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

(Draft version 14 October 2014)

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1 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]

[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;

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.

2 Objectives

The key objectives of this document are:

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

- Provide guidance to global 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 basic approaches and principles are similar to those currently required for investigating and responding to any polio outbreak. However, strategic actions following detection of 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**).

3 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 recommended to gauge global readiness for OPV2 cessation.[4]

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. In press

[4] See World Health Assembly. Poliomyelitis: intensification of the global eradication initiative. Report by the Secretariat. Geneva: World Health Organization, 2014 and Meeting of the Strategic Advisory Group of Experts on immunization, November 2013 – conclusions and recommendations. Weekly Epidemiological Record, 2014; 89(1):1–16.

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.

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. 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 that the country has adequate capacity to detect and respond to any type 2 poliovirus and that 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 will be reviewed by SAGE for possible endorsement by the WHA. 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 need to be complemented by additional supplies of IPV held in a rotating stockpile by manufacturers in order to provide a minimum buffer stock which can be utilized to supplement an outbreak response if necessary[5].[(See Response component below.)

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.

[5] 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; and Yen C, et al. Global Vaccine Stockpiles: a brief review and factors to consider for establishing future stockpiles. Lancet (Forthcoming).

The first two criteria are key measures which directly reflect preparations for identifying and dealing with any outbreak of type 2 poliovirus as part of the readiness steps, which must be attained prior to OPV2 cessation. The trigger for setting a definitive date for the final action will be the absence of all persistent circulating vaccine-derived type 2 polioviruses for at least six months.

4 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. Validating the absence of poliovirus type 2 in the population and the environment following the outbreak response; and
5. Using established mOPV2 [and IPV] stockpile(s) for outbreak response under a strict release protocol endorsed by the World Health Assembly (WHA).

5 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;
- 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.

6 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 the withdrawal of OPV2 includes 6 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 along several fronts.

6.1 Detection

All countries must maintain sensitive surveillance systems, including necessary laboratory capacity, in order to rapidly detect any circulating poliovirus, to uncover situations of risk so they can be investigated, and to further identify high risk areas. 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.[6] 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 acute flaccid paralysis (AFP) from diseases other than poliovirus.[7] 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 utilized increasingly 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 wild poliovirus (WPV) transmission can be sustained for over one year without being detected through AFP surveillance in areas with exclusive IPV use.[8] 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 Global Polio Eradication Initiative (GPEI) is jointly working with specific countries on a strategic expansion plan to include at least 15-20 additional sampling sites by the end of 2015.[9] Environmental surveillance 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 this environmental surveillance 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[10] 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,

[6] http://www.polioeradication.org/Dataandmonitoring/Surveillance.aspx.
[7] http://www.polioeradication.org/Dataandmonitoring/Surveillance/GlobalPolioLaboratoryNetwork.aspx
[8] 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
[9] http://www.polioeradication.org/resourcelibrary/strategyandwork.aspx
[10] 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 environmental surveillance samples. Priority should be given to developing tools which can be rapidly scaled up for use in difficult field environments.

6.2 Notification

Currently, the treaty obligations under the International Health Regulations (2005) specifically designate detection of a wild type poliovirus 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'.[11] Post cessation of OPV2 and confirmation of the elimination of cVDPV2, the interpretation of this criterion should be expanded to include detection of any poliovirus type 2 (wild, vaccine derived, or Sabin) in any sample of any provenance as a notifiable event under IHR.

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. However, these situations, as well as concerns about suboptimal surveillance, should be thoroughly investigated at the appropriate national/sub-national level.

6.3 Investigation and Risk Assessment

6.3.1 Objectives

In addition to the notification to WHO required under the IHR, discovery of any type 2 poliovirus isolate from either AFP or environmental surveillance should initiate an immediate investigation in order 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.

[11] International Health Regulations (2005)

6.3.2 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** provides additional indication of the expected steps depending on the scenarios outlined by the strength of evidence for transmission. (Further detailed guidelines for the enhanced surveillance review and required epidemiologic field investigation are outlined in recent GPEI guidelines for investigating and responding to a polio outbreak[12].)

Beyond the standard approaches to dealing with a 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** provides an overall timeline of required activities, the agency or persons with primary responsibility, and the expected time frame for completing the action.

6.3.3 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. In addition, 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.

[12] "Guidelines for investigating a polio outbreak or AFP case clustering" (http://www.polioeradication.org/Portals/0/Document/Resources/PolioEradicators/6b.InvestigatingPolioOutbreakorAFPcaseClustering20110107.pdf

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 some specific questions and approaches.

The critical outcome of the risk assessment step is to characterize the virus through addressing two key questions: *What is the nature of the virus (e.g. WPV, Sabin, or VDPV)? Is there evidence of circulation?*

Initial detection of a poliovirus isolate 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. Given the extended period since a circulating WPV2 has been detected, further emergence of this virus is remote; however, transmission could take place depending on population immunity in the affected location. Detection of a Sabin type 2 poliovirus is also unlikely. However, in the first two to three months post OPV2 cessation, discovery of a single Sabin type 2 in an environmental sample may reflect the residual excretions from the last tOPV use in routine immunization or campaigns. The research in New Zealand indicated that OPV die out following the switch to IPV only[13] (). While this detection should prompt increased vigilance through AFP and environmental surveillance, the risk for this occurrence should rapidly diminish with time.[14] 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.

The most common virus to be detected following withdrawal of OPV2 will be a VDPV. 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 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 at least two AFP cases 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 (e.g. are either clinical isolates from persons with no known immunodeficiency and no evidence of transmission, or sewage isolates whose source is unknown.

A cVDPV demonstrates already ongoing circulation in the community and represents the same public health threat as a WPV thus requiring an aggressive response.[15] In situations in which a VDPV is isolated from a single AFP case or from an apparently healthy individual, intensive investigation should be made to determine if additional cases are occurring in the community. In addition to case-finding and enhanced surveillance, the case investigation should determine whether the individual VDPV case

[13] Huang QS et al., Persistence of oral polio vaccine virus after its removal from the immunisation schedule in New Zealand. Lancet. 2005; 366(9483):394–396

[14] 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 .

[15] Kew O et al. Vaccine-derived polioviruses and the endgame strategy for global polio eradication. Annu Rev Microbiol. 2005;59:587-635.

represents a long-term carrier for poliovirus and thus evidence of an iVDPV. However, initial diagnosis of an iVDPV can require extensive follow-up and use of sophisticated molecular level testing. In case of single or multiple sequential isolates (i.e., aVDPV) from environmental sources, further molecular investigations are needed to determine whether these may be cVDPV or iVDPV. This could include full-genome sequencing, deep-sequencing of the environmental sample, other investigations and determinations. Detection of iVDPVs is rare (e.g. ~100 cases worldwide since 1961) and have predominantly been detected in developed countries.[16] However, recent studies in developing and middle income countries have demonstrated that such cases may occur more frequently than previously thought.[17] Since individuals with iVDPV infections can transmit poliovirus to others, a community immunization response may be required.

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. Possible classifications of type 2 poliovirus transmission

Transmission of detected poliovirus	Evidence	Potential Risk for further transmission*
Confirmed	detection of an infected individual –WPV or VDPV-without documented physical exposure to a virus in a laboratory or a vaccine production facility	High
Probable	detection of genetically related viruses from 2 or more environmental samples over time and space consistent with circulation in the population based on further molecular investigation of isolates (e.g. cVDPV) or detection of an iVDPV	Medium
Possible	isolation of a type 2 virus in a single environmental sample or in an individual with documented exposure[18]	Low

*NOTE: Additional factors, such as the force-of-infection, will ultimately determine the extent of further transmission and directly influence the required type and scale of response.

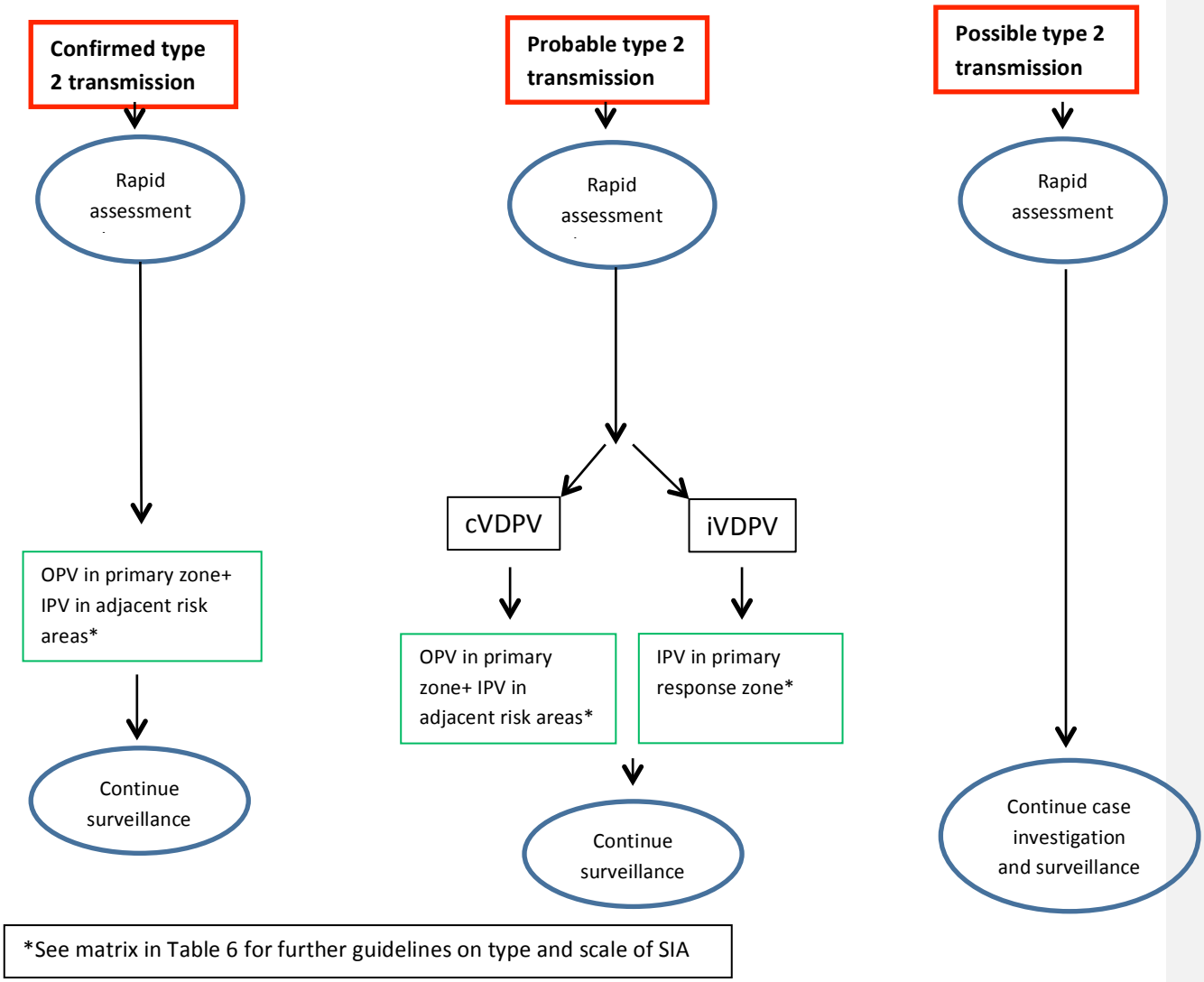
If the initial investigation and risk assessment conclude that either 'confirmed' or 'probable' type 2 poliovirus transmission has been detected, further assessment to determine an appropriate response is required, specifically whether to recommend proceeding with immunization, and, if so, which vaccine to utilize. This decision is critical given the risks associated with mOPV2 use following OPV2 withdrawal. If 'possible' type 2 transmission is found, the primary response will be to continue active case investigation and intensified surveillance (See **Figure 2**)

[16] 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

[17] 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. In press 2014.

[18] When an individual is known to be significantly exposed to the contaminated material (e.g. exposed to highly concentrated vaccine bulk in the vaccine production facility.

Figure 2. General response strategies by detection scenarios



6.4 Response

6.4.1 Factors influencing type and scale of response

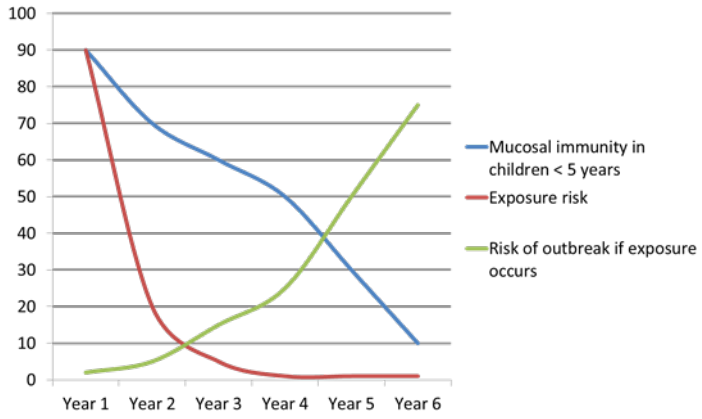
The risk for emergence of any type 2 poliovirus following withdrawal of OPV2 is not homogenous across countries or even within large countries. Two dynamically inter-related trends determine post-cessation risk of cVDPV emergence: decreasing population immunity to transmission and decreasing OPV-related virus presence[19] . 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 to consider include:

[19] See Thompson KM, Duintjer Tebbens RJ. Modeling the dynamics of oral poliovirus vaccine cessation. *J Infect Dis*. In press.

6.4.1.1 *Time*

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

Figure 3. Risk of cVDPV over time (Schematic)



While dependent on the level of population immunity to transmission just prior to stopping the use of OPV2, the risk of cVDPV emergence from Sabin viruses circulating at the time of OPV2 cessation is highest within 12 months after OPV2 cessation (although cVDPV detection will depend on the nature and quality of surveillance). Due to the declining mucosal immunity to type 2, particularly among younger age groups, the magnitude of an outbreak will rise exponentially with time elapsed since OPV2 cessation.

Based on the time elapsed, three phases can be identified which reflect the risk for the initial type 2 occurrence and for further transmission. Modelling has shown that the risk of cVDPV emergence is real depends on the population immunity to transmission prior to OPV2 withdrawal, and that any emergences associated with Sabin viruses circulating at the time of OPV2 withdrawal will most likely occur within the first 12 months following OPV2 withdrawal. Note that Phase 1 (within 2 years of cessation of OPV2) has the highest risk of initial occurrence of a type 2 virus emergence; 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 (6+ years since cessation of OPV2) will have the lowest risk of initial occurrence of a poliovirus type 2 virus emergence, because of the absence of any introductions of Sabin type 2 viruses into the population, 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 2 years	General population immunity remains high. Mucosal immunity absent in only 2 – 6% of the population.	High	Low
2	3-5 years	General immunity still reasonably high, mucosal immunity absent in 7 – 15% of the population	Medium	Medium
3	6 or more years	Mucosal immunity absent in more than 15% of the population and rising.	Low	High

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

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

Prior 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.

6.4.1.3 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 and types of vaccine used from both EPI and any SIAs in the area can be useful 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. Dose histories of children will need to consider their prior exposure to type 2 containing vaccine and should not include any mOPV or bOPV SIAs, which may complicate the analysis. In many situations, vaccination coverage may be unknown but other population characteristics (e.g. marginalized or underserved mobile, conflict-affected, history of immunization refusal, etc.) or limited use of tOPV in SIAs prior to OPV2 withdrawal in the affected community may be indicative of low immunity to type 2. Detection of poliovirus in a mobile community may be of special concern of further spread.

Location and population characteristics may be categorized into three general 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 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 analysis of the risk of further transmission (and thus the type and scale of required response) depends on an overall evaluation of the 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 (and thus in Zone 2).

6.4.2 Key principles of Response

- *Speed*: Modeling[20] 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 responding to an emergence of type 2 poliovirus given the potential ramifications for spread. Planning, decisions, and implementation must take place on an expedited timeframe.

- *Appropriate tools* (i.e., primarily vaccine): mOPV2 is the vaccine of choice for response to stop type 2 poliovirus circulations and to limit their spread. However, every effort should be made to limit the exposure to Sabin type 2 to the outbreak area (i.e., to contain both the cVPDV2 virus causing the outbreak and the mOPV2 used in response) in order to reduce the risk of emergence of new cVDPV outside of the outbreak area. Inactivated poliovirus vaccine (IPV) may have a potential role depending on the following circumstance: 1) simultaneous administration with mOPV2 to enhance the speed of immunity in poorly immunized populations and reduce viral shedding; and 2) boost immunization around the primary outbreak response zone to raise immunity levels. GPEI should maintain a stockpile of mOPV2 and manufacturers should retain a rotating stockpile of IPV that can be rapidly released.

  Additional tools for responding to iVDPV or Sabin viruses are under development. 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[21]

- *Operational flexibility*: Local environmental, infrastructure, security, and programmatic factors will help determine the required operational approaches required. 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. Wide target age ranges and multiple mOPV response rounds may be required to ensure transmission is halted.

6.4.3 Key steps

Initial response planning, including the activation of a National Emergency Response Team (ERT)[22] and designation of global/regional focal points should begin within the first day after detection of a type 2

[20] 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

[21] 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.

[22] 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.

poliovirus. The ERT should initiate planning for a possible immunization response in parallel with the investigation and rapid assessments (See **Table 2** and **Figure 1**). 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 Supplementary Immunization Activities (SIA), will be primarily driven by the immediate evidence for poliovirus type 2 transmission and the risk/benefit analysis of introducing mOPV2 into the community.

In general, if there is evidence of confirmed or probably type 2 transmission, an immunization response should proceed. However, the selection of the vaccine as well as the type and scale of response will be determined by the outcome of the risk assessment (See **Figure 2 and Table 6**). 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.

6.4.4 Approach—type and scale of response

In the situation of "confirmed transmission", the vaccine of choice to stop poliovirus circulation is mOPV2 in the primary response area and IPV in the adjacent risk areas.[23] The parameters of the primary response area will be situational dependent, but in general should cover a wide geographic area up to 1 million population. The size of the adjacent risk areas will also vary depending on the assessed risk of neighboring populations, transportation links to the affected community, etc.

In the situation of "probable transmission", if a cVDPV has been detected, respond with mOPV2 in the primary response area and IPV in the adjacent risk area as in the situation of confirmed transmission. If an iVDPV is detected, respond only with IPV in the primary response area. Continue investigation, especially enhanced surveillance in the adjacent risk areas.

The changes in the risk profile over time primarily due to the declining population mucosal immunity are reflected in the scale of the immunization response. 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 both Zone 1 and Zone 2; however, the scope may be slightly smaller in the latter scenario.

In the situation of "possible type 2 transmission", no immediate immunization response is recommended. Continue investigation of any suspected case, and seek rapid virologic confirmation. If a Sabin virus is detected in the environment, 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.

[23] Additional control measures, including additional use of IPV in the primary response area if the force of transmission is assessed as exceedingly high.

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. General recommendations are provided in **Table 6,** 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.)

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.

6.5 Travelers and Quarantine

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 transmission, 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).

In order to stop type 2 poliovirus transmission, the general recommendation is to restrict travel in and out of the outbreak response area to the largest degree possible. The specific boundaries of this affected area should be determined by local situations taking into account epidemiologic, geographic, and population mobility factors as well as practical issues of enforcement. 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. In addition to limiting population movement, public health officials should require that people undertaking essential travel in or out of an infected area must receive a booster dose of IPV.

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.[24] International traveler verification of IPV vaccination should follow guidance in the IHR (2005).

6.6 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.[25] 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 if required
- Continue OPV immunization response until at least 3 rounds after the last detection
- 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.

[24] See IHR (2005) http://whqlibdoc.who.int/publications/2008/9789241580410_eng.pdf?ua=1
[25] See Global Guidelines for Independent monitoring of polio SIA. http://www.polioeradication.org/Portals/0/Document/Resources/PolioEradicators/IndependentMonitoringGuidelines_20101124.pdf

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	*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	Expected within 2 weeks of virus detection	Required within 7 days of virus detection
Key steps		Time since OPV2 cessation is a key factor
Response		
Vaccine of choice	mOPV or bOPV from national stocks or procured on the global market	mOPV2 from global stockpiles, IPV from rotating stockpile has potential role
Speed of Initial immunization response	Within 28 days of virus detection	Within 14 days of virus detection; larger scale response within 4 weeks
Target population	Usually 0-5 years	Expanded age groups—including 0-15+ yrs and potentially to the whole population—at least for the first two rounds; minimum of 1 million
Number of rounds	Usually 3	3-5
Interval between first three rounds	4-6 weeks	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	May impose quarantine of polio cases and/or strict travel restrictions into/out of affected communities as well as for international travel. Strict vaccination requirements for essential travelers.
Follow-up	Usually monitor response strategy at 6 and 12 months	Continue active surveillance for at least 12 months post detection of last virus. Monitor response strategies at 1 and 3 months.

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																	

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	**Confirmed type 2 transmission**[26]		**Probable type 2 transmission**[27]		**Possible type 2 transmission**[28]	
	Action Step	***Time frame***	***Action Step***	***Time frame***	***Action Step***	***Time frame***
	Trigger: detection of type 2 poliovirus (Day 0)					
Notification						
Communicate information[29]	✓ Notify responsible MoH and national polio certification committee	Within 24 hours	✓ Notify responsible MoH and national polio certification committee	Within 24 hours	✓ Notify responsible MoH and national polio certification committee	Within 24 hours
	✓ Notify WHO	Within 24 hours	✓ Notify WHO	Within 24 hours	✓ Notify WHO	Within 24 hours
Rapid Assessment						
Enhance virologic investigation[30]	✓ Expedite intratypic differentiation (ITD) and sequencing	Send within 24 hours; results within 10 days	✓ Expedite intratypic differentiation (ITD) and sequencing	Send within 24 hours; results within 10 days	✓ 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	✓ Carefully review relevant laboratory indicators	Initiate within 24 hours; complete within 2 weeks	✓ Carefully review relevant laboratory indicators	Initiate within 24 hours; complete within 2 weeks
Enhance surveillance[3132]	✓ Notify all reporting units and heighten active AFP surveillance	Within 72 hours and continue for at least 12 months (see Follow-up)	✓ Notify all reporting units and heighten active AFP surveillance	Within 72 hours and continue for at least 12 months (see Follow-up)	✓ Notify all reporting units and heighten active AFP surveillance	Within 72 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	✓ Assess AFP and environmental surveillance performance quality for the previous 12 months	Within 7 days	✓ Assess AFP and environmental surveillance performance quality for the previous 12 months	Within 7 days

[26] "Detection of an infected individual without documented physical exposure to a virus in a laboratory or a vaccine production facility"
[27] "Detection of genetically related viruses from 2 or more environmental samples over time and space consistent with circulation in the population"
[28] "Isolation of a type 2 virus in a single environmental sample or in an individual with documented exposure"
[29] See IHR (2005) at http://www.who.int/ihr/publications/9789241596664/en/
[30] See "Polio Laboratory Manual" (http://whqlibdoc.who.int/hq/2004/WHO_IVB_04.10.pdf)
[31] See minimum expected surveillance standards (http://www.polioeradication.org/Dataandmonitoring/Surveillance.aspx)
[32] See "Guidelines for environmental surveillance of poliovirus circulation" (http://whqlibdoc.who.int/hq/2003/who_v&b_03.03.pdf)

	✓ Increase frequency of any existing environmental sampling	Within 7 days	✓ Increase frequency of environmental sampling	Within 7 days		
	✓ Consider expanding or initiating environmental sampling sites	Within 3 months	✓ Consider expanding environmental sampling sites	Within 3 months		
Conduct epidemiologic investigation[33]	✓ Initiate field investigation of AFP case and conduct active case search in community and AFP reporting sites	Initiate within 72 hours and complete within 7 days	✓ Initiate active case search in area of environmental sampling	Initiate within 72 hours and complete within 7 days	✓ Initiate field investigation of AFP case (including any laboratory or vaccine production site) and/or active case search in area of environmental sampling	Initiate within 72 hours and complete within 7 days
Conduct Risk Assessment [34]	✓ Assess polio immunization coverage and EPI program capacity	Initiate within 72 hours and complete within 7 days	✓ 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 and international transmission	Initiate within 72 hours and complete within 7 days	✓ Assess other key factors impacting risk for local and international transmission	Initiate within 72 hours and complete within 7 days		
	✓ Make recommendations for next steps, including +/- immunization response.	Within 7 days	✓ Make recommendations for next steps, including +/- immunization response	Within 7 days	✓ Make recommendations for next steps, including +/- immunization response	Within 7 days
Response						

[33] See "Guidelines for investigating a polio outbreak or AFP case clustering" (http://www.polioeradication.org/Portals/0/Document/Resources/PolioEradicators/6b.InvestigatingPolioOutbreakorAFPcaseClustering20110107.pdf)

[34] Major risk factors include: 1) the nature of the virus; 2) time since OPV2 withdrawal, 3) geography, 4) other population characteristics

Initiate response planning [35][36]	✓ Establish a National Emergency Response (ERT)Team	Within 24 hours	✓ Establish a National Emergency Response (ERT)Team	Within 24 hours	✓ Establish a National Emergency Response (ERT)Team	Within 24 hours
	✓ WHO appoints regional and global focal points to coordinate partner inputs	Within 24 hours	✓ WHO appoints regional and global focal points to coordinate partner inputs	Within 24 hours	✓ WHO appoints regional and global focal points to coordinate partner inputs	Within 24 hours
	✓ Partners provide 'surge' technical support as requested	Within 4 hours and continue for up to 6 months as needed	✓ Partners provide 'surge' technical support as requested	Within 4 hours and continue for up to 6 months as needed	✓ Partners provide 'surge' technical support as requested	Within 4 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	✓ 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 8 days	✓ Final decision by ERT on immunization response; if +, initiate request for mOPV2 and/or IPV from stockpile	Within 8 days		
	✓ Release of vaccine from stockpiles determined by DG	Within 48 hours of request	✓ Release of vaccine from stockpiles determined by DG	Within 48 hours of request		
	✓ Start of initial immunization SIA. *Continue for at least*	Initial response within 14 days; larger scale	✓ Start of initial immunization SIA	Initial response within 14 days; larger scale		

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

[36] 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

	3 rounds after the last detection.	response within 30 days		response within 30 days		
	✓ Closely monitor SIAs	Along with SIA	✓ Closely monitor SIAs	Along with SIA		
Traveler considerations						
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	✓ Determine and initiate local and/or international traveler restrictions	Within 72 hours	✓ Determine and initiate local and/or international traveler or quarantine restrictions	Within 24 hours for case quarantine; 72 hours for travelers
Follow-up						
Confirm end of outbreak transmission	✓ Maintain enhanced surveillance	Continue for minimum of 12 months following last virus detection in population	✓ Maintain enhanced surveillance	Continue for minimum of 12 months following last virus detection in environment	✓ Maintain enhanced surveillance	Continue for minimum of 12 months following last virus detection in population or environment
	✓ Analyze epidemiologic situation and evaluate status of the response	At 1 months and 3 months;	✓ Analyze epidemiologic situation and evaluate status of the response	At 1 months and 3 months	✓ Analyze epidemiologic situation and evaluate status of the response	At 3 months and 6 months
	✓ Analyze risks for further transmission and implement further mitigation steps as necessary	At 3 and 6 months after last detection	✓ Analyze risks for further transmission and implement further mitigation steps as necessary	At 3 and 6 months after last detection		

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

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*	*Min # of SIA*
Phase 1- Within 2 years post OPV2 with-drawal	0-10	1 million	Extend widely to adjacent communities	3
Phase 2—within 3-5 years	0-10	1 million		3
Phase 3—6+ years	0-15+	2 million		5

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***	***Min # of SIA***
Phase 1- Within 2 years post OPV2 with-drawal	**0-10**	0.5 million	**Extend widely to adjacent communities**	**3**
Phase 2—within 3-5 years	**0-10**	1 million		**3**
Phase 3—6+ years	**0-15+**	**2 million**		**5**

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 risk factors for sustained transmission			
	Minimum age group (yrs.)	***Minimum Target pop***	***Geographic scope beyond primary zone***	***Min # of SIA***
Phase 1- Within 2 years post OPV2 withdrawal	**0-5**	Situation dependent	**Extend widely to adjacent communities**	**3**
Phase 2—within 3-5 years	**0-5**			**3**
Phase 3—6+ years	**0-10**	**2 million**		**5**