradication Initiative.

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Printed by the WHO Document Production Services, Geneva, Switzerland

Editing and design by Inís Communication – www.iniscommunication.com

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World Health
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Abbreviations

| | | | |
|------------------|---|--------------|---|
| AFP | acute flaccid paralysis | tOPV | trivalent oral polio vaccine (contains Sabin 1, 2 and 3) |
| a/c/iVDPV | ambiguous/circulating/ immunodeficiency-associated vaccine-derived poliovirus | VDPV | vaccine-derived poliovirus |
| BOPV | bivalent oral polio vaccine (contains Sabin 1 and 3) | VDPV2 | VDPV type 2 |
| DTP3 | diphtheria-tetanus-pertussis | WHA | World Health Assembly |
| EC | Emergency Committee | WHO | World Health Organization |
| EOMG | Eradication and Outbreak Management Group | WPV | wild poliovirus |
| EOC | Emergency Operations Centre | WPV2 | WPV type 2 |
| GAPIII | Global Action Plan III | | |
| GPEI | Global Polio Eradication Initiative | | |
| GPLN | Global Polio Laboratory Network | | |
| IHR | International Health Regulations | | |
| IPV | inactivated polio vaccine | | |
| ITD | intratypic differentiation | | |
| mOPV2 | monovalent oral polio vaccine type 2 | | |
| OPV | oral polio vaccine | | |
| SAGE | Strategic Advisory Group of Experts | | |
| SIA | supplementary immunization activity | | |

Summary of technical updates for a type 2 poliovirus event and outbreak response

The Standard operating procedures (SOPs) for responding to a poliovirus event and outbreak – Parts 1 and 2 were released in April 2016 to coincide with the globally synchronized switch from trivalent oral polio vaccine (tOPV) to bivalent oral polio vaccine (bOPV). The recommendations in this version 2.1 focused on response in the first 12 months following the switch (e.g. Phase 1, 1 May 2016 to 30 April 2017). However, due to severe global shortage in the inactivated polio vaccine (IPV) supply, version 2.2 was published in August 2016 to change the recommended use of IPV in outbreak response campaigns from full-dose intramuscular injections to fractional doses delivered intradermally. In May 2017, version 2.3 reflect updated guidance on response planning, particularly for type 2 events and outbreaks, from the Polio Working Group of the WHO Strategic Advisory Group of Experts on Immunization (SAGE, February 2017). There were minor clarifications in other sections of the SOPs at this time.

Version 2.4: revised recommendations

The current minor update (version 2.4) reflects the greater emphasis on the importance of the quality and reach of supplementary immunization activities (SIAs) as recommended by SAGE and technical advisors within the Global Polio Eradication Initiative (GPEI). The key objectives, strategic principles, and general operational components of poliovirus response remain largely unchanged. Relevant sections that have been modified from the previous versions are noted below.

Quality, scope & speed considerations

For Part 2, section 4.4 Response: High quality SIAs for event and outbreak response

| Current | Revision |
|--|--|
| All polio outbreaks and any type 2 polio event that are assessed to meet the criteria for high risk of transmission will require implementation of vaccine campaigns within 14 days to stop any further transmission of the virus. | <p>Initiating the first SIA within 14 days of notification is recommended where high vaccination coverage can be achieved. A detailed risk assessment by country and GPEI experts must be completed in order to set start date to ensure quality implementation.</p> <p>Use of a preparedness dashboard is now required to be presented to relevant GPEI guidance or expert advisory body to track country readiness to launch SIA (e.g. mOPV2 advisory group and/or outbreak preparedness and response task team (OPRTT)). Response options include initial response SIA in limited geographic scope within 14 days, followed by SIA1 for larger population when intensified planning can maximize quality.</p> |

Rationale: reflects the increased emphasis on quality, particularly in the context of the complex settings where poliovirus outbreaks may occur and, for type 2 poliovirus, that risks of poor coverage or missed populations continue to increase as population mucosal immunity decreases in the post-switch context.

Prior updates Version 2.3: summary of recommendations

Detection of any type 2 poliovirus remains a public health emergency. The primary modifications reflect specific alterations in the response strategies as well as updated Global Polio Eradication Initiative (GPEI) guidelines on definition of the circulating vaccine-derived polioviruses (cVDPV) classification¹ and management of unused stocks of mOPV2.² Relevant sections that have been modified from the previous versions are noted below.

4.3. Investigation and risk assessment: key questions and determinations for risk assessment

Definition of cVDPV

| Current | Revision |
|----------------------------------|--|
| See cVDPV definition on page 14. | Revise definition of cVDPV to remove the reference to classification based on number of nucleotide changes |

Rationale: reflects update from Global Polio Laboratory Network (GPLN) that nucleotide changes alone are an imprecise determination of circulating virus. Available at: http://polioeradication.org/wp-content/uploads/2016/09/Reporting-and-Classification-of-VDPVs_Aug2016_EN.pdf

¹ GPEI. Classification and reporting of vaccine-derived polioviruses (VDPV), August 2016.

² GPEI. mOPV2 vaccine management, monitoring, removal and validation, October 2016.

4.3. Risk assessment: factors influencing type and scale of response

Transmission risk zones elements of risk for further transmission

| Current | Revision (see Annex for further details) |
|--|---|
| Three zones based on country and population characteristics, primarily based on anticipated immunity levels (page 20) | <p>Determine whether a type 2 poliovirus isolation represents a high- or medium-low-“risk scenario” for transmission based on qualitative assessments in three categories:</p> <ul style="list-style-type: none"> • <i>virological risk</i> (e.g. degree of genetic deviation from parent Sabin), • <i>contextual risk</i> (e.g. limited access due to conflict, recent poliovirus detection, high force of infection, population movement, etc.), and • <i>potential risk for international spread</i> (border area with high population mobility, etc.). <p>Qualitatively rank each factor as high/medium/low and assign overall risk to determine response:</p> <p>High risk: vaccination <i>plus</i> enhanced surveillance and investigation</p> <p>Medium/low: enhanced surveillance and/or investigation</p> |
| <p>Rationale: simplify criteria and provide more flexibility in assessment. The Annex provides further guidance. Population immunity to type 2 poliovirus by itself will decline in all areas without adequate routine immunization (RI) with IPV.</p> <p>NOTE: cVDPV is by definition evidence of a high-risk scenario. Concurrent wild poliovirus (WPV)1 and any VDPV2 circulation is inherently high risk and may require specifically tailored interventions. See below for additional response implications.</p> | |

4.4. Response: response strategies for Phase 1 (approximately 12–18 months post switch)

Vaccine choice

| Current | Revision |
|---|--|
| Use monovalent oral polio vaccine (mOPV)2 as the vaccine of choice but follow specific targeted roles for the use of fractional-dose IPV (fIPV) injected intradermally: (1) use in one supplementary immunization activity (SIA) along with mOPV2 to vaccinate expanded target of high-risk subpopulations in response to cVDPV; (2) vaccinate close contacts of immunodeficiency-related vaccine-derived poliovirus (iVDPV) cases. | Utilize mOPV2 as the vaccine of choice. fIPV is no longer recommended for responding to cVDPV2 or VDPV2s deemed to be “high risk”. Continue to vaccinate close contacts of iVDPV cases with IPV. |
| <p>Rationale: the SAGE Working Group has recommended that current supply constraints require prioritization of IPV use to provide protection to the general population through RI in countries at risk of VDPV2 emergence and spread (tiers 1 and 2) rather than in response to outbreaks where the impact is less pronounced.</p> | |

4.4. Response: response strategies for Phase 1 – vaccination response parameters

Optimal number of SIAs, timing, interval and target population for outbreak responses

| Current | Revision for all vaccination responses |
|--|---|
| <ul style="list-style-type: none"> • Conduct 4–5 SIAs using mOPV2 in response to a cVPDV and 3 SIAs using mOPV2 in response to an aVPDV. • Conduct SIA1 within 14 days of initial sequencing results and subsequent SIAs at 2–3-week intervals (but could be extended for mOPV+IPV round). • SIA1 (rapid response round): 500 000 children under 5 years of age; subsequent SIAs should target a minimum of 2 million children but could be expanded based on local conditions. | <p>Plan and implement 2 SIAs with mOPV2 in all outbreak and high-risk areas. Closely monitor SIA quality (i.e. coverage >90% and ensure that there is no evidence of persistently missed children or continued transmission). Add additional SIA(s) if quality is not satisfactory.</p> <ul style="list-style-type: none"> • Conduct SIA1 within 14 days of initial sequencing results and subsequent SIAs at 2–3-week intervals. • Target approximately 1–2 million children under 5 years of age for each SIA, with final size to be determined upon review of the risk assessment. Additional populations and further extension of the scope of outbreak response should occur if warranted due to extraordinary circumstances of high population mobility or other risk factors. |

Rationale: additional evidence has become available demonstrating the high efficacy of mOPV2 and its effectiveness in stopping transmission as long as “high quality” is achieved through high coverage and targeting missed children in subsequent SIAs. Countries and vaccine delivery systems have demonstrated the capacity to successfully organize and implement large-scale SIAs within 14 days. Local circumstances will dictate the scope of the target population, but it is important to identify and address the contiguous high-risk populations in an outbreak area, even if this extends across an international border. At this time, the risk of ongoing transmission outweighs the risk of seeding additional VDPVs from using mOPV2. In all situations, the target populations should be defined by risk, and implementation strategies to vaccinate target populations should not exceed the capacity of the programme to attain high coverage.

4.4. Response: response scenarios for Phase 1 (approximately 12–18 months post switch)

cVDPV2 (see Fig. 3a)

| Current | Revision |
|--|--|
| Initial small-scale SIA for all areas. For transmission risk zones 1 or 2, follow with SIA2 using mOPV2+IPV and SIAs3, 4, 5 using mOPV2. For transmission risk zone 3, follow with SIAs3, 4 using mOPV2. | See revised recommendations above that apply to revisions for all vaccination responses. |

Rationale: provides most efficient and effective response to evidence of type 2 transmission (e.g. cVDPV2 detected in infected individual or the environment).

4.4. Response: response scenarios for Phase 1 (approximately 12–18 months post switch)

“new” or “unclassified” VDPV2 (see Fig. 3a)

| Current | Revision |
|--|--|
| Presumed as “probable transmission” so initiate rapid response SIA1 with mOPV2 unless “low risk” (e.g. default is to respond) | Proceed with SIA response only if considered to be at high risk for transmission. (See 4.4 above on risk scenarios). Otherwise, intensify field investigation, enhance surveillance and, where appropriate, implement supplemental case detection activities. |
| If further field and sequencing results show links to prior VDPV, classify as cVDPV and follow relevant vaccination protocol with multiple SIAs depending on transmission risk zone. | If further investigation results in classification as cVDPV, initiate appropriate vaccination response. If further investigation results in classification as ambiguous vaccine-derived poliovirus (aVDPV) deemed to be at high risk for transmission, proceed with a vaccination response. |
| If further field and sequencing results rule out iVPD and no links to prior VDPV, classify as aVDPV and consider two additional SIAs with mOPV2. | If further investigation results in classification as iVDPV, proceed with limited response as outlined in current version. |
| Rationale: reflects experience that expanded environmental surveillance has been able to detect multiple VDPVs with only a small number of nucleotide changes that present minimal risk to continued transmission. Provides flexibility but also focuses on the use of mOPV2 in areas with presumed high risk. | |

4.4. Response scenarios for Phase 1 (approximately 12–18 months post switch)

WPV2 human case (see Fig. 3b)

| Current | Revision |
|---|---|
| For WPV human case without known exposure, proceed with multiple SIAs as outlined for situations of confirmed transmission based on transmission risk zone. | For WPV human case without known exposure, proceed with “high-risk” vaccination response as identified in revised parameters. |
| Rationale: reflects new vaccination parameters for all high-risk scenarios. | |

4.4. Response scenarios for Phase 1 (approximately 12–18 months post switch)

Sabin 2 human or environmental case

| Current | Revision |
|--|--|
| Notify International Health Regulations (IHR) authorities and conduct further aggressive investigation and active surveillance for any Sabin 2 detected >4 months post switch (or last mOPV2 use). | Notify IHR authorities, and conduct aggressive investigation and active surveillance. Additional tools and references provided: See: GPEI. <i>A guide for investigation of Sabin Like 2 (SL2) poliovirus in a human or in the environment</i> . March 2017. See: GPEI. <i>A tool for investigation of Sabin Like 2 (SL2) poliovirus isolation in a human or in the environment</i> . March 2017. |

Rationale: due to sporadic but persistent discovery of Sabin2 >4 months post switch, additional guidance has been developed to assist with the recommended follow up. Available at: <http://polioeradication.org/tools-and-library/resources-for-polio-eradicators/gpei-tools-protocols-and-guidelines/>

Annex 1.7d. Operational framework – logistics

General guidance on management of unused stocks of mOPV2

| Current | Revision |
|---|---|
| Provisions as outlined in <i>Standard operating procedures for vaccine management</i> | See new GPEI guidelines: <i>Technical guidance mOPV2 vaccine management, monitoring, removal and validation</i> . October 2016. |

Rationale: the new guidelines reflect more specific and detailed recommendations required for situations dealing with unused stocks of mOPV2. Available at: http://polioeradication.org/wp-content/uploads/2016/11/Technical-guidance-mOPV2-management-monitoring-removal-and-validation_Oct2016_EN.pdf

Other: Special situations

Endemic areas (co-circulating WPV1 and VDPV2) – often includes conflict-affected areas

| Current | Revision |
|---------------|---|
| Not addressed | In addition to WPV1, an immediate and adequate response to cVDPV2 should be implemented with high priority in all instances. In situations where both bOPV and mOPV2 are required, the two OPVs may be given separately 2 weeks (or less if operationally feasible) apart from each other. For example, one SIA round could be given with mOPV2 followed 10–14 days later by one SIA with bOPV. |

Rationale: in endemic countries, the need to interrupt both WPV and cVDPV2 is critical. There is an increasing risk of significant type 2 outbreaks due to waning type 2 mucosal immunity and a long-standing tradition of placing considerably more focus on interrupting transmission of WPV than cVDPV.

Executive summary

The Polio Eradication and Endgame Strategic Plan calls for poliovirus outbreaks to be stopped within 120 days of detection. Since the switch from trivalent oral polio vaccine (tOPV) to bivalent OPV (bOPV), the detection of **any** type 2 poliovirus (wild, vaccine-derived, or Sabin) in any sample from any source is generally considered to be a global public health emergency. Type 2 outbreak threats include: a high, but primarily short-term risk of vaccine-derived poliovirus emergence (VDPV2); a low, long term risk of poliovirus escaping from a manufacturing site or laboratory; and a future threat posed by prolonged or chronic poliovirus excretion by persons with B-cell related primary immunodeficiency (e.g. immunodeficiency-associated VDPV (iVDPV)).

Key objectives of the protocol are to: (i) outline strategies to detect and respond appropriately to any type 2 poliovirus; and (ii) provide guidance to global, regional and national public health officials and policy makers for the necessary steps required.

The strategic actions following the detection of a type 2 poliovirus isolate after OPV2 cessation have the same basic approaches and principles to those currently required for investigating and responding to any polio outbreak as outlined in *Responding to a poliovirus event or outbreak, Part 1: General (SOPs)*.

Timeframe and target audience. This protocol lays out overall strategic imperatives for dealing with all future type 2 outbreaks, **and provides revised recommendations and guidance for the six month period of 1 November 2017 to 30 April 2018.**

Key strategic principles for responding to a type 2 poliovirus.

- Prompt response in a sufficiently large population to rapidly stop virus circulation.
- Use vaccines from a global outbreak response stockpile for all countries, regardless of whether they previously procured vaccines through UNICEF
- Limit exposure to Sabin 2 poliovirus (e.g. from mOPV2) among populations not directly affected by the outbreak to prevent emergence of a new circulating VDPV type 2 (cVDPV2).
- Validate the absence of poliovirus type 2 in the population and the environment following the outbreak response.

Detection of a type 2 poliovirus will continue to depend on sensitive acute flaccid paralysis (AFP) surveillance and environmental surveillance in areas at high risk for cVDPV emergence, areas at risk of silent transmission and circulation of poliovirus, and areas at risk due to vaccine production.

Notification. Detection of **any poliovirus type 2** (wild, vaccine-derived Sabin2) must be reported to WHO under International Health Regulations (2005).

Investigation and risk assessment. When any type 2 poliovirus is detected, countries must: conduct a rapid field investigation and risk assessment, enhance virologic investigation, and strengthen surveillance. The nature of the virus (e.g. WPV, VDPV, or Sabin) and strength of

evidence of circulation will determine the risk of further poliovirus type 2 transmission. Travel and migration patterns within affected communities can have a significant impact on the risk and extent of poliovirus circulation.

Determine whether a type 2 emergence represents a high or medium-low risk for further transmission based on assessment of virologic risk, local context and potential for international spread. The risk designation will help determine the appropriate response.

Response. Preparations for a vaccination response should proceed immediately upon receipt of initial sequencing results and should not wait for a complete epidemiologic investigation or final classification of an isolate.

- Detecting a cVDPV2 or WPV2 without confirmed exposure is evidence of transmission and de facto indicates a high risk situation requiring a vaccination response. Plan and implement 2 SIAs with mOPV2 in all outbreak and high risk areas. Closely monitor SIA quality (i.e. aim for coverage >90% and no persistently missed children or continued transmission). Add additional SIA(s) if quality is not satisfactory. Conduct SIA1 within 14 days of initial sequencing results where high vaccination coverage can be achieved and subsequent SIAs at 2–3 week intervals. Target approximately 1–2 million children under 5 years of age for each SIA – determine final scope after a detailed risk assessment. The scope of outbreak response may be extended where there is high population mobility or other risk factors.
- If a new VDPV2 is detected, proceed with SIA response only if the situation is deemed high risk for further transmission. If assessed as a medium-low risk, intensify field investigation, enhance surveillance, and where appropriate implement supplemental case detection activities.
- If further investigation results in classification as aVDPV deemed to be at high risk for transmission, proceed with a vaccination response.
- If further investigation results in classification as iVDPV proceed with limited case management to protect both case and close contacts.

Countries apply to WHO to request release of mOPV2 from the global stockpile. Release of the vaccine can only be authorized by the WHO Director General.

Detection of any Sabin type 2 (SIA2) isolate in either an AFP/human case or environmental sample in any country post-switch or in those countries having used mOPV2, more than four months post use of mOPV2 in an event/outbreak response should prompt a full investigation to determine whether tOPV (or mOPV2) are still in use or if there may be a containment breach.

Outbreak/event response assessment and follow-up. Conduct independent SIA monitoring and LQAS at least by SIA2, and a full outbreak/event response assessment by the third month from Day 0 and quarterly thereafter until 12 months have passed without a type 2 poliovirus isolate. It is critically important to confirm the end of the outbreak by validating the absence of poliovirus type 2 in the population and the environment 6–12 months after the onset or collection of the most recent case or isolate plus at least one month to account for case

detection, investigation, testing and reporting of all pending results, or as per criteria set by the International Health Regulations – Emergency Committee (IHR-EC) for classifying “States no longer infected (detection of no new wild poliovirus or cVDPV)”.

Conclusions. The Polio Eradication and Endgame Strategic Plan calls for any poliovirus outbreak to be stopped within 120 days of detection. While wild poliovirus is still endemic in three countries, VDPVs continue to emerge in parts of endemic and non-endemic countries where there is persistently low population immunity. Implementation of high quality eradication strategies is the responsibility of national governments while GPEI partners provide necessary guidance and support. These SOPs were endorsed by the WHO Strategic Advisory Group of Experts (SAGE) on Immunization will assist countries and GPEI partners to develop effective and appropriate response strategies to poliovirus events and outbreaks following the global withdrawal of type-2 containing oral polio vaccine.

Introduction

The last detected case of wild poliovirus type 2 (WPV2) in the world occurred in 1999. On 20 September 2015, the Global Commission for the Certification of Poliomyelitis Eradication formally declared that WPV2 had been eradicated (1). However, use of oral polio vaccine type 2 component (OPV2) continued to cause emergence of circulating vaccine-derived poliovirus (cVDPV) and a substantial portion of vaccine-associated paralytic poliomyelitis cases. In order to address this situation and the wider implications of OPV use after global WPV eradication, Objective 2 of the *Polio Eradication and Endgame Strategic Plan* (2) proposed an endgame strategy of three steps: (i) introduce at least one dose of inactivated polio vaccine (IPV) into routine immunization; (ii) cease use of OPV2 by a globally-coordinated switch from trivalent OPV (tOPV) to bivalent OPV (bOPV); and (ii) eventually, globally coordinate the withdrawal of all OPV (3,4).

By April 2016, all 156 countries and territories using tOPV had introduced IPV in their immunization programs or made a commitment to do so. The global switch from tOPV to bOPV ensued between 17 April and 1 May 2016.

Following OPV2 cessation, population immunity (especially intestinal immunity) declined rapidly, increasing the risk of an outbreak should type 2 poliovirus exposure occur (5). There are three main threats following OPV2 cessation: (i) a relatively high short-term risk of emergence of cVDPV; (ii) a low long-term risk of poliovirus from a manufacturing site or laboratory; and (iii) possible transmission from prolonged or chronic poliovirus excretion by persons with primary immunodeficiency (e.g. immunodeficiency-related vaccine-derived poliovirus (iVDPV)) (6).

Since WPV2 was declared eradicated and tOPV use ceased, the detection of any poliovirus type 2 (wild, vaccine derived, or Sabin) in any sample from any source is generally considered a public health emergency which requires rapid and high-quality coordinated action from national health authorities and the Global Polio Eradication Initiative (GPEI). A global stockpile of monovalent OPV2 has been constituted for response to specific and identified threats.

Since April 2016, three cVDPV2 and many more VDPV2s emerged. The response to detection of a type 2 poliovirus isolate after OPV2 cessation follows the same principles to those required for investigating and responding to any polio outbreak as outlined in the *Responding to a poliovirus event or outbreak. Part 1: General SOPs*. However, the post-tOPV era requires a heightened sense of urgency, vigilant surveillance, a carefully planned risk assessment, and a specific vaccine response due to the risk of re-introduction of type 2 virus.

2

Protocol, objectives and scope

The objectives of the protocol for poliovirus type 2 are listed below.

1. Outline the strategy to detect and respond to any type 2 poliovirus from environmental sources or circulating in the population post OPV2 cessation.
2. Provide guidance to global, regional and national public health officials and policy makers on the steps required to rapidly notify authorities, conduct an initial risk assessment, and develop an effective response to promptly curtail any type 2 poliovirus emergence.

The proposed strategy is based on evidence from past and current programme experience in dealing with polioviruses as well as existing models projecting possible poliovirus epidemiology (7,8). These guidelines will continue to evolve as further evidence and experience are generated. **This version of the protocol lays out overall strategic guidance for dealing with type 2 outbreaks, with revised recommendations and guidance for the period of 1st November 2017 to 30th April 2018.**

While these guidelines offer concrete parameters for decision making, they cannot address every possible scenario. Decision makers should consider the local and national context, and their specific epidemiologic circumstances. In particular, recommendations for vaccine use in an outbreak response are specifically for countries which have used OPV2 within one year before the switch. However, any WPV2 or VDPV2 detected in any country (even in one with exclusive IPV use) must be considered a potential global risk. While protecting individuals, IPV use can mask ongoing poliovirus circulation. Given the potential for a Sabin type 2 poliovirus to evolve into a cVDPV2, detection of a Sabin type 2 poliovirus more than four months after any campaign use of monovalent OPV2 (mOPV2) for type 2 event or outbreak response in any country must also be considered a potential global risk. While detection of a type 2 poliovirus in one location may not always necessitate an immediate vaccination campaign, an urgent and aggressive investigation is still required to trace the origin of the virus in order to rapidly determine an appropriate response at both the location of identification and any more distant source.

3

Background: preparation for type 2 OPV withdrawal

In May 2014, the World Health Assembly (WHA) adopted criteria which the Strategic Advisory Group of Experts (SAGE) on Immunization recommended to gauge global readiness for OPV2 cessation (9,10). OPV2 withdrawal relied on satisfying these readiness criteria and the global interruption of persistent cVDPV2 transmission. They included the following:

Primary actions required at the global level by GPEI

- Establish a global stockpile of monovalent oral polio vaccine type 2 (mOPV2) for outbreak use (*completed. See Annex 2 for details on stockpile operations*).
- Provide global guidelines and technical assistance as required to implement Objective 2 (11). (*completed April 2016*)
- Confirm global eradication of WPV type 2 (*completed September 2015*).

Primary actions required at the national level by public health authorities

- Introduce at least one dose of IPV in routine immunization in countries using OPV only (12). (*phased according to vaccine availability, and underway. All Tier 1 and Tier 2 countries have introduced IPV*)
- Conduct one or more tOPV campaigns prior to OPV2 cessation (*completed April 2016*).
- Strengthen outbreak response capacity and ensure that public health officials are aware of the recommendations outlined in this protocol in the case of a type 2 outbreak. (*Several training workshops and outbreak simulations completed and several more planned*)
- Institute appropriate containment measures as required under the third edition of the Global Action Plan to minimize post-eradication poliovirus facility-associated risk (GAPIII) (13).
- Ensure that bOPV is licensed for routine immunization.

Most of these actions have been completed. However over 2015 and 2016, severe constraints emerged for the global IPV supply. Supply for countries most at risk was protected.

4

Poliovirus type 2 outbreak response strategy

Overall principles of the strategy to deal with detection of any type 2 poliovirus

- Ensure prompt detection and notification of all type 2 poliovirus strains.
- Ensure prompt response in a sufficiently large population to rapidly detect and stop type 2 poliovirus circulation.
- Utilize vaccines from the global outbreak response stockpile available for all countries whether or not they previously received vaccines through UNICEF.
- Limit exposure to Sabin 2 poliovirus (e.g. from mOPV2) among populations not directly affected by the outbreak to prevent emergence of a new cVDPV2.
- Validate absence of poliovirus type 2 in the population and the environment following the outbreak response.

The strategy to address risks associated with Sabin type 2 withdrawal has six components: (i) detection, (ii) notification, (iii) investigation/risk assessment, (iv) response, (v) traveler considerations (internal and international), and (vi) follow up. The proposed guidelines for each component are based on risk factors and epidemiological contexts. Although presented separately, action should proceed simultaneously.

4.1 Detection

Poliovirus surveillance includes multiple components (14). Acute flaccid paralysis (AFP) surveillance has been the gold standard for global polio eradication (15). The global, regional and national laboratories of the Global Polio Laboratory Network (GPLN) have comprehensive standards to distinguish poliovirus as a cause of AFP from other possible causes (16).

Environmental surveillance is an increasingly important adjunct to AFP surveillance. The GPEI is working with countries to expand the role and number of environmental surveillance sites (17). Environmental surveillance is being rolled out especially in: (i) areas at high risk for cVDPV emergence (e.g. low routine coverage and historical cVDPV cases), (ii) areas at risk of silent transmission and circulation of poliovirus (e.g. high force-of-poliovirus-infection), and (iii) areas at risk due to vaccine production. Environmental surveillance can also be instrumental in tracking the disappearance of Sabin 2 strain polioviruses, detecting any Sabin 2 strain polioviruses that subsequently might surface, and identifying any continued use of tOPV or mOPV2. Establishing environmental surveillance requires sufficient laboratory and staff resources as well as operational procedures following current World Health Organization (WHO) guidelines (18), and a collaborative global effort to enhance detection capacity for type 2 polioviruses.

Polioviruses may also be detected non-AFP clinical specimens or through a stool survey. Any such findings of type 2 poliovirus should be reported through the standard notification system (see section 4.2 *Notification*).

Primary actions required at the global/regional level by the GPEI/GPLN

- Assist countries to expand environmental surveillance.
- Adequately support national laboratories to ensure rapid and sensitive poliovirus isolation and characterization through intratypic differentiation (ITD). As a global priority, all laboratories must expedite processing and sequencing of any type 2 isolates.

Primary actions required at the national level by public health authorities

- Regularly monitor and evaluate AFP surveillance and laboratory networks to ensure that global quality standards are maintained even as WPV cases disappear (15).
- Collaborate with GPLN and GPEI to expand the environmental surveillance expansion plan. Countries not already engaged in environmental surveillance for polioviruses do **not** need to independently start environmental sampling for polioviruses solely for the purpose of detecting Sabin type 2 polioviruses as markers for post-switch use of tOPV.

4.2 Notification

Treaty obligations under the International Health Regulations (IHR, 2005) specifically designate detection of a WPV from a suspected case or from a close contact to be a notifiable event. Additionally, the isolation of any WPV or cVDPV from other human or non-human sources must also be notified to WHO under the separate notification requirement for ‘events which may constitute a public health emergency of international concern’ (19). The interpretation of this criterion is now expanded to include detection of **any poliovirus type 2** (wild, vaccine derived, or Sabin¹), in **any sample** (from clinical case or environment), of **any provenance** as a notifiable event under IHR (2005). The IHR-Emergency Committee (EC) on the international spread of poliovirus will advise the WHO Director General about the appropriate risk category of the affected country (20).

Primary actions required by national and/or regional laboratories

- Promptly notify national health authorities and WHO within 24 hours of obtaining results.

Primary actions required by national health authorities

- The National IHR Focal Point should notify WHO of any type 2 poliovirus detection within 24 hours as specified in the IHR (2005). The health ministry should likewise inform relevant national officials.

1 Sabin 2 has been notifiable under IHR since 1 August 2016 based on GAPIII containment criteria.

- Investigate non-laboratory confirmed cases, contradictory laboratory results, an unexpected cluster of AFP cases, or clusters of clinically compatible AFP cases that would not trigger global actions or notification under IHR (2005). These situations, as well as concerns about suboptimal surveillance should be thoroughly investigated at the appropriate national/subnational levels.

4.3 Investigation and risk assessment

Initial investigation

Discovery of **any** type 2 poliovirus isolate from AFP cases, contacts or environmental surveillance should trigger an immediate field investigation to: (i) confirm the outbreak/event; (ii) determine the number and characteristics of the case(s); (iii) identify the origin/causes for the outbreak/event; and (iv) assess the risk for occurrence and geographic extent of transmission.

Several steps may take place simultaneously. [Figure 1](#) provides an overall timeline of required activities, the agency or persons with primary responsibility, and the expected timeframe for completing the action. (For further details see *Responding to a poliovirus event and outbreak. Part 1: General SOPs for responding to a poliovirus event and outbreak (21).*)

Primary actions required by all relevant GPLN laboratories

- *Enhance virologic investigation:* Sequencing analysis beyond initial testing can aid in estimating the duration of poliovirus circulation. Laboratories responsible for covering the area where the poliovirus was detected should also carefully review relevant laboratory indicators (cell-sensitivity testing results, proficiency testing for viral isolation and ITD, accuracy of detection and testing, etc.) to ensure that the laboratory met the recommended standards before and at the time of type 2 detection.

Primary actions required by national public health authorities

- *Enhance surveillance:* In order to maximize quality and sensitivity of the surveillance system, it is important to strictly ensure completeness and timeliness of all AFP reporting. Minimum standards for the affected country and first administrative level should be increased to three non-polio AFP cases per 100 000 children under 15 years of age for 12 months following outbreak confirmation. Also, for the immediate assessment period, increase the frequency of environmental surveillance, if available. For the longer term, if any WPV2 or VDPV2 is detected, investigate with the GPEI about establishing or expanding local environmental sampling sites.
- *Conduct an epidemiologic investigation:* A prompt field investigation of any AFP case should include specific case characteristics as well as active case finding in the community and local reporting sites. A positive environmental sample should also trigger active case finding in the suspected community and/or catchment area of the environmental surveillance site.

- *Conduct a risk assessment:* Based on the findings of the epidemiologic and virologic investigations and the strength of evidence, characterize virus transmission and implications for further spread. Assess the critical factors which will influence the type and scale of response and make recommendations for appropriate actions (see *Key questions and determinations for risk assessment* below). Identify subpopulations outside the primarily affected area which are at-risk for possible transmission.

Risk assessment

It is critical to assess virologic and epidemiologic risk factors to inform the assessment of risk in a given context. For each type 2 virus detected, it must be determined whether this represents a high or medium-low risk of further transmission based on multiple factors in three areas (virology, local context, and risk of international spread). Rather than specific quantitative parameters, the assessment should reflect an overall evaluation of the situation. The relative ‘weight’ of each category will be situation dependent and any mitigating factors taken into consideration. (See Table 1 below and Annex 1 for further details.)

TABLE 1. Elements to assess risk for further type 2 poliovirus transmission and that will influence type and scale of response

| Criteria | Sample of elements considered (not exhaustive) |
|------------------------------------|---|
| Virologic risk | degree of genetic deviation from parent Sabin, virologist assessment / interpretation of types of nucleotide changes etc. |
| Contextual risk | limited access due to conflict, recent poliovirus detection, high force of infection, population movement etc. |
| Risk of international transmission | border area with high population mobility, nomadic or refugee populations etc. |

Process (see also Figures 2 & 3):

- Qualitatively rank each factor as high/medium/low.
- Assign overall risk as either High or Medium-Low.
- High risk: vaccination+; Med/Low: enhanced surveillance and/or investigation

FIGURE 1. Timeline and responsibility for actions following detection of type 2 poliovirus

| Action Steps | Days post sequencing results | | | | | | | | | | | | | | | | | | |
|---|------------------------------|---|---|---|---|---|---|---|---|---|---|----|----|----|----|----|-------|----|--|
| | <0 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15-30 | 30 | |
| Detection | | | | | | | | | | | | | | | | | | | |
| Virus isolation; ITD, sequencing by GPLN | █ | | | | | | | | | | | | | | | | | | |
| Notification | | | | | | | | | | | | | | | | | | | |
| Sequencing results notification to all GPEI by GPLN | █ | | | | | | | | | | | | | | | | | | |
| Notification to WHO headquarters under IHR | | | | | █ | | | | | | | | | | | | | | |
| Confirmation | | | | | | | | | | | | | | | | | | | |
| Initial event or outbreak confirmation by MoH | | | | █ | | | | | | | | | | | | | | | |
| Further confirmation by WHO Regional Office as required | | | | █ | | | | | | | | | | | | | | | |
| Final classification if required | | | | | | | | | | | | | | | █ | | | | |
| Investigation and Risk Assessment | | | | | | | | | | | | | | | | | | | |
| Enhance virologic investigation | | | | | | | | | | | | | | | | | | | |
| Enhance AFP and environmental surveillance | | | | | | | | | | | | | | | | | | | |
| Field investigation and/or active case search in area of environmental surveillance | | | | | | | | | | | | | | | | | | | |
| Conduct risk assessment | | | | | | | | | | | | | | | | | | | |
| Response | | | | | | | | | | | | | | | | | | | |
| Prepare SIA1 response plan and draft vaccine request | | | | | | | | | | | | | | | | | | | |
| Submit vaccine request | | | | | | | | | | | | | | | | | | | |
| EOMG prepares OPRTT response | | | | | | | | | | | | | | | | | | | |
| Risk assessment and vaccine request evaluated by Advisory Group (EOMG+) | | | | | | | | | | | | | | | | | | | |
| WHO DG authorizes release of mOPV2 from stockpile | | | | | | | | | | | | | | | | | | | |
| EOMG initiates surge support; country initiates response | | | | | | | | | | | | | | | | | | | |

| Action Steps | Days post sequencing results | | | | | | | | | | | | | | | | | | |
|---|------------------------------|---|---|---|---|------|---|---|--------|---|---|--------|----|----|----|----|-------|----|--------|
| | <0 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15-30 | 30 | |
| Official notification to vaccine manufacturer | | | | | | Red | | | | | | | | | | | | | |
| Manufacturer prepares shipment | | | | | | Blue | | | | | | | | | | | | | |
| Vaccine (and syringes) shipped to country | | | | | | | | | Purple | | | | | | | | | | |
| In-country processing and vaccine sent to field | | | | | | | | | | | | Yellow | | | | | | | |
| Start of SIA* | | | | | | | | | | | | | | | | | | | |
| Prepare SIA2 + response plan and submit Stage 2 vaccine request | | | | | | | | | | | | | | | | | | | |
| Other steps as above | | | | | | | | | | | | | | | | | | | Yellow |
| Start of SIA* | | | | | | | | | | | | | | | | | | | |
| <i>Primary responsibility</i> | | | | | | | | | | | | | | | | | | | |
| National health ministry and/or Emergency Operations Centre | | | | | | | | | | | | | | | | | | | |
| Global and regional partners | | | | | | | | | | | | | | | | | | | |
| Both health ministries and global partners | | | | | | | | | | | | | | | | | | | |
| Manufacturer | | | | | | | | | | | | | | | | | | | |
| WHO | | | | | | | | | | | | | | | | | | | |
| UNICEF | | | | | | | | | | | | | | | | | | | |

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* Where high coverage can be achieved (>90% and no persistently missed children)

Key questions and determinations for risk assessment

While laboratory and epidemiologic investigative steps correspond in general to standards for following-up any poliovirus detection, the risk assessment following the discovery of a type 2 isolate should focus specifically on addressing three core questions:

1. What is the nature of the virus (e.g. WPV, Sabin, or VDPV)?
2. Is there evidence of circulation?
3. What is the risk of further spread?

Following Initial detection, ITD and sequencing, a poliovirus isolate may be grouped into one of three categories: *WPVs*, *Sabin* (e.g. OPV strain), and *VDPVs* (>1% divergent (PV1 and PV3) or >0.6% divergent (PV2) from the corresponding OPV strain). A thorough risk assessment is required regardless of the isolate category.

WPV2. Given the extended period since a circulating WPV2 is detected, the possibility of emergence of this virus is remote. However, if an individual WPV2 infection is detected, rapid case investigation is mandatory since transmission could occur very rapidly. A WPV2 infection **without** a known exposure to a poliovirus in a laboratory or vaccine production facility should be considered evidence of *confirmed transmission*. A WPV2 infection **with** a known exposure in a containment breach is likely to be an isolated event but still a risk for *possible future transmission*. Likewise, a WPV2 isolate from an environmental sample is, in all probability, due to a containment breach in a laboratory or research facility. Nevertheless, a thorough investigation is warranted in the community catchment area surrounding the environmental surveillance site as well as in any nearby laboratory or research facility in order to identify an AFP case or rule out subclinical infection in an individual who is excreting poliovirus. A cautionary approach dictates that the discovery of a WPV2 in an environmental surveillance sample should initially be considered as evidence of *probable transmission*.

Sabin 2. Empirical evidence and modeling suggest that Sabin type 2 polioviruses remain detectable for approximately three months in the stool and four months in sewage samples after the last use of tOPV (and/or use of mOPV2) (5,22).² While this detection should prompt increased vigilance through AFP and environmental surveillance, the risk for this occurrence should rapidly diminish with time (3). Detection of Sabin type 2 polioviruses **after** three or more months following the switch (i.e. from September 2016 onwards) or last use of mOPV2 in a type 2 outbreak/event response suggests continued use of OPV2-containing vaccine, and represents a risk for *possible future transmission*. A single individual AFP case with a Sabin type 2 poliovirus could also indicate a rare isolated exposure in a vaccine production facility or research laboratory.³ This situation warrants a thorough case investigation, including checks for any remaining local stocks of tOPV/mOPV2 and review of containment procedures and good manufacturing practices at nearby facilities. See GPEI resources to help guide investigation of Sabin 2 poliovirus isolations.

² For an example of empirical evidence see (22). Modeling indicates that the mean time until OPV-related viruses die out is approximately four months (range 2–12 months), see (5).

³ GAPIII requires that all research laboratories or production facilities must have adequate containment procedures in place for Sabin 2 polioviruses no later than 1 August 2016.

VDPV2. Following large-scale use of type 2 containing vaccine, and aside from Sabin 2 isolates found within the first three months, the most commonly detected poliovirus will likely be a VDPV (23). Genetic sequencing through molecular and antigenic methods or real-time reverse transcription–polymerase chain reaction targeting sequences within the VP1 capsid region (selected for during replication of OPV in the human intestine) will provide more specific information. VDPVs are classified as: (i) circulating VDPVs (cVDPVs) when there is evidence of person-to-person transmission in the community; (ii) immunodeficiency-associated VDPVs (iVDPVs), isolated from persons with primary, B-cell immunodeficiencies; and (iii) ambiguous VDPVs (aVDPVs), which do not fit into the two other categories.

An isolate linked to a known cVDPV or a previously detected aVDPV demonstrates ongoing circulation and *confirmed transmission* in the community, presenting the same public health threat as a WPV (24). Given the critical importance of detecting and stopping cVDPV transmission, in July 2015 WHO increased the sensitivity of surveillance to include the following expanded definition:

cVDPV is a

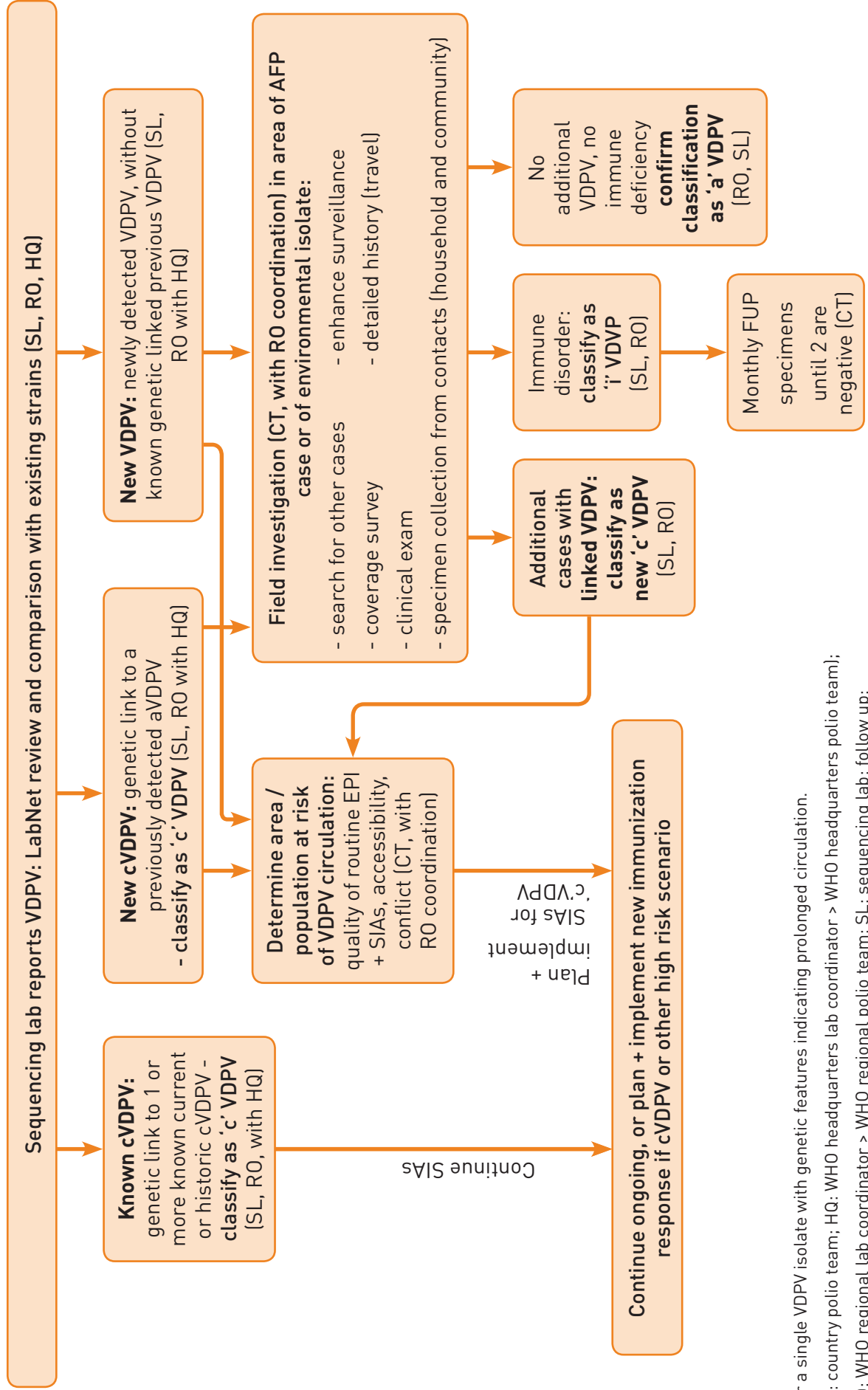
- genetically linked VDPVs, isolated:
 - i) from at least two individuals (not necessarily AFP cases), who are not household contacts,
 - ii) from one individual and one or more environmental surveillance samples, or
 - iii) from two or more environmental surveillance samples if they were collected at more than one distinct environmental surveillance collection site (no overlapping of catchment areas), or from one site if collection was more than two months apart
- OR
- a single VDPV isolate, with genetic features indicating prolonged circulation (i.e. a number of nucleotide changes suggesting >1.5 years of independent circulation) (25).

A sample that does not initially meet the above definition is considered a “new VDPV,” which requires intensive investigation to determine if additional infections are occurring in the community (Figure 2). A single VDPV2 without evidence of prolonged circulation or a single VDPV2 case not linked to a previously detected aVDPV may represent an isolated event without any other consequences. However, the circumstances surrounding this detection must be carefully assessed to determine whether this represents a high risk for transmission (See Risk Scenarios, Table 1). More particularly, multiple emergences of VDPVs in a population with significant immunity gaps must also be considered a red flag, and managed as a high risk situation.

Further active surveillance in the catchment area of an environmental sample or a community search and contact tracing of a human case may find additional case(s) linked to the new VDPV, which would lead to classification of the cases as cVDPVs.

FIGURE 2. Classification of and response to reported VDPV isolates

Reference: GPEI. *Reporting and classification of vaccine-derived polioviruses*. August 2016 (25).



*or a single VDPV isolate with genetic features indicating prolonged circulation.
 CT: country polio team; HQ: WHO headquarters lab coordinator > WHO headquarters polio team);
 RO: WHO regional lab coordinator > WHO regional polio team; SL: sequencing lab; follow up:

The investigation should also determine whether an individual VDPV case represents a long-term, immunodeficient carrier for poliovirus (i.e. an iVDPV). Classification of iVDPV should be made only after a thorough investigation including: detailed history, competently performed physical examination, and results of quantitative immunoglobulin testing.⁴ Acute or chronic malnutrition, which may cause a form of secondary depression of the immune system, should not be confused with serious primary immune deficiency (such as a- or hypogammaglobulinaemia, common variable immunodeficiency, x-linked a-gammaglobulinaemia, other antibody deficiency; or some form combined immunodeficiencies – most commonly, severe combined immunodeficiency).

Detection of iVDPVs is rare (e.g. ~100 known cases worldwide since 1961) and these cases have predominantly been found in developed countries (26). Recent studies in developing and middle-income countries have demonstrated that such cases may occur more frequently than previously thought. However, the survival rates for persons with primary immune deficiencies are probably very low in areas with the highest risk for polio transmission (27). With one possible exception (28), there is no evidence that iVDPV excretors have triggered substantial cVDPV transmission or outbreaks to date. However, all known iVDPV excretors have lived in settings of very high population immunity to poliovirus transmission and/or high hygiene and sanitation settings with reduced transmission potential of polioviruses. Therefore, especially in the first year following OPV2 cessation while type 2 immunity remains relatively high, the potential of further transmission from an iVDPV is deemed low in most countries but still *possible*. Modelling indicates that the future risk of live poliovirus reintroduction into the population from iVDPVs may rise considerably after global WPVs eradication and subsequent OPV cessation (6,8).

4.4 Response

Classification of poliovirus events/outbreaks, type 2 transmission, and further risk of post switch transmission

Based on the nature of the virus and strength of evidence of circulation (e.g. confirmed, probable, or possible), three scenarios emerge reflecting the potential risk for further poliovirus type 2 transmission: high, medium and low (Table 2). Note that unlike type 1 or 3 isolates, for type 2 isolates post switch, the transmission classification (not typology) determines the response. The level of concern should increase with the higher likelihood of further transmission.

⁴ If necessary, countries should contact WHO for assistance to conduct sophisticated molecular level testing of individuals suspected of being immunodeficient.

TABLE 2. Definitions of poliovirus events/outbreaks and classification of type 2 transmission during Phase 1 (12–18 months post switch)

| Typology | Sample source | Classifications |
|----------|------------------------|--|
| Event | Human/AFP ^b | “new VDPV2” awaiting classification |
| | | aVDPV2 |
| | | iVDPV2 |
| | Environmental | Sabin2 |
| | | WPV2 with documented exposure in a laboratory or vaccine production facility |
| | | VDPV2 single sample without evidence of a high risk scenario |
| Outbreak | Human/AFP ^b | WPV2 single sample without follow-up evidence of virus excretion ^c |
| | | Sabin2 |
| | | cVDPV2 |
| | Environmental | WPV2 without documented exposure in a laboratory or vaccine production facility |
| | | cVDPV2 |
| | | ≥2 separate WPV with genetic sequencing indicating sustained local transmission ^d |
| | | WPV2 single sample with follow-up evidence of virus excretion ^c and no documented exposure |

a Additional factors (e.g. force-of-infection, population density, season of the outbreak, indigenous vs. imported virus, etc.) will ultimately determine the risk of further transmission and directly influence the required type and scale of response.

b Infected individual can be an AFP case or an asymptomatic/healthy person.

c Evidence of virus excretion = identification of polio compatible AFP case or WFP infected individual.

d Collected at more than one distinct environmental surveillance collection site (no overlapping of catchment areas), or from one site if collection was more than two months apart.

Factors influencing type and scale of response

If the initial investigation and risk assessment indicate that either confirmed or a high risk for type 2 poliovirus transmission has been detected, an immunization response will most likely be required even before waiting for final classification. Further assessment to determine an appropriate type and scale of response is critical given the potential risks associated with mOPV2 use following OPV2 withdrawal and the need to balance this risk with the necessity to stop the type 2 transmission.

The risk for emergence of any type 2 poliovirus following withdrawal of OPV2 is not homogenous across countries or even within large countries. A significant factor will be the predominant polio vaccine in use within a country.

Countries exclusively using IPV

For countries that exclusively use IPV, the risk for cVDPVs (detected in either an environmental surveillance sample or an individual case) depends on their relatively limited risk of exposure to imported OPV through travelers or migrants. Even the definitions of confirmed or probable transmission for their situation may depend on whether the type 2 poliovirus isolates demonstrate genetic features consistent with local transmission versus importation. These countries may still be at risk, albeit at a low level, for discovery of WPV2 or Sabin2 virus that is traced to a breach in containment from a laboratory or vaccine production facility. Given the generally high vaccination coverage and levels of sanitation found in these countries, the risk of type 2 transmission is relatively low in all these circumstances but the poliovirus may still spread to under-vaccinated subpopulations (29). The level of concern (and associated degree of response) in these countries will thus depend on thorough virologic and epidemiologic investigations that are tailored to the individual situation.

However, from a global perspective, detection of any type 2 poliovirus should be a cause for concern. An attempt to identify the origin of any outbreak, including those due to importations, will be important in order to determine an appropriate response at the source. Nevertheless, the recommendations below regarding a vaccination response following the detection of a type 2 poliovirus are focused on countries that used tOPV within 12 months prior to the switch.

Countries using tOPV in the last 12 months prior to type 2 OPV withdrawal

For countries with recent use of OPV, two dynamically inter-related trends determine post cessation risk of cVDPV emergence: decreasing population immunity to transmission and decreasing OPV-related virus presence. These same factors that predispose for the emergence of a new poliovirus type 2 will also be critical in determining the potential risk for further transmission and the extent to which any transmission may occur.

Note: Risk factors and response strategies presented below apply to countries using tOPV within the last 12 months prior to the switch.

Critical factors for countries to consider in reaching response decisions include time, place and characteristics of the affected population.

Time: *How many months/years have elapsed between OPV2 cessation and detection of poliovirus type2?* Multiple high-quality supplementary immunization activities (SIAs) (i.e. ≥ 3 SIAs with $\geq 80\%$ coverage)* in the 4–6 months before the switch will significantly reduce the risk of emergence (5). However, modelling suggests a high probability that at least one cVDPV will emerge within 12 months of the switch.⁵ While specific cutoff dates cannot be determined, three broad phases – based on the time elapsed since tOPV cessation (shown in Table 3) – can be identified, which reflect exposure to type 2 poliovirus and risk for initial VDPV occurrence and further transmission.* Phase 1 (within 12–18 months of cessation of tOPV) has the highest risk of initial occurrence of a type 2 virus detection; however, assuming

5 Institute for Disease Modeling. Unpublished data, January 2016.

* Recommendation is now $>90\%$ coverage and no evidence of persistently missed children

that precessation mitigation activities (i.e., tOPV SIAs) have taken place prior to withdrawal of tOPV, this phase should have the lowest risk of further transmission. Phase 2 (2–3 years post-cessation) reflects medium risk of occurrence and further circulation. Phase 3 (4+ years since cessation of OPV2) will have the lowest exposure risk to type 2 virus, but will have an accelerating risk of further transmission due to waning mucosal immunity in the population.

TABLE 3. Phases of risk for type 2 poliovirus emergence and circulation^a

| Phase | Time after cessation of OPV2 | Comment | Relative risk for initial type 2 occurrence | Risk for further circulation |
|-------|------------------------------|---|---|------------------------------|
| 1 | 12–18 months | General population immunity remains high if mucosal immunity is boosted in <5 population by pre-switch tOPV SIAs | High | Low |
| 2 | 2–3 years | General immunity still reasonably high, but overall mucosal immunity declining and absent in new birth cohorts | Medium | Medium |
| 3 | ≥4 years | Mucosal immunity declines sharply | Low | High |

a The period of 18–24 months will be updated in the next version of the SOP

Occurrence of aVDPV2s is historically less responsive to immunity conditions and may be more difficult to predict in the context of rapidly decreasing population immunity to transmission after OPV2 cessation; however, a minimum of four aVDPVs could be expected in the first year following OPV2 cessation.⁶

Place (country or sub-national region with >10 million population): *What is the scope of the outbreak affected area and extent of epidemiologically linked populations?*

The geographic scope under consideration for a response should take into account epidemiologically-linked populations, including defined areas of ongoing circulation as well as other areas of high risk. The scope may include an entire country, or for large countries, could include a subnational region/urban area with at least 10 million population. Note that in some situations, epidemiologic links may include homogenous populations who regularly inter-mix and cross international borders, and thus areas of multiple countries may need to be included in the scope of the response.

The scope and scale of the response may also be influenced by characteristics of the place, such as environmental factors (e.g. poor sanitation and high force-of-infection), geo-political challenges (e.g. insecurity) and other geographic factors (e.g. transport links to high risk communities with immunity gaps).

Characteristics of the affected population: *What is the estimated immunity of the population in the area where the poliovirus was detected? Does the community in which the virus was*

6 Institute for Disease Modeling. Unpublished data, January 2016.

discovered have particular characteristics which may signal low immunity and/or an increased risk for transmission?

Although the greatest risk factor for the emergence of a VDPV2 is low overall population immunity to type 2 poliovirus transmission, other risk factors include high birth rate, high population size and density, low routine immunization coverage, failure to reach unvaccinated children in pre-switch SIAs, and other conditions associated with high levels of fecal–oral transmission.

Vaccination coverage rates from both routine immunization programmes and any SIAs in the area can be useful. However, this data must be analyzed in the context of what is about the immunogenicity of OPV in order to estimate population immunity. In many situations, vaccination coverage may be unknown but other population characteristics (e.g. marginalized or underserved, conflict-affected, history of immunization refusal, etc.) in the affected community may be indicative of low immunity. Detection of poliovirus in a mobile community or conflict zone may be of special concern for further spread.

- **Vaccine choice:** Use mOPV2 as the vaccine of choice to stop type 2 poliovirus circulation during Phase 1. NOTE: IPV (either fl ID or full dose IM) is no longer recommended for a type 2 outbreak response.) IPV may be used to strengthen routine immunization or in selected individuals to provide protection for close contacts of iVDPV or WPV2 cases.

Special circumstances: Although tOPV and mOPV2 have similar immunogenicity against type 2 (8), use of tOPV in the post switch era is not feasible due to containment imperatives. tOPV has been withdrawn from use and remaining stocks have been destroyed. bOPV is the vaccine of choice now to respond to PV1 or PV3. In endemic areas with co-circulation of WPV1 and cVPVD2 the need to interrupt both types of transmission is critical. In addition to an aggressive response to WPV1, an immediate and adequate response to cVDPV2 should be implemented with high priority in all instances. In situations where both bOPV and mOPV2 are required, the two OPVs may be given 2 weeks (or less if operationally feasible) apart.

mOPV2. Modeling suggests that a mOPV2 response sufficient to interrupt the live poliovirus transmission that caused the outbreak will not create new cVDPVs within the same population (5,8). However, exportation of the OPV-related virus to other susceptible neighbouring populations remains a concern. In addition, an inadequate response with mOPV2 long after initial SIAs have controlled an outbreak also creates the potential for vaccine virus transmission. Nevertheless, the risk of remaining cVPDV2 circulation far outweighs the risk of seeding type 2 virus through mOPV2 SIAs.

Other tools. The most common form of treatment for persons with primary immune deficiency disorders that may lead to an iVDPV is replacement therapy with intravenous immunoglobulin (IVIG). Polio antiviral compounds and monoclonal antibodies have demonstrated therapeutic value in limited studies, but additional research is being conducted urgently to make these options widely available as potentially useful prevention measures (33).

- **Vaccine stockpile.** Request mOPV2 for type 2 outbreak response through WHO for allocation from the global stockpile managed in collaboration with UNICEF Supply Division. Member States that decide to establish a national poliovirus vaccine stockpile

should maintain the stockpile in conditions of containment that are verified by the Regional Certification Commission for Polio Eradication to be compliant with the containment Global Action Plan and also seek authorization of the WHO Director General before release and use of mOPV2 (34) (see *Response scenarios* and *Annex 1* for further details).

In order to maximize the containment of type 2 poliovirus, the WHA has urged countries to rely on a global stockpile of mOPV2 managed under the authority of the WHO Director General. The WHO, in collaboration with the UNICEF Supply Division and vaccine manufacturers, has established a stockpile of mOPV2 which can be rapidly provided to Member States based on an established request procedure in case of a type 2 outbreak. In line with the guidelines for a type 2 outbreak response in this protocol, countries should file a request for mOPV2⁷ to WHO. A global advisory body will review the request and make a recommendation to the WHO Director General who can authorize the release of mOPV2.

- **Optimal number of supplemental immunization activities (SIAs):** Plan and implement 2 SIAs with mOPV2 in all outbreak and high risk areas. Closely monitor SIA quality (defined as coverage >90% and no evidence exists of persistently missed children or continued transmission). Add additional SIA(s) if quality is not satisfactory.
- **Speed of supplemental immunization activities (SIAs):** Conduct the first ‘rapid response’ SIA (e.g. SIA1) within 14 days of initial sequencing results provided by the GPLN where it is possible to achieve high coverage (>90% and no persistently missed children).
- **High quality supplemental immunization activities (SIAs):** High quality campaigns are essential to achieve rapid interruption of transmission and timeline for implementation may be adjusted slightly to help achieve quality. Decisions about timing of vaccination response should be made in consultation with WHO RO and HQ, and supported by GPEI technical experts. Please refer to guidance in section 2.7, SOP part 1.

Modeling (35) and multiple years of experience in responding to prior outbreaks of WPV and cVDPV have demonstrated that conducting an immunization response quickly even with moderate coverage for the first round will stop transmission in fewer rounds than waiting to intervene later in the hope of maximizing coverage through better organization. The implications are even greater in responding to an emergence of type 2 poliovirus given the potential ramifications of spread.

- **Interval of SIAs:** After SIA1, conduct subsequent SIAs (if required) within 2–3 week intervals as long as coverage is not compromised. It is critical to ensure that second and any subsequent rounds of vaccination response reach every child. Local operational feasibility based on environmental, infrastructure, security, and programmatic factors should ultimately determine the intervals required to ensure safety and effectiveness.
- **Target age group:** During the period 12–18 months after tOPV cessation, target **all** children under five years of age. To minimize the use of mOPV2 in the population, expanded age groups are not routinely recommended for a type 2 immunization response unless there is evidence of circulation among older persons.

⁷ If only a very limited number of doses of IPV are required (i.e. to vaccinate household contacts) countries should use their own national stocks, or if unavailable, request from UNICEF.

- **Target population:** Target approximately 1–2 million children under 5 years of age for each SIA, with final size to be determined upon review of the risk assessment. Where two million children do not exist within a reasonable radius, all children, or children of 10 million total population could be targeted. Consider increasing the scope further in densely populated areas **or** if there is evidence of extensive circulation (e.g. population mobility or other risk factors). However, in all situations, the target population should not be increased beyond the capacity of the programme to attain high coverage.

The priority where high coverage (>90% and no persistently missed children) can be achieved is for the initial SIA to begin vaccination within 14 days of sequencing results. In circumstances where high quality cannot be achieved, determine start date in consultation with country and GPEI experts. Use of a preparedness dashboard should help guide this process. Please refer to guidance in section 2.7, SOP part 1.

The minimum target for SIAs needs to balance the requirement to stop transmission while minimizing the chances of reseeding the vaccine virus elsewhere. Related modeling shows that the exportation risk is low during the period that population immunity for type 2 remains high (e.g. during Phase 1) in most countries.⁸ However the risk for exportation increases if initial post switch immunity was low or has not been addressed through IPV use in routine immunization. The target of two million reflects successful experience in the precessation era. With high coverage, this target should be adequate to stop transmission in most areas, but could be expanded based on analysis of local risk factors.

Response scenarios for Phase 1

The general GPEI performance standards for any poliovirus response are detailed elsewhere (21). Figure 1 summarizes general steps and the specific measures required for a type 2 response. Depending on the situation, an outbreak or an event may trigger a vaccination response.

VDPVs (Figure 3a).

Initial sequencing results of a cVDPV should prompt a rapid vaccination response. Plan and implement 2 SIAs with mOPV2 in all outbreak and high risk areas. NOTE: fIPV is no longer recommended for use in outbreak response. Closely monitor SIA quality (defined as coverage >90% and no evidence of persistently missed children or continued transmission). Add additional SIA(s) if quality is not satisfactory. Conduct SIA1 within 14 days of initial sequencing results and subsequent SIAs at 2–3 week intervals where high coverage can be achieved (>90% and no evidence of persistently missed children). Please refer to guidance in section 2.7, SOP part 1 for further detail. Target approximately 1–2 million children under 5 years of age for each SIA, with final scope to be guided by the risk assessment. The scope of outbreak response may be further extended in circumstances of high population mobility or other risk factors.

- If a new VDPV2 is detected proceed with SIA response only if considered to be at high risk for further transmission. If assessed as a medium-low risk situation, intensify field investigation, enhance surveillance, and undertake supplemental case detection activities.

⁸ See Institute for Disease Modeling. Unpublished data, January 2016.

Note: In the situation of detecting a cVDPV or a new VDPV in a high risk context, implementing a rapid response SIA should not wait for full case or community investigation or for laboratory testing to rule out an iVDPV.

- If further contact tracing finds additional VDPV cases linked to the original isolate, classify as a 'new cVDPV' and continue with vaccination response SIAs
- If further investigation results in classification as aVDPV deemed to be at high risk for transmission, proceed with a vaccination response.
- If further investigation results in classification as iVDPV proceed with limited response to protect both case and close contacts.

Treat the individual with IVIG and/or antivirals (when available) plus give IPV to any household members or close contacts. SIAs are not routinely recommended in response to iVDPVs whether the classification is made based on initial sequencing or after identification of an immunocompromised individual. However, one to three SIAs (each with a target of 500,000 children) may be considered in high-risk areas around the immunodeficient case, especially if the iVDPV is detected late in Phase 1 when type 2 immunity will have declined.

If further investigation does not determine either a new cVDPV or iVDPV, consider the isolate an **aVDPV**. Historically, most aVDPVs have occurred in isolation, but in the context of decreasing population immunity a higher fraction of aVDPVs may go on to become cVDPVs. Therefore, classification of an aVDPV should lead to close monitoring of surveillance performance standards for the next three to six months. Additionally, a more aggressive vaccination response to an aVDPV may be required if it meets one of these three criteria: (i) interval from the switch is >6 months; **or** (ii) occurrence in an area with prior cVDPV emergence; **or** (iii) substantial genetic deviation from a parent Sabin virus (e.g. evidenced by nucleotide deviations or recombination with class C enterovirus). In these situations or in an area otherwise considered as high risk for transmission, after the initial rapid response SIA, proceed with at least two more SIAs each targeting two million children with mOPV2.

WPV (Figure 3b). In the unlikely event of detecting a **WPV2 human/AFP case**, promptly determine whether the individual has a known type 2 exposure due to a containment breach. In the instance of known, documented exposure, vaccinate close contacts with IPV; but no further vaccination response is required unless active surveillance provides evidence of other cases. If no exposure can be documented, respond aggressively according to the *vaccination response* scenario for a cVDPV.

For a single **WPV2 environmental surveillance sample**, rapidly assess the community for evidence of an individual excreting the virus (e.g. a polio compatible AFP case or a WPV case). Multiple environmental surveillance samples with sequencing which indicates >1 infected individual⁹ may also demonstrate virus excretion in the community. If evidence of excretion is found, respond according to the WPV2 case scenario. If no evidence is found, consider at least one rapid response SIA especially in any area deemed to be at high risk.

⁹ For example, samples collected at more than one distinct environmental surveillance collection site (no overlapping of catchment areas), or from one site if collection was more than two months apart.

FIGURE 3A. General response strategies by detection scenarios of a VDPV2 isolate during Phase 1 (12–18 months post switch)

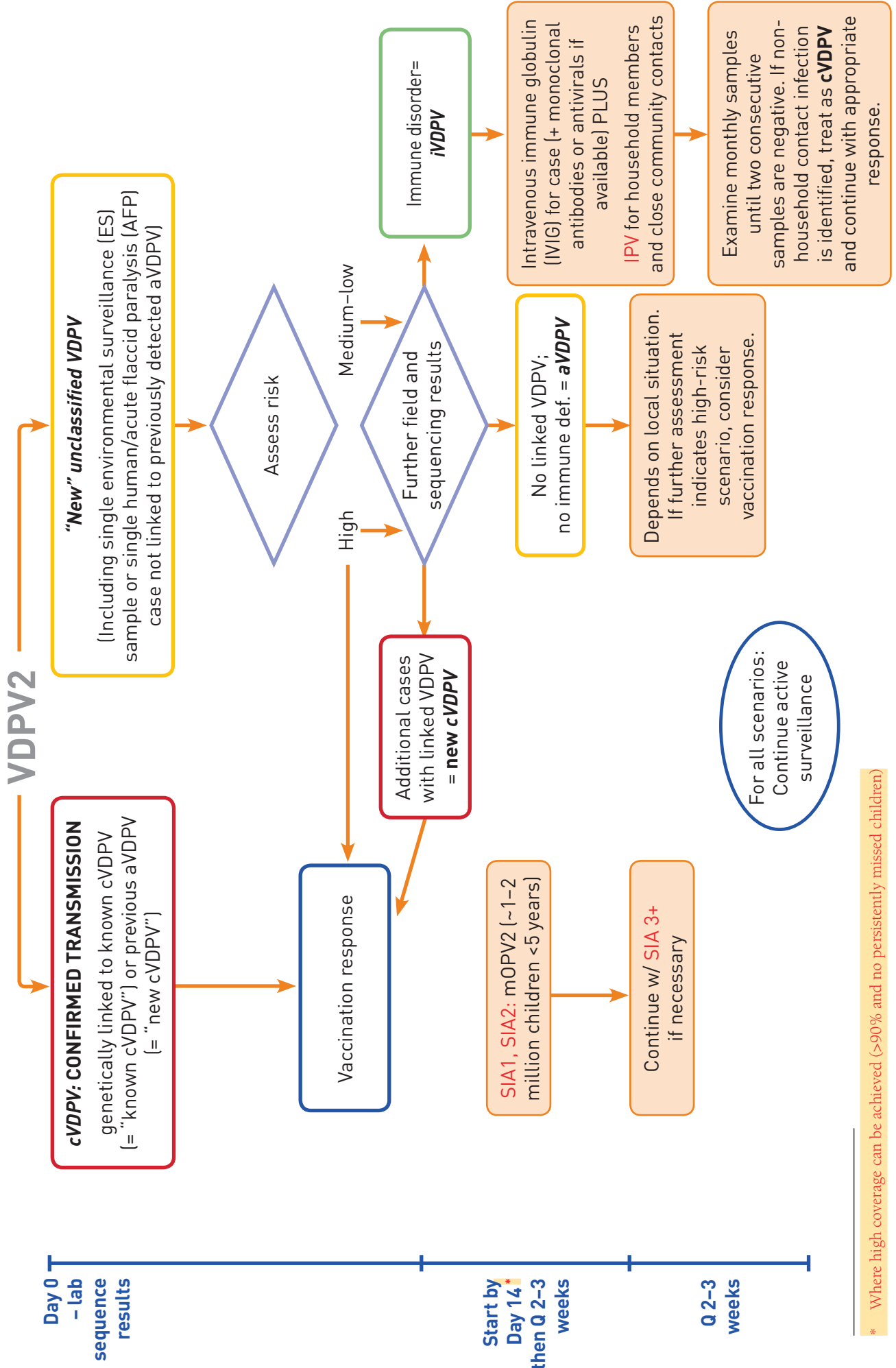
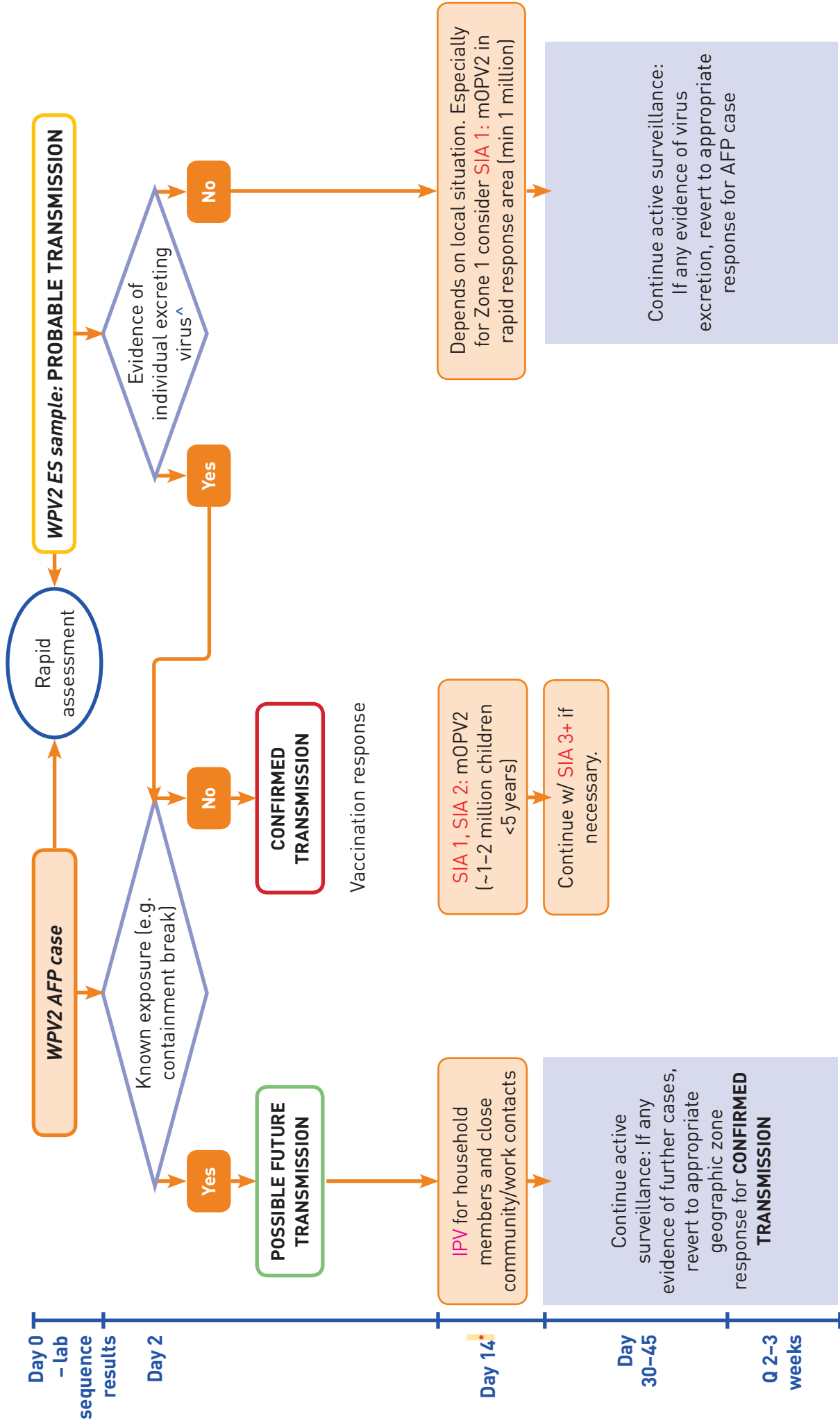


FIGURE 3B. General response strategies by detection scenarios of a WPV2 isolate during Phase 1 (12–18 months post switch)



[^] polio compatible AFP case, WPV infected person(s), or multiple environmental surveillance samples indicating > 1 infected individual

* Where high coverage can be achieved (>90% and no persistently missed children)

Sabin environmental surveillance sample or individual (Figure 3c). Detection of Sabin type 2 poliovirus in the stool within three months or in sewage within four months of the switch (and/or mOPV2 response immunization) should encourage continued monitoring for Sabin type 2 poliovirus, but does not need to automatically trigger a search for OPV2-containing vaccine in the community. However, if there are any nearby laboratories or vaccine production facilities, prompt investigation should be undertaken to discover any breach in containment, to test workers as possible sources of poliovirus, and to review safety protocols, particularly in light of the deadline for all Sabin type 2 polioviruses globally to be contained or destroyed within three months of the switch (13).

Detection of Sabin type 2 poliovirus more than three months after the switch (or mOPV2 use) in stool and more than four months of the switch (or mOPV2 use) in sewage suggests possible containment breach or continued use of tOPV or mOPV2 after the switch. The sequencing of the isolated Sabin type 2 poliovirus, and if there are multiple isolates, analysis of trends in the detection of Sabin type 2 polioviruses, should guide further action. If the detected isolate sequence is $\geq 99.7\%$ similar to the parent Sabin type 2 poliovirus sequence, the isolate probably originated from tOPV/mOPV2 administered after the switch or a breach in containment and a search should be conducted for tOPV/mOPV2 in use or storage in the area in which the Sabin type 2 poliovirus was found. If the detected isolate sequence is $< 99.7\%$ similar to the parent Sabin type 2 poliovirus sequence, the isolate may have originated from tOPV administered prior to the switch and may represent an outlier in excretion descended from polio vaccine viruses. A search for tOPV may still be warranted unless sequencing results compared to prior Sabin type 2 samples demonstrate a continued decline in similarity to the parent Sabin strain.

Primary actions required by national public health authorities

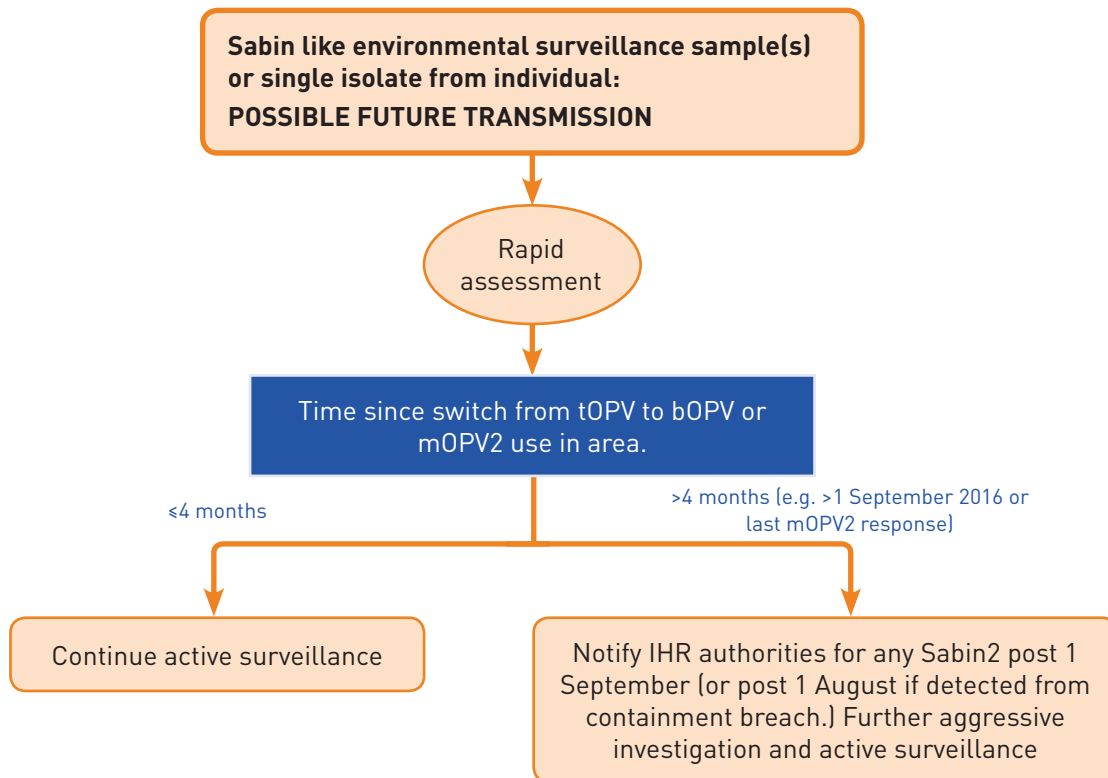
- Based on the risk assessment (Tables 1 and 3) and strategies noted above, implement the recommended response according to the appropriate scenario of type 2 virus classification (Table 2).

If indicated, request mOPV2 for type 2 outbreak response through WHO for allocation from the global stockpile. Requests should be submitted in two stages. Submit the Stage 1 request for vaccines required for SIA1 within 24 hours of validation of sequencing results. The Stage 2 request covering vaccines needed for all subsequent SIAs should be submitted within the two weeks following outbreak/event confirmation (see Annex 2 for details).

For any Sabin 2 detected > 4 months post switch (or last mOPV2 use) conduct further aggressive investigation and active surveillance according to new guidelines and tools developed by GPEI.¹⁰

¹⁰ See: GPEI. A guide for investigation of Sabin Like 2 (SL2) poliovirus in a human or in the environment. March 2017 and GPEI. A tool for investigation of Sabin Like 2 (SL2) poliovirus isolation in human or in the environment. March 2017. <http://polioeradication.org/tools-and-library/resources-for-polio-eradicators/gpei-tools-protocols-and-guidelines/>

FIGURE 3C. General response strategies by detection scenarios for a Sabin 2 isolate during Phase 1 for countries with use of OPV within 1 year prior to type 2 OPV withdrawal



Travel and migration patterns in and out of affected communities can have a significant impact on the risk and extent of poliovirus circulation. Therefore, in the situation of a type 2 poliovirus outbreak, local epidemiologic, geographic and population mobility factors should be used to determine the specific boundaries of the outbreak affected area.

Primary actions required by national public health authorities

- Consider imposing a local quarantine in situations where a single individual has a documented exposure to poliovirus type 2 (e.g. in a laboratory or vaccine production facility). Continue further investigation and close surveillance of family members and/or co-workers for at least 60 days post initial case detection.
- Based on local feasibility and assessed risk, consider implementing local travel restrictions and/or proof of polio vaccination for travelers of any age into/out of the outbreak area. Community organizers may be mobilized to engage the population in risk reduction behaviours, including vaccination and voluntarily restricting travel.

On 5 May 2014, the WHO Director General declared the international spread of WPV a public health emergency of international concern under the International Health Regulations (2005) (36). Since then, the IHR-Emergency Committee (EC) has met regularly to issue advisories to polio-affected countries regarding measures they should undertake to restrict the international spread of poliovirus, including heightened surveillance and traveler vaccination (37).

Primary actions required by WHO and national public health authorities

- In accordance with national regulations and IHR (2005) Articles 30–32 (19), WHO and national health authorities should collaborate to implement international travel restrictions as necessary. International traveler verification of IPV vaccination should follow guidance in the IHR (2005).

4.5 Outbreak/event response assessment and follow-up steps

The urgency of stopping any type 2 poliovirus transmission as soon as possible underscores the need to follow up the initial response steps with ongoing evaluation of the impact. Since poliovirus transmission has been declared a public health emergency of international concern, specific oversight and reporting requirements will be required under IHR (2005).

Primary actions required by national public health authorities

- As with any SIA, institute adequate supervision, lot quality assurance and independent monitoring of immunization activities to ensure the quality of interventions (38).
- Submit regular updates to the IHR-EC as requested.

Primary actions required by GPEI (39)

- Conduct independent monitoring at least by SIA2. Also conduct outbreak/event response assessments by the third month from Day 0 and continuing quarterly thereafter until 12 months have passed without a type 2 poliovirus identification.
- Confirm the end of the outbreak by validating the absence of poliovirus type 2 in the population and the environment 12 months after the onset date of the most recent case plus one month to account for case detection, investigation, laboratory testing and reporting period (20). The final assessment should be submitted to the Global Commission for Certification of the Eradication of Poliomyelitis for final verification that the outbreak has ended.
- Develop a six-month plan for strengthening surveillance which should be monitored quarterly.
- Provide “surge” technical support graded to risk of transmission and local response capacity.

Annexes

Annex 1. Summary of factors contributing to risk categorization for virologic, contextual, and international transmission spread of poliovirus

Objective is to identify elements of 'high risk' scenarios based on a risk assessment that considers multiple factors in three categorical areas (virology, context, and international spread). Rather than specific quantitated parameters, the assessment should be based on an overall evaluation of the specific situation. The relative 'weight' of each category will be situation dependent and any mitigating factors taken into consideration.

TABLE A1-1. Factors of virologic, contextual, and international transmission spread that influence risk assessment

| Risk Category | High | Medium-Low | Comment |
|--|---|----------------------|--|
| Virology | | | |
| cVDPV | Automatically defined as a high risk situation | | |
| Other immunological & virological evidence | <ul style="list-style-type: none"> • Co-circulating WPV1 • Detection of other (un-related) aVDPV2 or cVDPV since switch in same region • Substantial genetic deviation from parent Sabin | Absent or low number | Based on present/past laboratory data Expert virologist assessment |
| Context | | | |
| Case characteristics | <ul style="list-style-type: none"> • Member of known 'high risk'/underserved population (minority, refugee, mobile, IDP, etc.) • 0 dose or 'under'-vaccinated • Age >5 years | Absent | Based on local case investigation |
| Coverage data | <ul style="list-style-type: none"> • Poor RI coverage (IPV if available-otherwise DPT3) in infected Admin 1 level • Poor quality of prior SIAs (if relevant) | | 'Pop immunity' by itself may be a problematic risk factor as this will decline in all areas w/o adequate RI IPV. High IPV coverage alone may also mask ongoing risk for 'silent' transmission. |

| Risk Category | High | Medium-Low | Comment |
|-------------------------------|--|---|---|
| Surveillance quality | Evidence of surveillance gaps (e.g. sub-standard AFP indicators, infrequent or absent ES, orphan virus) in infected Admin 1 level | Adequate surveillance | Based on routine AFP/ES monitoring data + any available recnt surveillance assessment |
| Admin level 1 context | <ul style="list-style-type: none"> • Large, densely populated area • Predominance of known 'high risk populations' (e.g. mobile, refugee, IDP) • Insecure and/or inaccessible area • Environmental conditions associated with high levels of fecal-oral transmission | Stable, accessible population | Based on local investigation |
| International spread | | | |
| Proximity to border | Contiguous or direct transport link to int'l border (especially if other area is known high risk) | Absent | Based on local investigation and/or available data |
| Population mobility-migration | Evidence of high levels of migration (from sequencing data, available cell phone data, prior migration patterns, etc.) | Absent | Based on local investigation and/or available data |
| Context of neighboring areas | Evidence of surveillance gaps or other high risk factors in neighboring areas susceptible to importation from affected area | Absent | |
| Summary | | | |
| | Significant risk of continuation and international spread of transmission due to evidence of recent/ongoing polio virus transmission, significant gaps in population immunity, major vulnerable population clusters, a history of multi-country involvement, high security threats and access challenges, | Minimal to Moderate risk of continuation and international spread of transmission | |
| Actions to consider | <p>Vaccination response per protocol</p> <p>Enhanced surveillance</p> <p>Continued field investigation as required</p> | <p>Enhanced surveillance</p> <p>Continued field investigation as required</p> | |

Annex 2. Operational framework for monovalent oral poliovirus type 2 (mOPV2) stockpile deployment and replenishment after OPV2 cessation

1. Stockpile objectives

In May 2014, the WHA endorsed the SAGE recommendation to establish a global stockpile of mOPV2 for responding to type 2 outbreaks post OPV2 cessation (40).

The primary objectives of the stock pile are to: (i) ensure rapid, universal supplies of mOPV2 for countries experiencing outbreaks of VDPV2 or WPV2; and (ii) maximize the containment of Sabin type 2 poliovirus. Specific quantities of the vaccine will be released upon authorization of the WHO Director General.

2. Eligibility

All countries, whether or not they have previously received vaccines through UNICEF, are eligible to access the stockpile.

The SAGE has strongly advised that all countries should rely on this global stock. In May 2015, the WHA directed that any country that decides to establish their own national stock of mOPV2 should maintain the stockpile in conditions of containment that are verified by their Regional Certification Commission for Polio Eradication to be compliant with the GAPIII guidelines (10) and to seek authorization from the WHO Director General for its release and use (34).

3. Stockpile content

The WHO and the UNICEF supply divisions have collaborated with two vaccine manufacturers to establish a stockpile of bulk mOPV2. Both manufacturers of mOPV2 vaccines have been licensed in the country of origin and their vaccines are prequalified by WHO (41).

As of March 2016, the stockpile contains 519 million doses of mOPV2: 419 million doses of bulk vaccine (shelf life of 20 years), 50 million doses of the finished product ready for deployment by April 2016 and 50 million doses in semi-finished product (vials without labels) available by July 2016 which can be converted to the finished product between September and December 2016. The vaccine will be processed to replenish the supply of the finished product upon request from the GPEI to maintain stock levels.

4. Stockpile location, management and governance

The roles and responsibilities of each party (e.g. manufacturers, WHO, UNICEF) are outlined in a contract for services with the manufacturers which builds on a Letter of Agreement between WHO and UNICEF. WHO maintains ownership of the stockpile. The manufacturers are responsible for storing and maintaining the stockpile under appropriate containment and quality assurance standards as well as preparing the vaccine for delivery in line with the agreed lead times. UNICEF has the responsibility for procuring and coordinating the delivery of the vaccine to recipient countries when authorized by the WHO Director General based on national requests.

5. Decision-making for release of vaccine

The objective of establishing the stockpile is to manage stocks of mOPV2 which will be required in all vaccination responses (see Response strategies for Phase 1). Countries (even

those with their own national stocks) should submit a request for mOPV2 to a global advisory committee (the Eradication and Outbreak Management Group (EOMG) plus other technical experts). This committee will make a recommendation to the WHO Director General whose authorization permits the release of mOPV2 from a national or global stockpile and initiates the process for shipping the vaccine to the requesting country as necessary.

Fractional dose IPV (fIPV) is no longer recommended for outbreak response to cVDPV. The SAGE WG has recommended that IPV be prioritized to provide general population protection through routine immunization in countries at risk of VDPV2 emergence and spread (tier 1 and 2), rather than in response to outbreaks. The priority in outbreak response remains high quality OPV response and there is limited added benefit from fIPV. Continue to vaccinate close contacts of iVDPV cases with IPV. For such limited number of doses, countries should use their own national stocks.

Table A1–1 provides a summary of the steps required for notification, confirmation and response to a type 2 outbreak/event. Note that the steps and timeframe may be revised based on experience and implementation of new laboratory procedures.

6. Stages in accessing vaccine stockpile (see also [Figure 2](#) in the main text)

The vaccine will be requested in two stages: Stage 1 which covers only the mOPV2 vaccine required for SIA1; and Stage 2 which covers vaccines (mOPV2 and if necessary, IPV) for all further planned SIAs.

Stage 1. In order to ensure a rapid response, the initial request (**see Annex B**) should be prepared within 24 hours of validation of sequencing results and include:

- Relevant laboratory and epidemiologic information of the investigation to date
- Basic profile of the affected population (e.g. vaccination coverage rates, summary of other risk factors, etc.)
- General response plan for SIA1 only, including requested quantities of mOPV2 vaccine
- Authorization for emergency use of mOPV2 based on WHO prequalification (see Regulatory considerations below).

Stage 2. Planning for subsequent response strategies will usually require further field investigation. Submit a request for all subsequent SIAs together. The Stage 2 request form should contain:

- Results of any further laboratory and epidemiologic investigations
- Response plan for all further SIAs (including specific number of vaccine doses required) and number of doses of any existing stocks of mOPV2 from SIA1.

TABLE A2-1. Steps for notification, confirmation, and response to a type 2 outbreak/event^a

| Step | Action | Comments | Responsibility | Timeframe | Data or decision reported to | Days to notification of sequencing results |
|---|--|---|--|--|--|--|
| Notification and response preparation for all type 2 poliovirus isolations (cVDPV2s, VDPV2 and Sabin 2 isolations) | | | | | | |
| 1 | Laboratory notification of type 2 poliovirus isolate sequencing results | | Global Polio Laboratory Network (GPLN) | <ul style="list-style-type: none"> Complete within 14 days of initial isolation Report within 24 hours of results | Notification to health ministry, GPEI partners (including UNICEF Supply Division) | Day 0 |
| 2a | Initial confirmation of outbreak/event and risk assessment <i>national level</i> | Conduct rapid case confirmation and risk assessment; further investigation should continue to aid in final classification (<i>see step 14</i>) | <ul style="list-style-type: none"> Health ministry/EOC (with local GPEI support if needed and available). If outbreak/event is confirmed, IHR focal point has reporting responsibility | <ul style="list-style-type: none"> Complete in <48 hours; report findings immediately If outbreak/event is confirmed to meet IHR criteria, report in <24 hours of completing assessment through IHR protocol | <ul style="list-style-type: none"> Report initial findings to WHO country and Regional Office. Report to WHO IHR contact point | Day 0-2 |
| 2b | Confirmation of outbreak/event <i>regional/global level</i> | Follow-up with health ministry upon receiving lab notification; if any concerns, verify lab results with GPLN regional reference lab | WHO Regional Office polio focal point | Report immediately or in <24 hours of completing assessment | Notification to regional and global GPEI partners | Day 2 |
| 3a | Response preparation <i>global level</i> | Prepare OPRTT response <ul style="list-style-type: none"> Identify potential technical assistance Prepare funding | EOMG | Begin <24 hours from lab notification | | Days 0-2 |
| 3b | Response preparation <i>national level</i> | Draft response plan and vaccine request where indicated due to risk & virologic characteristics simultaneously with rapid investigation | Health ministry/EOC (with GPEI if needed & available) | Begin <24 hours from lab notification; complete within 48 hours | | Days 1-2 |

| Step | Action | Comments | Responsibility | Timeframe | Data or decision reported to | Days to notification of sequencing results |
|---|---|---|--|--|---|--|
| Stage 1: Response Implementation | | | | | | |
| 4 | Submit SIA1 vaccine request upon confirmation of outbreak/high risk event | Complete initial risk assessment; finalize vaccine requirements per response plan | Health ministry/EOC (consult with WHO/ UNICEF in-country) | <24 hours from confirmation of outbreak or event | EOMG | Day 2 |
| 5 | Vaccine request evaluated at global level | Assisted by WHO/POL as secretariat | Advisory Group (EOMG+) | <24 hours | WHO Director General | Day 3 |
| 6 | Vaccine stockpile release authorized | WHO Director General reviews Advisory Group recommendation | WHO Director General | <24 hours | Authorization sent to UNICEF, health ministry | Day 4 |
| 7 | GPEI response initiated | OPRTT support implementation <ul style="list-style-type: none"> • Grading • Technical assistance staff deployed • No regret funds released | EOMG/OPRTT | <72 hours from Director General's authorization | Communicates with other GPEI partners at all levels and health ministries | Days 4–6 |
| 8 | Official notification to prepare vaccines for delivery | Purchase Order issued to manufacturer | UNICEF Supply Division | <24 hrs from receipt of Director General's authorization | Vaccine manufacturer | Day 4 |
| 9 | Prepare shipment | | Manufacturer–vaccine; UNICEF (or WHO)– syringes and safety boxes if required | 3 working days | UNICEF | Days 4–6 |
| 10 | Ship to recipient country | | UNICEF Supply Division (or WHO) | <72 hours | Recipient health ministry | Days 7–9 |
| 11 | In-country processing and transport | Includes customs clearances; delivery to field level | Health ministry/EOC | <5 days | | Days 10–14 |

| Step | Action | Comments | Responsibility | Timeframe | Data or decision reported to | Days to notification of sequencing results |
|---|--|--|---|---|------------------------------|--|
| 12 | SIA 1 | | Health ministry/EOC + EOMG rapid response team | 3–5 days | | Day 14+ |
| Stage 2: Response preparation and implementation | | | | | | |
| 13 | Conduct further field + laboratory investigation to reach final classification | Simultaneous with Stage 1; includes contact tracing, further labs to rule out immunodeficiency. | Health ministry/EOC + EOMG rapid response team | 7–14 days; further time may be required in some circumstances | | Day 0–13 |
| 14 | Prepare further response plans (SIA2+) and Stage 2 vaccine request | Simultaneous with Stage 1; request should include vaccines required for all additional planned SIAs. | Health ministry/EOC + EOMG rapid response team | 7–14 days | WHO headquarters | By day 14 ^a |
| | Repeat steps 4–12 | Delivery may take longer than in Stage 1 when syringes required. | All | 16 days | | Days 15–30 |
| | Implement SIA2 and additional SIAs | | Health ministry/EOC + EOMG support as necessary | | | By day 30–45; then 2–3 weeks apart |
| | Proper containment and disposal of mOPV2 | Should take place after each SIA with validation after last SIA. | Health ministry with assistance from GPEI | Final stock report within 2 weeks of last SIA | | |

^a Steps and timeframe may be revised based on experience and implementation of new laboratory procedures.

^b All timeframes indicate intended targets. Some steps may be accomplished quicker; others, particularly for logistics, may take longer depending on local conditions, flight schedules, etc. EOC: Emergency Operations Centre; EOMG: Eradication and Outbreak Management Group; OPRTT: Outbreak Preparedness and Response Task Team

* Where high coverage can be achieved (>90% and no persistently missed children)

7. Logistics

a. Shipping

UNICEF will coordinate with the supplier to organize the shipment of mOPV2.

b. Documentation

The list of documents in the packing list to accompany each vaccine consignment is listed in the contract for services with the manufacturer and includes: invoice; airway bill; release certificate issued by the national regulatory authority of the country of manufacture for each lot of vaccine supplied; and the 'vaccine arrival report'. Temperature recorders will be included in the consignment as per guidelines for international shipping of the vaccine. A 'vaccine vial monitor' will be placed on each vaccine vial as for any WHO prequalified OPV vaccine. Any additional documentation requirements from recipient countries will not be accommodated and will need to be waived to ensure timely delivery.

c. Vaccine specifications and storage at country level

WHO and UNICEF will work closely with the recipient country to assess the storage volume required for the outbreak response vaccine and ensure sufficient cold room space at -20°C or 2°C to 8°C at the national level as well as adequate capacity at all relevant links of the cold chain. Vial sizes will depend on available supply. Refer to the request form for estimated volumes and storage requirements for mOPV2.

d. Management of unused stocks

The programme should rigorously manage and monitor utilization of mOPV2 stocks (42). After each SIA, all vaccine doses utilized and balance stock remaining (unopened vials) should be reported to the district level within two days of completion of the round. These **unopened** vials should be retrieved by the district level cold store within five days of completion of the round. The district level cold store should report mOPV2 stock levels to the national EPI manager within one week of SIA completion. Supplies to the district for the next mOPV2 SIA round should be adjusted against these available stocks.

The district level cold chain manager should clearly segregate and store any retrieved mOPV2 vials separately from bOPV stocks. **Open** vials of mOPV2 remaining after each SIA should be securely disposed at the local level using the same guidelines issued for disposal of tOPV (43).

Within two weeks of completing the last SIA required in the response plan, countries must report their remaining stock levels of mOPV2 to WHO and UNICEF as outlined in the revised *Technical guidance for mOPV2 vaccine management, monitoring, removal and validation* (44).

All district stores should take the remaining unopened mOPV2 vials out of the cold chain, and label and mark them clearly as explained in tOPV-bOPV switch guidelines. These vials should then be collected at the regional stores and disposed of properly as per national regulatory procedures.

Further detailed guidance for country programmes is being developed by the GPEI.

5. Regulatory considerations

a. Role of national regulatory authority in licensing and oversight

The Sixty-eighth World health Assembly urged all Member States to establish procedures to authorize the import and use of mOPV2 in the event of a type 2 outbreak. Since the procedure to license the vaccine even in the case of a fast track procedure may be time consuming, high-risk countries (e.g. those in transmission risk zones 1 and 2) should take steps in advance to ensure that mOPV2 can be rapidly deployed if necessary. WHO will provide technical support to these countries to facilitate implementation of this authorization procedure. Recipient countries may preemptively authorize the use of mOPV2 based on licensure issued by the stringent national regulatory authority process in the producing country and the knowledge that the vaccine is prequalified by the WHO. If not already completed, this authorization should be included as part of the vaccine request and will confirm that the recipient country will accept the vaccine and has the regulatory procedure in place to sanction its intended use.

b. Prequalification

The mOPV2 products in the stockpile for outbreaks are licensed in the country of origin and WHO prequalified. As for any vaccine supplied through UNICEF, the manufacturers are responsible for submission for WHO prequalification and for maintaining the prequalification status to cover the period of the stockpile contract.

Annex 3. Vaccine request forms

- **mOPV2 vaccine request form** can be found on the GPEI website: http://www.polioeradication.org/Portals/0/Document/Resources/PolioEradicators/SOP_AnnexB_mOPV.doc

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