Protocol for notification, risk assessment, and response following detection of poliovirus type 2 following globally-coordinated cessation of serotype 2-containing oral polio vaccine

Global Polio Eradication Initiative

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Introduction

Although no naturally circulating wild polio virus (WPV) type 2 (WPV2) has been detected globally since 1999, the oral polio vaccine (OPV) type 2 component (OPV2) currently is responsible for the vast majority of circulating vaccine derived poliovirus (cVDPV) cases and a substantial portion of vaccine associated paralytic poliomyelitis (VAPP) cases. In order to address this situation and the wider implications of OPV use after global wild poliovirus eradication, the *Polio Eradication and Endgame Strategic Plan 2013-2018*[1] proposes an endgame strategy (Objective 2) through three sequential steps: 1. Introduce at least one dose of inactivated polio vaccine (IPV) into routine immunization in all countries; 2. Cease using type 2-containing oral polio vaccine (OPV2) by a globally-coordinated switch from trivalent OPV (tOPV) to bivalent OPV (bOPV); and 3. Eventually globally-coordinate withdrawal of all OPV. [2]

Following OPV2 cessation, population immunity and especially intestinal immunity and secondary spread of type 2 OPV-related viruses will decline, which will increase the risk of an outbreak if exposure to a type 2 poliovirus occurs. Three main outbreak threats following OPV2 cessation are: a relatively higher, but time-limited risk of the emergence of cVDPV; a lower, long term risk of poliovirus re-introduction from a manufacturing site or laboratory; and a small, potential threat posed by prolonged poliovirus infection in individuals with B-cell related immunodeficiencies (e.g. immunodeficiency-related vaccine-derived poliovirus [iVDPV]).[3] Consequently, detection of any poliovirus type 2 (wild, vaccine derived, or Sabin) in any sample of any source will be considered a global public health emergency that requires rapid and high-quality coordinated action from global, national, and sub-national health agencies.

Objectives

The key objectives of this document are:

1. Outline the main elements of the strategy to detect and respond appropriately to any type 2 polio viruses from environmental sources or circulating in the population post OPV2 cessation.

[1] http://www.polioeradication.org/resourcelibrary/strategyandwork.aspx

[2] For a detailed analysis for the rational to withdraw OPV post WPV eradication see: Duintjer Tebbens RJ, et al. Risks of paralytic disease due to wild or vaccine-derived poliovirus after eradication. Risk Analysis 2006; 26(6):1471-1505 and Thompson KM et al. The risks, costs, and benefits of future global policies for managing polioviruses. American Journal of Public Health 2008; 98(7):1322-1330.

[3] For modeling of the risks associated with withdrawal of OPV see: Thompson KM, Duintjer Tebbens RJ. Modeling the dynamics of oral poliovirus vaccine cessation. J Infect Dis. (2014) 210 (suppl 1): S475-S484

This proposed strategy is based on evidence from past and current program experience dealing with polio viruses as well as existing models projecting possible scenarios. Development of these guidelines is an iterative process that will evolve as further evidence and experience are generated.

2. Provide guidance to global, regional and national public health officials and policy makers for the necessary steps required to rapidly notify the proper authorities, conduct an initial risk assessment, and develop an effective response to promptly curtail any type 2 poliovirus transmission.

The guidelines are intended to provide concrete parameters for decision making, yet they cannot address every possible scenario. Decision makers should flexibly interpret the protocol and actively consider their specific epidemiologic circumstances. However, any type2 outbreak in the post-switch era must be considered a potential global risk. While detection of a type2 poliovirus in one location may not generate sufficient concern of further transmission to necessitate an immediate local vaccination campaign, an aggressive investigation may still be required to trace the origin of the virus in order to determine an appropriate response at the initial source of the outbreak.

The basic approaches and principles are similar to those currently required for investigating and responding to any polio outbreak.[4] However, strategic actions following detection of a type 2 poliovirus isolate following OPV2 cessation require a heightened urgency and a carefully planned risk assessment and response due to the world entering truly new territory with associated uncertainties surrounding the possibility of introducing an eradicated pathogen and concerns about ensuing transmission. (See **Table 1,** page 27.)

Background: Criteria to gauge readiness for type 2 OPV withdrawal

In May 2014, the World Health Assembly (WHA) adopted five criteria which the Strategic Advisory Group of Experts on Immunization (SAGE) recommended to gauge global readiness for OPV2 cessation.[5] OPV2 withdrawal, scheduled for April 2016, is dependent on the global interruption of persistent cVDPV2 transmission and satisfactorily meeting all these readiness criteria. The first two criteria are specifically relevant to this protocol as they directly reflect preparations for identifying and dealing with any outbreak of type 2 poliovirus.

[4] See Global Polio Eradication Initiative. Responding to a poliovirus outbreak: Standard Operating Procedures for a new polio outbreak in a polio-free country. Geneva. February 2015. http://www.polioeradication.org/Portals/0/Document/Resources/PolioEradicators/1a.PolioOutbreakGuideline20150220.pdf

[5] See World Health Assembly. Poliomyelitis: intensification of the global eradication initiative. Report by the Secretariat. Geneva: World Health Organization, 2014 http://apps.who.int/gb/ebwha/pdf_files/WHA67/A67_38-en.pdf and Meeting of the Strategic Advisory Group of Experts on immunization, November 2013 – conclusions and recommendations. Weekly Epidemiological Record, 2014; 89(1):1–16. http://www.who.int/wer/2014/wer8901.pdf

a. Introduce at least one dose of IPV in OPV-only using countries.

All OPV-using countries should add at least one dose of IPV to the national immunization schedule in order to: (a) reduce the risk of paralytic poliomyelitis if exposure to a type 2 virus occurred after OPV2 withdrawal, (b) improve response to any future use of a monovalent type 2 polio vaccine in the case of an outbreak, (c) reduce transmission of a reintroduced type 2 virus; and (d) boost immunity to the remaining wild poliovirus serotypes 1 and 3. Specific guidelines for implementing this step are outlined elsewhere. [6]

While adding a single dose of IPV into routine immunization increases population immunity, implementing tOPV campaigns shortly before OPV2 withdrawal may be of even more benefit in decreasing the risk of cVDPV in some countries.[7] However, the use of tOPV campaigns in these situations may not be sufficient to prevent the development of cVDPVs if not appropriately planned and implemented. Before proceeding, countries should undertake an analysis of risk factors (e.g. location, historical VDPV emergence, population size, and population susceptibility) as well as taking steps to ensure maximum coverage and boost population immunity before OPV2 withdrawal.

b. Implementation of surveillance and response protocols for type 2 poliovirus (including constitution of a stockpile of monovalent oral polio vaccine (mOPV) type 2 (mOPV2).

Consistent with this global strategic document, each country should update its national surveillance and outbreak response plans to ensure the country has adequate capacity to detect and respond to any type 2 poliovirus and all relevant health officials are aware of the expanded notification requirements. On the global level, the Global Polio Eradication Initiative (GPEI) has established a stockpile of mOPV2 available to all countries specifically for outbreak response. Along with a comprehensive plan for stockpile management, a comprehensive release protocol including the criteria and procedures for use of the vaccine has been developed and reviewed by SAGE for possible endorsement by the WHA[8]. Since most OPV suppliers are expected to cease production of Sabin 2 virus due to the absence of constant demand and the implementation of stringent containment requirements, the potential for Sabin-IPV production sites to produce extra mOPV2 should be explored. The mOPV2 stockpile will be complemented by additional supplies of IPV held in a rotating stockpile by manufacturers to provide a minimum buffer stock which can also be utilized for an outbreak response[9]. (See **Response**, page 10.)

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[6] See http://www.who.int/immunization/diseases/poliomyelitis/endgame_objective2/en

[7] Thompson KM and Duintjer Tebbens RJ. Modeling the dynamics of oral poliovirus vaccine cessation. J Infect Dis. (2014) 210 (suppl 1): S475-484

[8] WHO. Operational Framework for monovalent oral poliovirus type 2 (mOPV2) deployment and replenishment. Draft October 2014. (http://www.who.int/immunization/sage/meetings/2014/october/4_Polio_mOPV2_stockpile_v4_09_10_2014.pdf

[9] For discussion on global vaccine stockpiles for VPDs see: Thompson KM, Duintjer Tebbens RJ. Framework for Optimal Global Vaccine Stockpile Design for Vaccine-Preventable Diseases: Application to Measles and Cholera Vaccines as Contrasting Examples, Risk Analysis 11 AUG 2014 DOI: 10.1111/risa.12265 (http://www.ncbi.nlm.nih.gov/pubmed/25109229); and Yen C, et al. Global Vaccine Stockpiles: a brief review and factors to consider for establishing future stockpiles. Lancet Published online February 6, 2015. (http://dx.doi.org/10.1016/S1473-3099(14)7099-5).

c. access to a bivalent oral polio vaccine that is licensed for routine immunization;

d. completion of phase 1 poliovirus containment activities, with appropriate handling of residual type 2 materials; and

e. verification of global eradication of wild poliovirus type 2.

Overall objectives of the strategy to deal with detection of a type 2 poliovirus

1. Prompt detection and notification of all type 2 poliovirus strains;
2. Rapid cessation of type 2 poliovirus circulation;
3. Instituting appropriate control activities as soon as possible that limit exposure of populations to Sabin 2 poliovirus from mOPV2 used in the outbreak response to prevent emergence of a new cVDPV type 2 (cVDPV2);
4. Using established mOPV2 and IPV stockpiles for outbreak response under a strict release protocol endorsed by the WHA; and
5. Validating the absence of poliovirus type 2 in the population and the environment following the outbreak response.

Explicit assumptions underlying the strategy

Implementation of the strategy to deal with the detection of a type 2 poliovirus requires certain key public health systems' operational and governance capacities and capabilities at the global, regional, national, and sub-national levels, including:

- Successful global coordination of OPV2 withdrawal ;
- Functional national surveillance system to detect poliovirus;
- Functional national and sub-national polio laboratory capacity , as well as regional and global reference laboratories;
- Willingness of national authorities to rapidly notify WHO of any type 2 poliovirus detection and to participate in a globally coordinated response;
- Sufficient qualified staff , financing, and logistical resources to meet the operational imperatives to rapidly plan and implement an investigation and, if necessary, an immunization response;
- Adequate stockpile of response tools, especially appropriate vaccine(s);
- Strong political will and governance structures to promptly make decisions and endorse the required actions at the national and global levels;
- Effective community mobilization and engagement to collaboratively support necessary response activities.

Components

In addition to incorporating the several preparatory steps which are also required for initiating Sabin type 2 withdrawal , the strategy for addressing the risks associated with withdrawal of OPV2 includes six components: detection, notification, investigation/risk assessment, response, traveler considerations (internal, and international), and follow-up. The proposed guidelines for each component are based on

risk factors and epidemiological contexts. Although presented separately, some components should proceed simultaneously.

1. Detection

All countries must maintain sensitive surveillance systems, including necessary laboratory capacity, to rapidly detect any circulating poliovirus and to uncover areas at risk of developing circulating polioviruses due to low population immunity. Global and regional systems should continue to support these vital national efforts.

Acute Flaccid Paralysis (AFP) surveillance has been the gold standard for global polio eradication and will remain the primary focus for detecting any type 2 virus in the post cessation era. Global and national guidelines are currently in place to provide required procedures and standards. [10] AFP surveillance is linked to global, regional, and national laboratories which are part of the Global Polio Laboratory Network (GPLN) with comprehensive, standardized guidelines to distinguish poliovirus as a cause of AFP from diseases other than poliovirus. [11] WHO and Ministries of Health should regularly monitor and evaluate AFP surveillance and laboratory networks to ensure global quality standards are maintained even as wild poliovirus cases disappear.

Environmental sampling has been increasingly utilized in key countries to supplement polio eradication efforts, especially in areas where deficiencies in AFP surveillance are suspected or populations are at high risk for poliovirus circulation due to low vaccine coverage or importation. However, the 2013 experience in Israel demonstrated that WPV transmission can be sustained for over one year without being detected through AFP surveillance in areas with exclusive IPV use.[12] This situation underscores the importance of targeted expansion of environmental surveillance in the post-cessation era in a wide range of situations. As proposed in *the Polio Eradication and Endgame Strategic Plan 2013-2018* the GPEI is working jointly with specific countries on a strategic expansion plan to include at least 15-20 additional sampling sites by the end of 2015.[13] Environmental surveillance (ES) will be targeted especially in areas of high risk for cVDPV emergence (e.g. low routine coverage and historical cVDPV cases), areas where there is a risk of silent transmission and circulation of poliovirus (e.g. high force-of-poliovirus-infection), and areas at risk due to vaccine production. Establishing ES as a fundamental part of the surveillance strategy for OPV2 withdrawal requires sufficient laboratory and staff resources as well as operations following current WHO guidelines [14] and should be instituted through a collaborative strategic global effort to enhance detection capacity for type 2 polioviruses.

Polioviruses may also be detected as an incidental finding in a non-AFP clinical specimen or through a stool survey. Currently, this detection method is not an important surveillance source. Nevertheless,

[10] http://www.polioeradication.org/Dataandmonitoring/Surveillance.aspx.
[11] http://www.polioeradication.org/Dataandmonitoring/Surveillance/GlobalPolioLaboratoryNetwork.aspx
[12] Anis E, Kopel E, Singer SR, et al. Insidious reintroduction of wild poliovirus into Israel, 2013. Euro Surveill 2013 Sep 19;18(38):pii=20586 (http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20586)
[13] http://www.polioeradication.org/resourcelibrary/strategyandwork.aspx
[14] http://whqlibdoc.who.int/hq/2003/who_v&b_03.03.pdf

any incidental findings of type 2 polio virus should be reported through the standard notification system. (See ***Notification***.)

Further operational research is needed to accelerate the timeliness and sensitivity of detection, reporting, and monitoring of type 2 poliovirus. New and emerging technologies should be fostered to develop point-of-contact diagnostics and to facilitate faster and simpler methods for collection and processing of ES samples. Priority should be given to developing tools which can be rapidly scaled up for use in difficult field environments.

2. Notification

Currently, treaty obligations under the International Health Regulations (2005) [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 generally also be notified to WHO under the separate notification requirement for 'events which may constitute a public health emergency of international concern'. [15] Post cessation of OPV2 and confirmation of the elimination of cVDPV2 the interpretation of this criterion should be expanded to include detection of <u>any</u> poliovirus type 2 (wild, vaccine derived, or Sabin) in <u>any</u> sample of <u>any</u> provenance as a notifiable event under IHR (2005).

The National IHR Focal Point should notify WHO of a confirmed, probable, or possible type 2 poliovirus detection within 24 hours as specified in the IHR (2005). The Ministry of Health should likewise inform relevant national officials. In this situation, even a single poliovirus isolate should be considered an outbreak and trigger an immediate assessment and outbreak response planning.

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

3. Investigation and Risk Assessment

<u>Objectives</u>
In addition to notification to WHO as required under IHR (2005), discovery of <u>any</u> type 2 poliovirus isolate from either AFP or environmental surveillance should initiate an immediate investigation to:

1. Confirm the outbreak;
2. Determine extent and duration of poliovirus circulation;
3. Define population characteristics of the case(s);
4. Identify the origin/causes for the outbreak;
5. Assess the risk for occurrence and extent of transmission.

[15] International Health Regulations (2005)

General Approach

While the general investigative approach is the same regardless whether the source of the isolate is from AFP or environmental surveillance, precise steps should be tailored to the specific situation. The key steps in the investigation phase are outlined below. **Table 2** (see pages 28-29) provides additional indication of the expected steps. (Further detailed guidelines for enhanced surveillance review and required epidemiologic field investigation are outlined in recent GPEI guidelines for investigating and responding to a polio outbreak[16].)

Beyond the standard approaches to dealing with any poliovirus outbreak, responding to the detection of a type 2 poliovirus following OPV2 cessation will require a heightened urgency with very rapid decision making as well as more intensive investigation, detailed planning, and close follow-up. Several steps may take place simultaneously. **Figure 1** (see page 19) provides an overall timeline of required activities, the agency or persons with primary responsibility, and the expected time frame for completing the action.

Key Steps

- Enhance virologic investigation: Further characterization of poliovirus isolates for intratypic differentiation (ITD) and sequencing should proceed in WHO accredited laboratories as a priority action. Additionally, laboratories responsible for covering the area where the poliovirus was detected should 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 recommended standards before and at the time of type 2 detection.

- Enhance surveillance: In order to maximize quality and sensitivity of the surveillance system, ensure strict attention to completeness and timeliness of all AFP reporting. In the immediate assessment period, increase frequency of environmental surveillance if the virus was discovered in areas where this is operational. For the longer term, in close collaboration with the GPEI, investigate expanding the number of local sampling sites or establishing environmental surveillance in the country if it is not yet operational.

- Conduct an epidemiologic investigation: A prompt field investigation of any AFP case should investigate the 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.

- Conduct a risk assessment: Based on the findings of the epidemiologic and virologic investigations and the strength of evidence, characterize the virus transmission and the implications for further spread. A follow-up step is to assess the critical factors which will influence the type and scale of response and make recommendations for appropriate actions.

[16]GPEI. Responding to a poliovirus outbreak: Standard Operating Procedures for a new polio outbreak in a polio-free country. Geneva. February 2015.

Key Questions and Determinations for the Risk Assessment

While the other laboratory and epidemiologic investigative steps correspond in general to standardized guidelines for following-up any poliovirus detection, the discovery of a type 2 isolate should generate a risk assessment which seeks to specifically address two core questions:

1. *What is the nature of the virus (e.g. WPV, Sabin, or VDPV)?;* and
2. *Is there evidence of circulation?*

Following Initial detection of a poliovirus isolate, its nature should be further characterized through ITD. Poliovirus isolates may be grouped into three categories: 1) WPVs, 2) Sabin (e.g. OPV strain), and 3) VDPVs (>1% divergent [PV1 and PV3] or >0.6% divergent [PV2] from the corresponding OPV strain). A thorough risk assessment is required regardless of isolate category.

WPV2. Given the extended period since a circulating WPV2 has been detected, the possibility of further emergence of this virus is very remote. However, if an individual WPV2 case is discovered, rapid case investigation is mandatory since transmission could rapidly take place depending on local population immunity. A WPV2 infected individual with no known exposure to a polio virus in a laboratory or vaccine production facility should be treated as evidence of *confirmed* transmission. A WPV2 isolate from an environmental sample is, in all probability, due to a containment break in a laboratory or research facility. Nevertheless, a thorough investigation is warranted in order to rule out an individual with ongoing sub-clinical infection who is excreting poliovirus. In any case, discovery of a WPV2 in an ES sample represents a *probable* risk for transmission. An infected individual with a known exposure to a break in containment is most likely an isolated event but is a risk for *possible* further transmission.

Sabin 2. Detection of a Sabin type 2 poliovirus is unlikely, but also represents a *possible* risk for transmission. In the first two to four months post OPV2 cessation, discovery of a single Sabin type 2 in an environmental sample may reflect residual excretions from the last tOPV campaigns.[17] While this detection should prompt increased vigilance through AFP and environmental surveillance, the risk for this occurrence should rapidly diminish with time.[18] A single individual AFP case with a Sabin type 2 poliovirus would also be rare, but could represent an isolated exposure in a vaccine production facility or research laboratory. This situation warrants a thorough case investigation and review of containment procedures and/or good manufacturing practices.

VDPV2. The most common poliovirus to be detected following withdrawal of OPV2 will be a VDPV.[19] Genetic sequencing of the detected poliovirus through a combination of molecular and antigenic methods or real-time reverse transcription–polymerase chain reaction (rRT-PCR) targeting sequences

[17] For empirical evidence see Wahjuhono G, et al. Switch from oral to inactivated poliovirus vaccine in Yogyakarta Province, Indonesia: summary of coverage, immunity, and environmental surveillance. J Infect Dis. (2014) 210 (suppl 1): S347-352. Modeling indicates that the mean time until OPV-related viruses die out is 3.7 months (range 2-12 months). See Thompson KM and Duintjer Tebbens RJ. Modeling the dynamics of oral poliovirus vaccine cessation. J Infect Dis. (2014) 210 (suppl 1): S475-484.

[18] Tebbens, R. J. D et al. Risks of Paralytic Disease Due to Wild or Vaccine-Derived Poliovirus After Eradication. Risk Analysis, 2006. 26: 1471–1505.

[19] For a comprehensive review of VDPVs, see Burns C, Diop OM, Sutter RW, and Kew OM. Vaccine-derived polioviruses. J Infect Dis 2014:210 (Supl 1):S283-293.

within the VP1 capsid region that are selected for during replication of OPV in the human intestine will provide more specific categorization. VDPVs are further classified as: 1) cVDPVs when there is evidence of person-to-person transmission in the community; 2) iVDPVs, which are isolated from persons with primary, B-cell immunodeficiencies; and 3) ambiguous VDPVs (aVDPVs), which do not fit into the other two categories.

As a cVDPV demonstrates ongoing circulation and *confirmed* transmission in the community it represents the same public health threat as a WPV.[20] Given the critical importance of detecting and stopping cVDPV transmission during the Endgame, in July 2015 WHO increased the sensitivity of surveillance to include the following expanded definition:

cVDPV

- '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 (ES) samples, or
iii) from two or more ES samples if they were collected at more than one distinct ES collection site (no overlapping of catchment areas), or from one site if collection was more than two months apart (NOTE: Classification as 'c'VDPV' for this scenario should apply only after detailed joint review of complete epidemiological and virological evidence between regional and global polio laboratory coordinator and other Global Polio Laboratory Network experts)

or

- a single VDPV isolate, with genetic features indicating prolonged circulation (i.e. $\geq$ 15 nucleotide changes).[21]

A sample that does not meet one of the above criteria requires more intensive investigation to determine if additional cases are occurring in the community. (See **Figure 2,** page 20.) A single VDPV2 ES sample without evidence of prolonged circulation (i.e. <15 nucleotide changes) or a single VDPV2 case may only represent an isolated event which will eventually disappear without further transmission. However, given the large risks inherent in failing to promptly respond to even low level type 2 spread, initial discovery of these scenarios should be treated as evidence of *probable* transmission.

In addition to case-finding and enhanced surveillance, the case investigation should determine whether an individual VDPV case or ES sample represents a long-term carrier for poliovirus (e.g.an iVDPV). Initial diagnosis of an iVDPV can require extensive follow-up and use of sophisticated molecular level testing. Detection of iVDPVs is rare (e.g. ~100 cases worldwide since 1961) and these cases have predominantly been found in developed countries.[22] 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

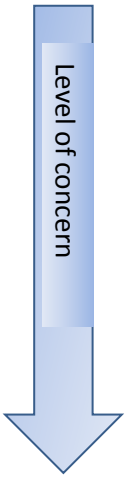
[20] See Kew O et al. Vaccine-derived polioviruses and the endgame strategy for global polio eradication. Annu Rev Microbiol. 2005; 59:587-635.
[21] WHO. Reporting and classification of vaccine-derived polioviruses. (Draft- 29 July 2015)
[22] Diop OM, Burns CC, Wassilak SG, Kew OM. Update on vaccine-derived polioviruses - worldwide, July 2012-December 2013. MMWR Morb Mortal Wkly Rep. 2014 Mar 21;63(11):242-8 http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6311a5.htm

areas with the highest risk for polio transmission.[23] With one possible exception[24], there is no evidence that iVDPV excretors will trigger cVDPV outbreaks. Therefore, the potential risk of further transmission from an iVDPV is deemed low, but still *possible*.

Based on the nature of the virus and strength of evidence of circulation, three possible scenarios emerge reflecting the risk of further transmission (see **Table 3**).

Table 3. Classifications of type 2 poliovirus transmission

Transmission risk of detected poliovirus	Evidence	Potential Risk for further transmission*
Confirmed	1.. Detection of single or multiple WPV2 infected individual(s) without documented physical exposure to a virus in a laboratory or a vaccine production facility *OR* 2. Detection of single or multiple cVDPVs	High
Probable	1. Detection of WPV2 in an ES sample *OR* 2. Detection of single VDPV2 in an ES with <15 NT changes *OR* 3. Detection of a single VDPV2-infected individual	Medium
Possible	1.Isolation of a WPV2 in an individual with documented exposure *OR* 2..Detection of a single Sabin2 isolate from an ES sample or individual *OR* 3. Detection of an iVDPV	Low



*NOTE: 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.

4. Response

If the initial investigation and risk assessment conclude that either *confirmed* or *probable* type 2 poliovirus transmission has been detected, further assessment to determine an appropriate response is required, specifically whether to recommend proceeding with immunization, and, if so, which vaccine to utilize. This decision is critical given the potential risks associated with mOPV2 use following OPV2 withdrawal and the differential impact of IPV depending on the time since withdrawal of tOPV. In general, evidence of *confirmed* transmission warrants an aggressive outbreak response. Scenarios of p*robable* transmission also require specific interventions aimed at mitigating risks for the potential spread of any type 2 poliovirus. If *possible* type 2 transmission is found, the primary response will be to continue active case investigation and intensified surveillance along with a very limited vaccination response to protect selected individuals at risk of infection. (See **Figures 3a, b, c and 4a, b, c,** pages 21-26.)

[23] Li L, Ivanova O, Triki H, et al. Poliovirus excretion among persons with primary immune deficiency disorders: summary of a seven-country study series. J Infect Dis. 2014:210 (Supl 1):S368-72.

[24] Alexander JP, et al. Transmission of imported vaccine-derived poliovirus in an under vaccinated community in Minnesota. J Infect Dis 2009; 199:391-7.

Factors influencing type and scale of response

The risk for emergence of any type 2 poliovirus following withdrawal of OPV2 is not homogenous across countries or even within large countries.

Countries exclusively using IPV

For countries which exclusively use IPV, the risk for cVDPVs (detected in either in an ES sample or an individual case) is dependent 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 demonstrates genetic features consistent with indigenous transmission vs. importations. These countries may still be at risk, albeit at a low level, for discovery of WPV2 or Sabin2 virus traced to a break 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 poliovirus may still spread to under-vaccinated sub-populations[25]. The level of concern (and associated degree of response) in these countries will thus depend on a thorough virologic and epidemiologic investigation. However, from a global perspective, detection of any type 2 poliovirus should be a cause of 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.

Countries with prior use of OPV

For countries with prior 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 of any transmission which might occur.

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

a) Time

How many months/years have elapsed between OPV2 cessation and detection of poliovirus type2?

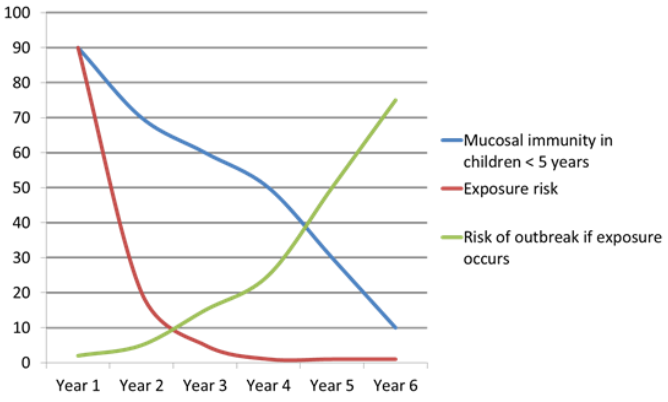


Figure 7. Risk of cVDPV over time

While dependent on the level of population immunity to transmission just prior to stopping the use of OPV2, the risk of cVDPV emergency is highest within 12 months after OPV2 cessation and subsequently decreases rapidly. However, due to the declining mucosal immunity to type 2 particularly among younger age groups, the magnitude of an outbreak will

[25] Oostvogel PM, et al. Poliomyelitis outbreak in an unvaccinated community in The Netherlands, 1992-93. Lancet. 1994 Sep 3;344(8923):665-70

rise exponentially with time elapsed since OPV2 cessation.

Based on the time elapsed, three broad phases can be identified which reflect the risk for the initial type 2 occurrence and for further transmission. While specific cutoff dates for each phase cannot be determined, extensive modelling has shown that the risk of cVDPV emergence depends on the population immunity to transmission prior to OPV2 withdrawal and that emergences associated with Sabin viruses circulating at the time of OPV2 withdrawal will most likely occur within the first 12 months following OPV2 withdrawal[26]. Note that Phase 1 (within 1 year of cessation of OPV2) has the highest risk of initial occurrence of a type 2 virus detection; however, assuming mitigation activities have taken place prior to withdrawal of tOPV, this phase should have the lowest risk of further transmission spread. Similarly, Phase 3 (4+ years since cessation of OPV2) will have the lowest risk of initial occurrence of a poliovirus type 2 virus detection, but will have the highest risk of further transmission due to waning mucosal immunity in the population.

Table 4. Phases of risk for type 2 poliovirus emergence and circulation

Phase	**Time after cessation of OPV2**	**Comment**	**Relative Risk for initial type 2 occurrence**	**Risk for further circulation**
1	Within 1 year	General population immunity remains high. Mucosal immunity absent in only a small percentage of the population	High	Low
2	2-3years	General immunity still reasonably high, but overall mucosal immunity declining and absent in new birth cohorts	Medium	Medium
3	4 or more years	Mucosal immunity declines sharply	Low	High

b) Place (country or sub-national region w/ >10 million population)

Does the country/region have a history of poliovirus transmission (WPV or cVDPV) since the year 2000? Does the affected area have clear links to high risk communities with immunity gaps?

Recent history of WPV and/or cVDPV transmission in a country or sub-national area may be indicative of environmental factors (e.g. poor sanitation and high force-of-infection) that will impact on the force of immunogenicity of OPV. Evidence of sustained transmission in an area may also indicate programmatic challenges (e.g. insecurity) which could influence the efficiency of a response and thus affect further spread of a poliovirus. The assessment should also evaluate the proximity and likelihood of exposure (e.g. population movements, transport links, etc.) to high risk communities with immunity gaps.

[26] See Thompson KM and Duintjer Tebbens RJ. Modeling the dynamics of oral poliovirus vaccine cessation. J Infect Dis. (2014) 210 (suppl 1): S475-484 and Chabot-Couture G and Lyons H. How can we reduce the risk of cVDPV emergences after OPV cessation? unpublished presentation, July 2014.

c) Characteristics of the affected population.

What are the estimated immunity levels of the population in the area where the poliovirus was detected? Does the community in which the virus was discovered have particular characteristics which may signal low immunity and/or an increased risk for transmission?

Vaccination coverage rates from both EPI and any SIAs in the area can be useful input, but this data must be analyzed in the context of any known information on the immunogenicity of OPV in order to provide an indication of 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 of further spread.

Location and population characteristics may be categorized into three general Geographic Zones which influence the risk and extent of any transmission (see **Table 5**).

Table 5. Geographic zones of risk for type 2 poliovirus transmission

Zone	Country/area and Population Characteristics	Risk for further transmission
1	Clear history of sustained WPV or reported cVDPV2 since 2000; OR affected community with other risks for low immunity or high mobility links to susceptible communities	High
2	Consistently low DTP3 coverage <80% in the previous 3 years; OR history of imported WPV or any cVDPV in the previous 3 years; OR with DTP3 coverage <90% and adjacent to affected area	High- Medium
3	DTP3 coverage consistently >80%; affected community with few risk factors for sustained transmission	Low

A final determination of the type and scale of required response depends on an overall evaluation of these multiple factors and a subjective weighting of the results from the different determinants. Not all criteria need to be met in order for the risk of transmission to be judged as high. For example, the risk may be assessed as high if the detected virus has *confirmed* transmission even though the affected area may not have had a recent history of a WPV or cVDPV outbreak.

<u>Key principles of Response</u>

- *Speed*: Modeling[27] and multiple years of experience in responding to prior outbreaks of WPV and cVDVP have demonstrated that conducting an immunization response quickly with moderate coverage will stop transmission in fewer rounds than waiting to intervene later hoping to maximize coverage through better organization. The implications are even greater in

[27] See Thompson KM, Duintjer Tebbens RJ, Pallansch MA. Evaluation of response scenarios to potential polio outbreaks using mathematical models. Risk Analysis 2006; 26(6):1541-1556. Risk Anal, 2006

responding to an emergence of type 2 poliovirus given the potential ramifications of spread. Planning, decisions, and implementation must take place on an expedited timeframe.

- *Appropriate tools* (i.e., primarily vaccine): The specific vaccine(s) to employ in the outbreak response may depend on local contextual factors, including risk zone , estimated immunity levels, and timing of the outbreak in relation to the withdrawal of tOPV. In general, mOPV2 is the vaccine of choice for response to stop type 2 poliovirus circulations, but there are specific roles for the use of inactivated polio vaccine (IPV)[28] Modeling demonstrates that a mOPV2 response sufficient to interrupt live poliovirus transmission will not create new cVDPVs within the same population[29]. Nevertheless, exportation of the OPV-related virus to other susceptible neighboring populations remains a concern unless the initial response is adequately aggressive. An inadequate response with mOPV2 also creates the potential for vaccine virus transmission. Trade-offs in risk mitigation may provide the opportunity to utilize IPV in both the short and longer term response to a type 2 outbreak. Areas where transmission is predominantly oropharyngeal may also opt to utilize IPV as an initial response vaccine.

  SAGE has already recommended the addition of one dose of IPV prior to OPV2 withdrawal in all routine immunization programs for countries using OPV-only primarily to mitigate risk of type2.[30] While modeling has shown that a single dose may have a modest impact on the probability of cVDPV emergence, a second IPV dose given in an outbreak response is expected to rapidly boost individual antibody titers.[31] A recent study has also provided strong evidence that IPV given to OPV-primed children can boost mucosal immunity and thus potentially contribute to stopping transmission.[32] However, if the population is primarily OPV-naïve, IPV alone will do very little to provide intestinal immunity and therefore has a limited role compared to a mOPV2 response in situations with primarily fecal-oral transmission.[33] Accordingly, the impact of IPV for halting transmission may be most effective in the 6-12 months post OPV2 cessation when the OPV immunity is likely to be highest.

  Vaccine availability may constrain the choice of vaccine for an outbreak response. GPEI should maintain a stockpile of mOPV2 and manufacturers should retain a rotating stockpile of IPV that can be rapidly released. However, the projected limited global supply of IPV through at least the

[28] tOPV should also be considered in areas where there is persistent transmission of WPV1 or 3.
[29] Thompson KM and Duintjer Tebbens RJ. Modeling the dynamics of oral poliovirus vaccine cessation. J Infect Dis. (2014) 210 (suppl 1): S475-484
[30] WHO. Meeting of the Strategic Advisory Group of Experts on immunization, November 2012. Weekly Epidemiologic Rec. 2013. 88,1-6. (http://www.who.int/wer/2013/wer8801.pdf)
[31] See Duintjer Tebbens RJ and Thompson KM. Modeling the potential role of inactivated poliovirus vaccine to manage the risk of oral poliovirus vaccine cessation. J Infect Dis. (2014) 210 (suppl 1): S485-497.
[32] Jafari H, et al. Efficacy of inactivated poliovirus vaccine in India. Science. August 2014; 345:922-925.
[33] O'Ryan GM, et al. Inactivated poliovirus vaccine given alone or in a sequential schedule with bivalent oral poliovirus vaccine in Chilean infants: a randomized, controlled, open-label, phase 4, non-inferiority study. www.thelancet.com/infection. Published online August 27, 2015 (http://dx.doi.org/10.1016/S1473-3099(15)00219-4)

end of 2016 may present practical limitations. Multiple studies have demonstrated the efficacy and operational feasibility of fractional dosing for IPV through intradermal administration. This delivery system should be actively considered as a mechanism to stretch limited IPV supply. [34]

Additional tools for responding to iVDPV or Sabin viruses are under development. The most common form of treatment for persons with primary immune deficiency disorders which may lead to an iVDPV is replacement therapy with intravenous immunoglobulin (IVIG). Anti-viral compounds and monoclonal antibodies have demonstrated therapeutic value in limited studies, but additional research should be urgently conducted to make these options widely available and potentially useful prevention measures[35]

- *Operational flexibility*: Local environmental, infrastructure, security, and programmatic factors will help determine the required operational approaches. Standard protocols for SIA may need to be modified to maximize efficiency and effectiveness in mitigating the risks of transmission as soon as possible. For example, short interval addition dose (SIAD) campaigns have demonstrated that intensified SIA with only 1-2 weeks or even less between rounds can still be effective.[36] Wide target age ranges and multiple mOPV response rounds may be required to ensure transmission is halted. [37] Epidemiologic and operational considerations should determine specific SIA parameters. Although an aggressive outbreak response in required, expanding age groups should not take precedence over the primary aim of effectively reaching new susceptibles with each subsequent round. [38]

Key steps

Initial response planning, including the activation of a National Emergency Response Team (ERT)[39] and designation of global/regional focal points should begin within the first day after detection of a type 2 poliovirus. The ERT should initiate planning for a possible immunization response in parallel with the investigation and rapid assessments (see **Table 2,** pages 28-29 and **Figure 1, p**age 19). However, the initiation of the response should be based on the outcome of the rapid assessment and analysis of the response determinants. The critical decision for the response, whether or not to proceed with implementation of a SIA, will be primarily driven by the immediate evidence for poliovirus type 2

[34] See Okayasu H, et al. Affordable inactivated poliovirus vaccine: strategies and progress. . J Infect Dis. (2014) 210 (suppl 1): S459-464.
[35] Puligedda RD et al. Human monoclonal antibodies that neutralize vaccine and wild-type poliovirus strains. Antiviral Res. 2014 Aug; 108:36-43. doi: 10.1016/j.antiviral.2014.05.005. Epub 2014 May 10.
[36] See GPEI. The Short Interval Additional Dose (SIAD) - An intensified campaign approach to deliver monovalent Oral Polio Vaccine (mOPV).
[37] See 2006 WHA resolution (http://www.polioeradication.org/Portals/0/Document/Resources/WHA59_1_Eradication_poliomyelitis.pdf) and GPEI. Responding to a poliovirus outbreak: Standard Operating Procedures for a new polio outbreak in a polio-free country. Geneva. February 2015
[38] See Duintjer Tbbens RJ, et al. The potential impact of expanding target age groups for polio immunization campaigns. BMC Infectious Diseases. http://www.biomedcentral.com/1471-2334/14/45.
[39] The ERT is whatever entity has been designated by the national emergency response plan to respond to a public health emergency or outbreak, usually within the Ministry of Health.

transmission and the risk/benefit analysis of introducing mOPV2 into the community. In all situations, enhanced surveillance and virologic investigations should continue as new data may dictate additional strategic actions.

There should be strict emphasis on the operational imperatives, including: rapid decision making multiple simultaneous steps, early involvement of global/regional partners, prompt preparation of appropriate budget, and accelerated planning.

Approach—type and scale of response

The highest risk for a type 2 outbreak is emergence of a VDPV during Phase 1. (See **Figure 3a,** page 21.) The usual scenario would be a cVDPV outbreak in a country with inadequate coverage of OPV prior to type 2 OPV withdrawal. In the situation of *confirmed* transmission in Geographic Zones 1 or 2, multiple rapid SIAs will be required. The first SIAD should use mOPV2 plus IPV in the primary affected area and only IPV in the adjacent risk area. Subsequent rounds should use mOPV2 alone in the primary response area. The scope of the primary response area will be situationally dependent, but in general should cover a wide geographic area up to 2 million population in the targeted age range. The size of the adjacent risk areas to vaccinate will also vary depending on the assessed risk of neighboring populations, transportation links to the affected community, etc. The response to *confirmed* transmission during Phase 1 in Geographic Zone 3 will rely on the expected background of high OPV coverage and utilize an initial SIA of only IPV in both the primary and adjacent areas. Any further evidence of transmission would be met by subsequent rounds using mOPV2.

In the situation of *probable* transmission related to a VDPV during Phase 1 (e.g. a single ES sample with<15 nucleotide changes or a single VDPV case), respond initially with a single round of IPV in both the primary response and adjacent risk areas as a mitigation measure. Any subsequent evidence of confirmed transmission warrants additional SIAs with mOPV2. (NOTE: Given the length of time often required to conduct a full genetic investigation, unless a VDPV is isolated from an individual with a known immunodeficiency, a mitigation response consistent with *probable* transmission should be initiated before a final classification is determined.)

Discovery of a WPV during phase 1 is unlikely but should be met with an aggressive response regardless of geographic zone. (See **Figure 3b,** page22.) Vaccinate with mOPV2 + IPV in the primary response area and IPV in adjacent risk areas for the first SIAD round in the situation of detecting either a WPV2 AFP case without known poliovirus exposure or detection of an individual with poliovirus infection secondary to an investigation from a positive ES sample. Follow-up SIAD rounds should use mOPV2 in the primary affected area. Respond initially to a WPV2 ES isolate without evidence of an individual excreting virus with a single SIA using IPV in both the primary and adjacent risk areas. Implement multiple rounds of mOPV2 for any subsequent evidence of type 2 transmission.

Since identification of a Sabin 2 virus in the first 4 months of Phase 1 would not be unexpected, only continued surveillance is required in this situation. If a Sabin virus is detected in the environment or isolated from an individual, prompt investigation should be undertaken in nearby laboratories or vaccine

production facilities to discover any break in containment, to test workers as possible sources of poliovirus, and to review safety protocols. (See **Figure 3c,** page23.)

The changes in the risk profile reflected in Phases 2 and 3 are primarily due to the declining population mucosal immunity. Concomitant changes in the response approach are reflected in the vaccine selection and the scale of the immunization response. Geographic zone will be less relevant and the priming effect of prior OPV use will have dissipated. For either a cVDPV or a WPV2 AFP case without know poliovirus exposure respond with mOPV2 in the primary affected area and IPV in the adjacent risk area. As in Phase 1, IPV will be the key vaccine in the scenario of *probable* transmission. (See **Figures 4a and b**—pages 24-25.)

For all phases, in the situation of *possible* type 2 transmission, no immediate wide scale vaccination response is recommended. If either an iVDPV or a WPV2 case with a known poliovirus exposure is detected, vaccinate household members and close community or work contacts with IPV. Continue investigation of any suspected case, seek rapid virologic confirmation, and sustain high level surveillance.

Decisions regarding the specific target population (including age group, number, and exact geographic scope) as well as the number of rounds will generally be dependent on specifics of the time and situation. As time progresses towards Phase 3 when risk for transmission will be highest and population immunity lowest, the age groups, minimum target population and minimum number of SIAs will all correspondingly expand. This general progression will be maintained in all Geographic Zones; however, the scope may be slightly smaller in Zone 3. General recommendations are provided in **Tables 6a, b, c** (pages 30-31) which provides a matrix utilizing the phase and zone determinations made during the rapid assessment. These recommendations in the matrix are based on prior experience gained from responding to WPV and cVDPV outbreaks during the eradication phase. However, the ERT will need to rely on their best judgment in order to balance the immediate need to stop transmission as soon as possible with the concurrent need to limit the population exposure to mOPV2 in order to minimize any risk for re-emergence of a cVDPV (Objectives 2 and 3 of the overall strategy.)

5. ***Travelers and Quarantine***

Beyond immunization, the response phase requires strict attention to enhanced surveillance in a wide geographic area regardless of the initial detection scenario. Additional steps may be required to address the risk posed by travelers or infected individuals.

In determining the appropriate local and international traveler or quarantine restrictions, public health officials will be required to address both overall strategic objective 2 (rapid cessation of poliovirus circulation) and objective 3 (limiting exposure of populations to Sabin 2 poliovirus from mOPV 2 used in the outbreak response).

In situations where a single individual has a documented exposure to poliovirus type 2 (e.g. in a laboratory or vaccine production facility), quarantine should be actively considered by the ERT. In these cases, further investigation and close surveillance of family members and/or co-workers for at least 60

days post detection will be required. Due to the high likelihood of ongoing undetected poliovirus circulation in the situations of "confirmed" or "probable" poliovirus type 2 transmissions, strict quarantine of individual polio cases will have limited impact on stopping the outbreak.

However, travel and migration patterns in and out of affected communities can have a significant impact on the risk and extent of poliovirus circulation. Drawing on national public health emergency regulations., national and/or local government officials should consider travel restrictions especially in situations where the initial transmission occurs in areas of high population density and/or active transport links to non-affected areas (either within the country or across international borders).

Even in the face of major epidemics such as Ebola in West Africa in 2014 enforcing local travel restrictions has proved problematic. In the situation of a polio outbreak, the specific boundaries of the primarily affected area should be determined by local situations taking into account epidemiologic, geographic, and population mobility factors. As noted in the risk assessment, links from the outbreak area to high risk communities with immunity gaps should influence decisions on the scope of travel restrictions and /or possible requirements for people undertaking travel in or out of an infected to receive a booster dose of IPV. Community organizers may be mobilized to engage the population in risk reduction behaviors, including vaccination and voluntarily restricting travel.

Restrictions on international travel from/to the affected area should also be considered. Such decisions will need to be coordinated among national and international authorities from WHO in accordance with national regulations and IHR (2005) Articles 30-32.[40] International traveler verification of IPV vaccination should follow guidance in the IHR (2005).

6. 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. As with any SIA, supervision and independent monitoring of immunization activities is a critical component to ensure the quality of the interventions.[41] In addition to this ongoing field monitoring, further recommended steps include:

- Assessments at *1 month & 3 months* after detection to enable changes in strategy or approach
- Six month plan for strengthening surveillance following assessments, monitored quarterly
- 'Surge' technical support maintained for > 6 months
- Full assessments of situation / risks at 6 months and 12 months *after last detection*

The concluding follow-up step is to confirm the end of outbreak by validating the absence of poliovirus type 2 in the population and the environment following the outbreak response. Transmission will not be considered closed out until a minimum of 12 months since last detection. The final assessment conducted 12 months after the last detected polio virus should be submitted by the Global Certification Committee for final verification that the outbreak has ended.

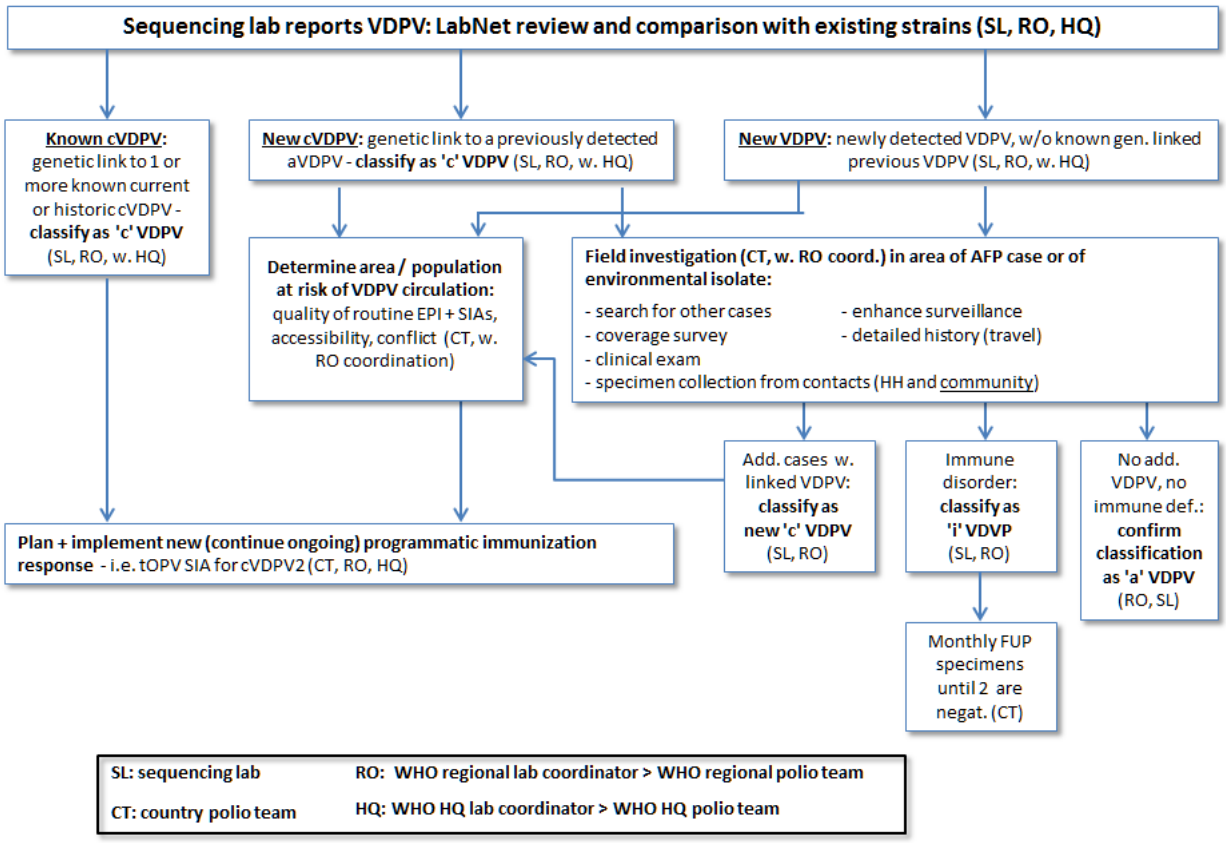
[40] See IHR (2005) http://whqlibdoc.who.int/publications/2008/9789241580410_eng.pdf?ua=1

[41] See Global Guidelines for Independent monitoring of polio SIA. http://www.polioeradication.org/Portals/0/Document/Resources/PolioEradicators/IndependentMonitoringGuidelines_20101124.pdf

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

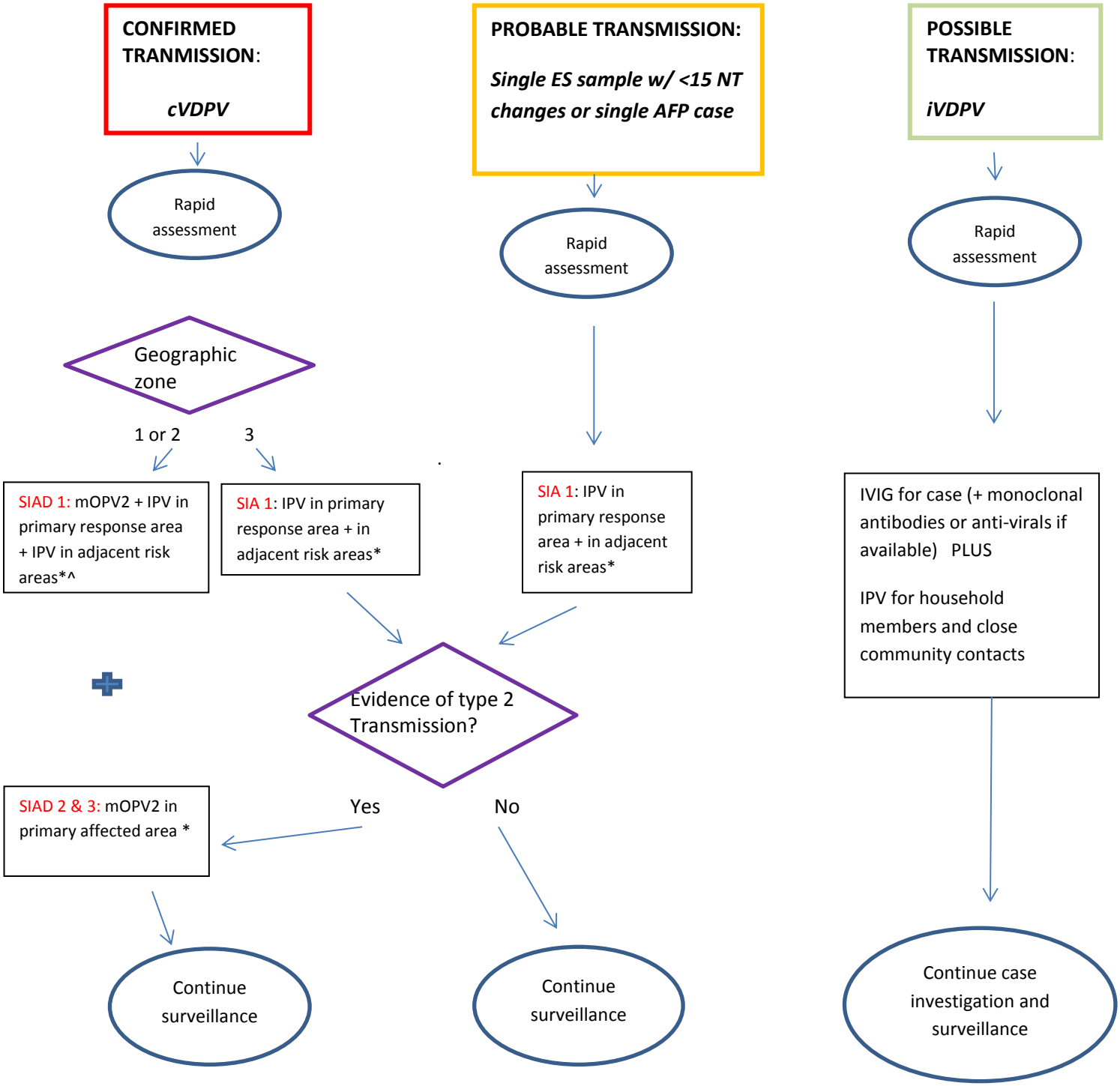
Action Steps	Days post virus detection														Primary responsibility	Comments
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Communicate information																
Notify responsible MoH and national polio certification committee																National IHR Focal Point	
Notify WHO																National IHR Focal Point	
Enhance virologic investigation																
Expedite intratypic differentiation (ITD) and sequencing																Nat'l polio lab and Regional Reference Lab	
Further investigate virus-negative AFP and environmental samples from within the last 6 months																Nat'l polio lab	
Enhance surveillance																	
Notify all reporting units and heighten active AFP surveillance																ERT	continue for 12 months
Assess AFP and environmental surveillance performance quality for the previous 12 months																ERT	
Increase frequency of environmental sampling (if ongoing)																Polio surveillance unit	
Consider initiating or expanding environmental sampling sites																MoH	
Conduct epidemiologic investigation																	
Initiate field investigation of AFP case and/or active case search in area of environmental sampling																ERT	
Review AFP reporting site records to search for possible missed cases																ERT	
Conduct Risk Assessment (and recommendation for immunization response)																	
Assess polio immunization coverage and EPI program capacity																ERT	
Assess other key factors impacting risk for local and international transmission																ERT	
Initiate response planning																	
Establish a National Emergency Response Team (ERT)																MoH	
Appoint regional and global focal points to coordinate partner inputs																WHO	
Prepare immunization response plan																ERT w/ partner support	
Determine and initiate local and/or international traveler restrictions (as required)																MoH and WHO	
Initiate immunization response (if required)																	
Release of vaccine from stockpile																WHO DG with inputs from expert panel	
Start of initial immunization SIA																	large scale SIA by day 30
Primary responsibility																	
National MoH and/or country level teams																	
Global and regional partners																	
Both																	

Figure 2: Classification of and response to reported VDPV isolates



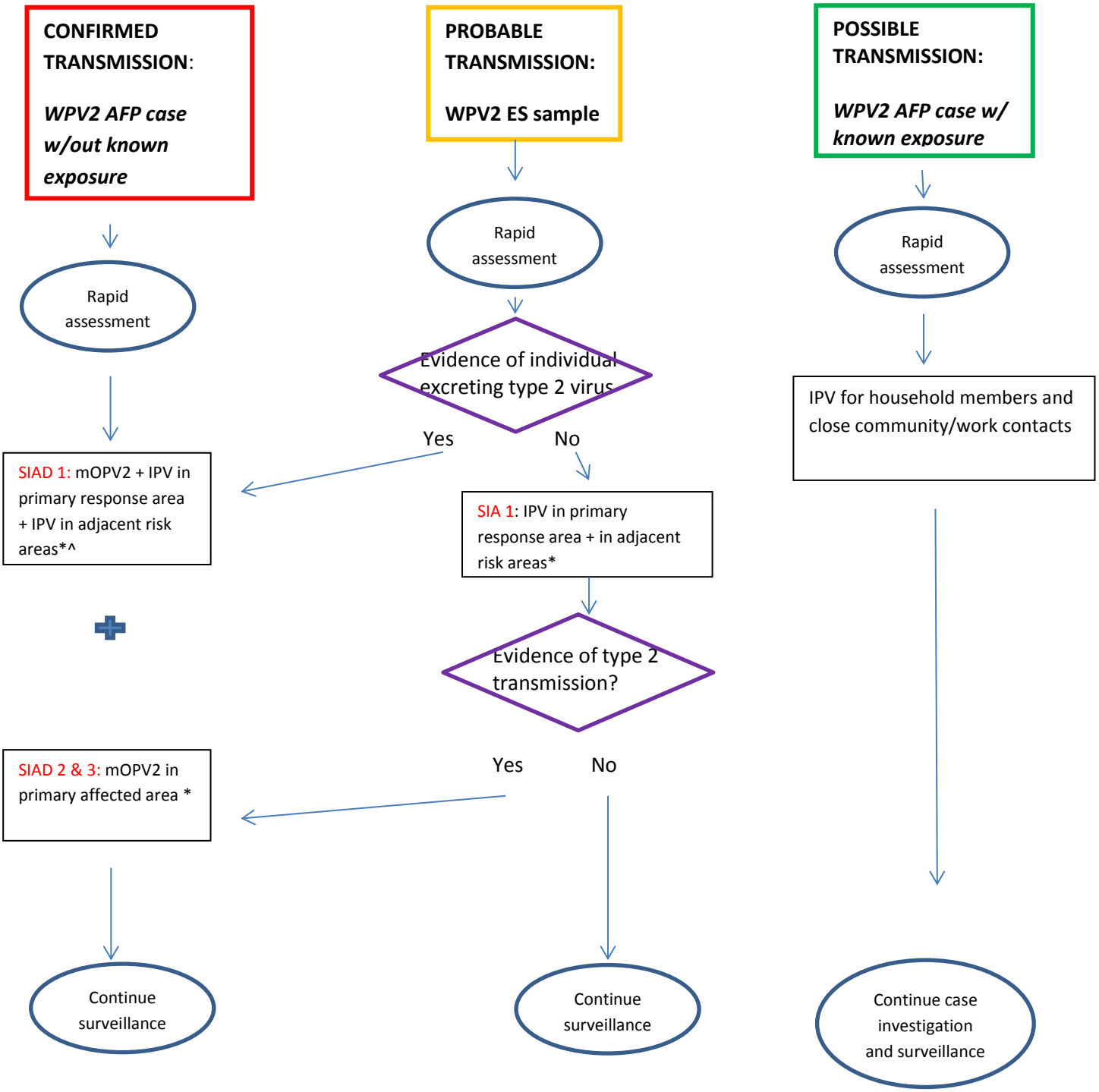
Source: WHO draft guidelines: Reporting and classification of vaccine-derived polioviruses (29 July 2015)
NOTE: The response with tOPV will be modified in the post-tOPV era. See sections on vaccine selection.

Figure 3a. General response strategies by detection scenarios of a VDPV2 isolate during Phase 1 for countries with recent use of OPV prior to type 2 OPV withdrawal



*See matrix in Table 6 for further guidelines on type and scale of SIA. ^ Given the importance of a rapid response, if operational constraints preclude using IPV within 8 days of the outbreak, response should continue with mOPV2 and IPV given in round 2.

Figure 3b. General response strategies by detection scenarios of a WPV2 isolate during Phase 1 for countries with recent use of OPV prior to type 2 OPV withdrawal



*See matrix in Table 6 for further guidelines on type and scale of SIA. ^ Given the importance of a rapid response, if operational constraints preclude using IPV within 8 days of the outbreak, response should continue with mOPV2 and IPV given in round 2.

Figure 3c. General response strategies by detection scenarios for a Sabin2 isolate during Phase 1 for countries with recent use of OPV prior to type 2 OPV withdrawal

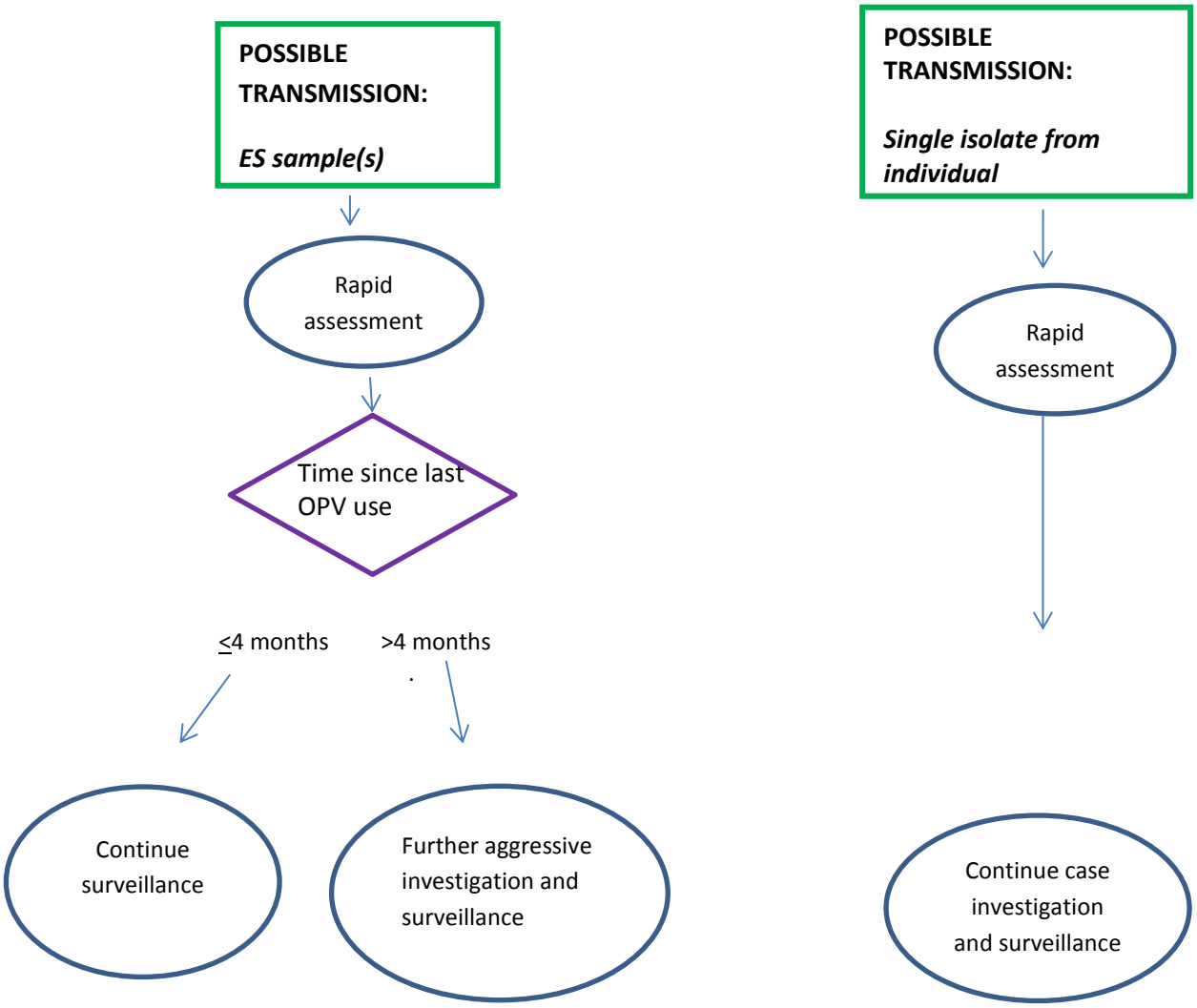
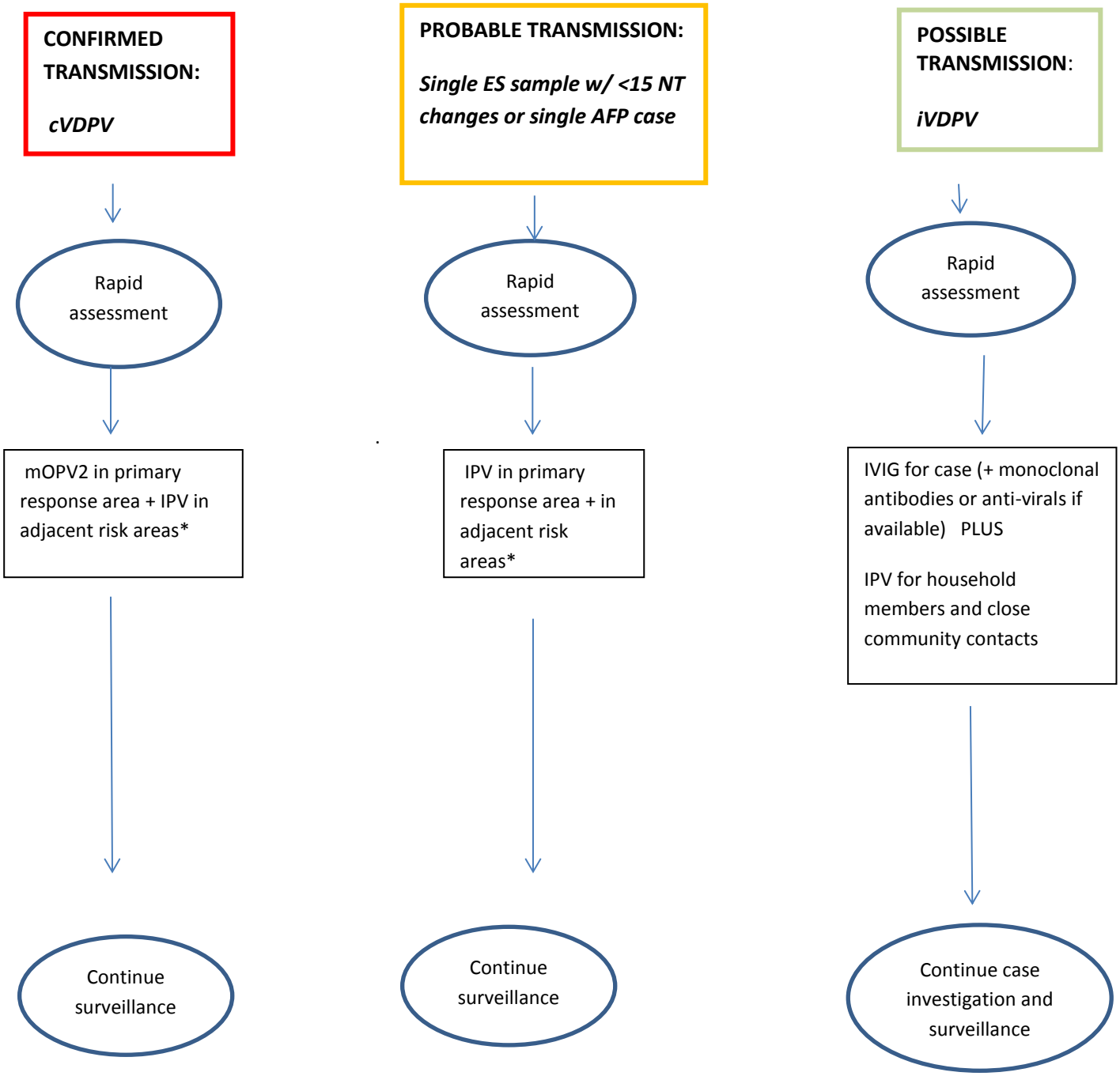
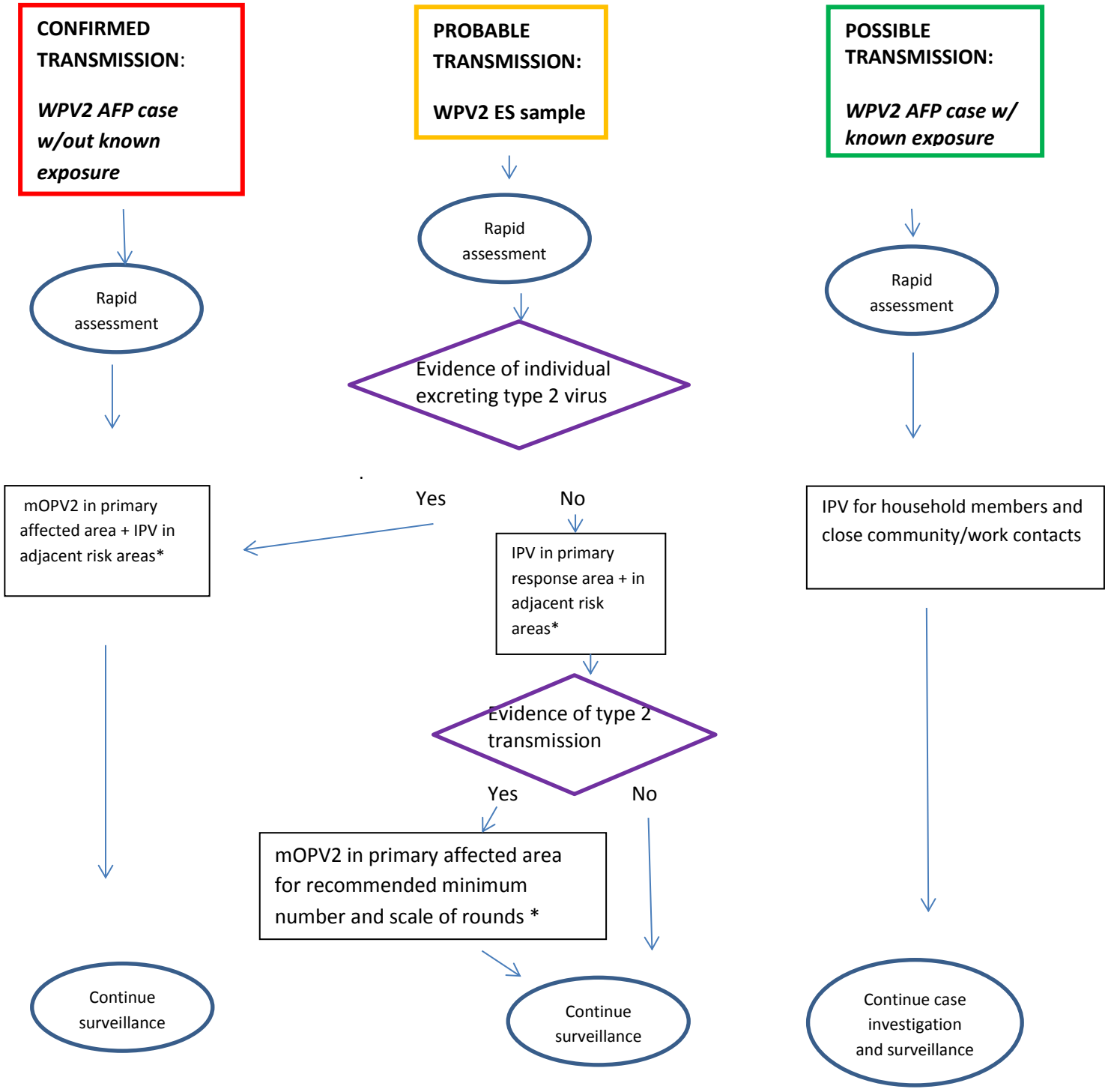


Figure 4a. General response strategies by detection scenarios for a VDPV2 isolate during Phases 2 and 3



*See matrix in Table 6 for further guidelines on type and scale of SIA

Figure4b. General response strategies by detection scenarios of a WPV2 isolate during Phases 2 and 3



*See matrix in Table 6 for further guidelines on type, number, and scale of SIA

Figure 4c. General response strategies by detection scenarios for a Sabin2 isolate during Phases 2 and 3

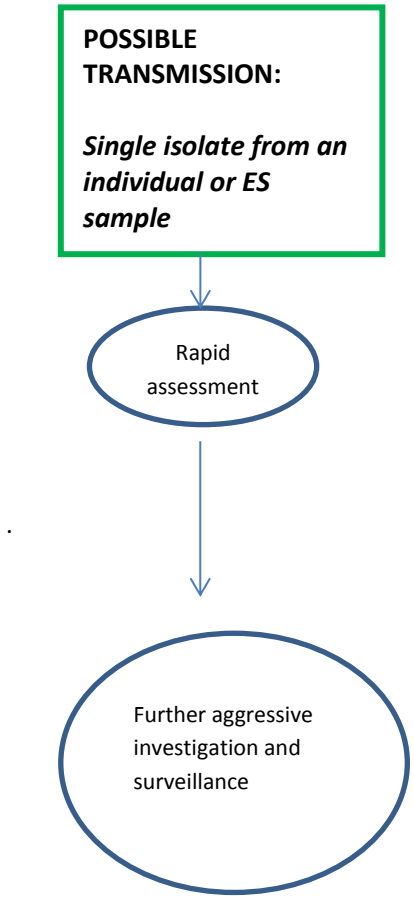


Table 1. Comparison of the standard strategies for responding to any polio outbreak and steps required post detection of a type 2 isolate post-cessation of OPV2

	Standard[42]	*Type 2 post cessation OPV2*
General approach	National responsibility with partner assistance as requested	Emphasis on operational imperatives, including: rapid decision making, multiple simultaneous steps, early involvement of global/regional partners, prompt preparation of appropriate budget, etc.
Detection	Driven by isolation of a poliovirus from a paralyzed child detected through AFP surveillance; supplemental role of environmental surveillance	AFP surveillance continues as a mainstay of surveillance, but environmental surveillance data will also be used more systematically to guide outbreak response planning and Implementation.
Notification-- Required notification as a "public health emergency"	WPV, cVDPV	WPV, cVDPV, and Sabin
Rapid Assessment		
Assessment and response plans	Initiate within 24 hours of case confirmation. Full response plans within 6-10 days.	Initiate within 24 hours of any confirmed, probable, or possible type 2 transmission. Full response plans required within 7 days of virus detection
Key assessment	Graded 1-3 according to risk of continuation	Risk classification based on evidence of transmission, time since OPV2 cessation , population characteristics, and geographic zone
Response		
Vaccine of choice	mOPV or bOPV from national stocks or procured on the global market	mOPV2 from global stockpiles, IPV from rotating stockpile
Speed of Initial immunization response	Within 14 days of outbreak confirmation (may include immediate local OPV round within 7 days)	Within 14 days of virus detection; larger scale response within 4 weeks (response dependent on receipt of stockpile vaccine.)
Target population	0-5 year olds + at least one SIA covering up to at least 10 years old; minimum of 2 million.	Expanded age groups depending on phase and geographic zone (see Table 6); minimum of 2 million
Number of rounds	5	1-5 (depending on phase and geographic zone). Balances objectives of halting transmission and limiting re-introduction of live polio vaccine.
Interval between first three rounds	preferably at 2-3 weeks intervals maximum.	Prioritize implementation speed with maximum of 2-3 weeks; short interval additional doses (SIADs) may be widely utilized
Travelers	Restrictions limited to requiring vaccination for those traveling internationally from endemic areas	Consider quarantine of polio cases and/or close community engagement to discuss local travel restrictions into/out of affected communities. Close coordination between national and international authorities for urgent implementation of international travel restrictions. Strict vaccination requirements for essential travelers.
Follow-up	Monitor response strategy at 1 month, 3 months, and quarterly up to 6 months after the last case.	Monitor response strategies at 1 and 3 months. Continue active surveillance for at least 12 months post detection of last virus.

[42] WHO. Responding to a polio outbreak: operational guidelines 2015 (draft 23 July 2015)

Table 2. Recommended key steps for initial rapid assessment and response following detection of type 2 poliovirus isolate

NOTE: Several strategic components may take place simultaneously (See Figure 1 for log frame and responsible agency)

Strategic component	**For any suspected type 2 transmission**	
	Action Step	***Time frame--trigger is detection of type 2 poliovirus (day 0)***
Communicate information[43]	✓ Notify responsible MoH and national polio certification committee	Within 24 hours
	✓ Notify WHO	Within 24 hours
Enhance virologic investigation[44]	✓ Expedite intratypic differentiation (ITD) and sequencing	Send within 24 hours; results within 10 days
	✓ Carefully review relevant laboratory indicators	Initiate within 24 hours; complete within 2 weeks
Enhance surveillance[4546]	✓ Notify all reporting units and heighten active AFP surveillance	Within 24 hours and continue for at least 12 months (see Follow-up)
	✓ Assess AFP and environmental surveillance performance quality for the previous 12 months	Within 7 days
	✓ Increase frequency of any existing environmental sampling	Within 7 days
	✓ Consider expanding or initiating environmental sampling sites	Within 3 months
Conduct epidemiologic investigation[47]	✓ Initiate field investigation of AFP case and conduct active case search in community, AFP reporting sites, and in area of environmental sampling	Initiate within24 hours and complete within 7 days
Conduct Risk Assessment [48]	✓ Assess polio immunization coverage and EPI program capacity	Initiate within 72 hours and complete within 7 days
	✓ Assess other key factors impacting risk for local	Initiate within 72 hours and complete within 7 days

[43] See IHR (2005) at http://www.who.int/ihr/publications/9789241596664/en/
[44] See "Polio Laboratory Manual" (http://whqlibdoc.who.int/hq/2004/WHO_IVB_04.10.pdf)
[45] See minimum expected surveillance standards (http://www.polioeradication.org/Dataandmonitoring/Surveillance.aspx)
[46] See "Guidelines for environmental surveillance of poliovirus circulation" (http://whqlibdoc.who.int/hq/2003/who_v&b_03.03.pdf)
[47] See "Guidelines for investigating a polio outbreak or AFP case clustering" (http://www.polioeradication.org/Portals/0/Document/Resources/PolioEradicators/6b.InvestigatingPolioOutbreakorAFPcaseClustering20110107.pdf)
[48] Major risk factors include: 1) the nature of the virus; 2) time since OPV2 withdrawal, 3) geography, 4) other population characteristics

	and international transmission	
	✓ Make recommendations for next steps, including +/- immunization response.	Initial response plan within 72 hours; more complete plan within 7 days
Initiate response planning [49][50]	✓ Establish a National Emergency Response (ERT)Team	Within 24-48 hours
	✓ GPEI appoints regional and global focal points to coordinate partner inputs	Within 24 hours
	✓ Partners provide 'surge' technical support as requested	Within -72 hours and continue for up to 6 months as needed
	✓ Prepare immunization response plan (including vaccine, target age group, geographic scope, # of rounds, etc.)	Completed and shared with all global partners within 7 days
Initiate immunization response (if required)	✓ Final decision by ERT on immunization response; if +, initiate request for mOPV2 and IPV from stockpiles	Within 7 days
	✓ Release of vaccine from stockpiles determined by DG	DG to make decision within 48 hours of request; vaccine to be released within 48 hours of approval.
	✓ Start of initial immunization SIA. May *continue for at least 3 rounds after the last detection*.	Initial response within 14 days; larger scale response within 30 days
	✓ Closely monitor SIAs	Along with SIA
Quarantine and travel restrictions	✓ Determine and initiate local and/or international traveler or quarantine restrictions	Within 24 hours for case quarantine; 72 hours for travelers
Confirm end of outbreak transmission	✓ Maintain enhanced surveillance	Continue for minimum of 12 months following last virus detection in population or ES
	✓ Analyze epidemiologic situation and evaluate status of the response	At 1 months and 3 months;
	✓ Analyze risks for further transmission and implement further mitigation steps as necessary	At 3 and 6 months after last detection

[49] See "Responding to a polio outbreak" (http://www.polioeradication.org/Portals/0/Document/Resources/PolioEradicators/1a.PolioOutbreakGuideline20110107.pdf)

[50] See various regional or country guidelines for SIA planning, .e.g. http://www.searo.who.int/india/topics/poliomyelitis/Operational_guidelines_for_Pulse_Polio_Immunization_in_India_February_2006.pdf?ua=1

Table 6a. Matrix for minimum scale of immunization response to confirmed or probable type 2 transmission—Zone 1.

	Zone 1 --Clear history of sustained WPV or reported cVDPV2 since 2000; OR affected community with other risks for low immunity or high mobility to susceptible communities			
	Minimum age group (yrs.)	*Minimum Target pop*	*Geographic scope beyond primary zone*	*Minimum # of SIA*
Phase 1- Within1 year post OPV2 withdrawal	0-5 (≥1 to cover up to at least 10 years)	2 million	Extend widely to adjacent communities	3
Phase 2—within 2-3 years	0-10	2 million		3
Phase 3—4+ years	0-15+	2-5 million		5

Table 6b. Matrix for minimum scale of immunization response to confirmed or probable type 2 transmission—Zone 2

	Zone 2-- Consistently low DTP3 coverage <80% in the previous 3 years; OR history of imported WPV or any cVDPV in the previous 3 years; OR with DTP3 coverage <90% and adjacent to affected area			
	Minimum age group (yrs.)	*Minimum Target pop*	*Geographic scope beyond primary zone*	*Minimum # of SIA*
Phase 1- Within 1 year post OPV2 withdrawal	**0-5 (>1SIA to cover up to at least 10 years)**	2million	**Extend widely to adjacent communities**	**3**
Phase 2—within 2-3 years	**0-10**	2 million		**3**
Phase 3—4+ years	**0-15+**	**2-5 million**		**5**

Table 6c. Matrix for minimum scale of immunization response to confirmed or probable type 2 transmission—Zone 3

	Zone 3-- DTP3 coverage consistently >80%; affected community with few risker factors for sustained transmission			
	Minimum age group (yrs.)	*Minimum Target pop*	*Geographic scope beyond primary zone*	*Minimum # of SIA*
Phase 1- Within 1 year post OPV2 withdrawal	**0-5 years**	0.5-1 million	**Extend widely to adjacent communities**	**1**
Phase 2—within 2-3 years	**0-5 years**	1 million		**3**
Phase 3—4+ years	**0-10 years**	**2 million**		**5**