

[Concept Note] Polio Environmental Surveillance Enhancement Following Detection of Vaccine-Related Type-2 Poliovirus

1. Goal and Objective:

Although acute flaccid paralysis surveillance is the gold standard of polio surveillance, supplemental surveillance methods (which includes environmental surveillance (ES)) provide additional information to assess the extent of poliovirus circulation. The purpose of this concept note is to provide a foundation for the development of a standard operating procedure for enhanced, reactive, short term ES to monitor for OPV2 virus (SL2) and VDPV2 pre- and post-outbreak response with monovalent OPV type 2 (mOPV2) or novel OPV type 2 (nOPV2). The goal is to establish standard, minimum guidelines for monitoring the presence or absence of vaccine-related virus through ES in special circumstances that can be adapted or broadened depending on the specific situation.

This document provides basic guidelines for polio ES enhancement following VDPV2 detection and is intended to serve as a basis for future development of more detailed Standard Operating Procedures or protocols as necessary. Also, the proposed ES enhancement is meant to be qualitatively and quantitatively different to previous “ES sweeps” in terms of site selection and frequency of sampling.

2. Intended Audience:

This document is intended for the various Global Polio Eradication (GPEI) working groups, to trigger the development of standard operating procedures.

3. Background and Rationale:

Following the global cessation of routine use of OPV2 in April/May 2016, immunity against infection with type 2 poliovirus is on the decline. Since cessation, new VDPV2s have emerged causing events/outbreaks due to ongoing transmission of OPV2-related viruses, suspected unauthorized use of trivalent OPV (tOPV), and use of type 2 monovalent OPV (mOPV2) for outbreak response. Risks of ongoing circulation of VDPV2s may also arise from immune-deficient, long-term VDPV excretors (iVDPV), or from circulating VDPV2 (cVDPV2) released from a laboratory. Circulation of type 2 poliovirus requires an urgent response with mOPV2 to interrupt transmission. However, a response with mOPV2 carries the risk of seeding subsequent outbreaks of vaccine-derived poliovirus (VDPV), which has been estimated to become greater over time due to the accumulation of OPV2-naïve children. Per modelling estimates, even if campaign coverage is relatively high in the response zone, connected (through geographic proximity and/or population movement) areas outside the response zone with OPV2-naïve individuals may be at risk of new VDPV transmission (particularly > 18 months after cessation). Although the overall risks of seeding new VDPV2 outbreaks may be low and difficult to specifically quantify, if such events do happen the progress to eradication will be impeded. A potential consequence of uncontrolled cVDPV2 outbreaks includes the need to restart OPV2 in routine immunization. In order to minimize this risk a new vaccine, nOPV2, is being rolled out in 2020 under a WHO emergency use listing (EUL). Studies to date have shown nOPV2 offers similar levels of protection as mOPV2, but with significantly reduced risk of seeding new outbreaks.

It is important to systematically enhance virus detection in/around areas when i) a VDPV2 is first reported to inform the response; ii) a response with mOPV2 or nOPV2 is conducted to closely monitor the impact

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of the response in interrupting VDPV2 transmission; iii) monitoring any inappropriate large-scale use of mOPV2 or nOPV2 after the official response; and iv) monitoring persistence of SL2 within the response region or in connected areas at risk.

ES for poliovirus supplements acute flaccid paralysis (AFP) surveillance and provides information on the presence and spatial scale of wild PV and VDPV transmission. It has played a critical role in monitoring cVDPV2 transmission and SL2 isolation from the mOPV2 responses in Nigeria and Pakistan post-OPV2 cessation. Furthermore, the GPEI 'standard operating procedures' for responding to a type 2 poliovirus event or outbreak state that ES should be considered to enhance surveillance following detection of type 2 poliovirus. For example, in scenarios where newly isolated VDPVs have an ambiguous definition (i.e. when a VDPV has only been isolated from a single AFP case or ES sample), ES can help determine the extent of virus circulation to inform the type of response required. Realizing the importance of ES in the post-cessation period where VDPV2 circulation and mOPV2 response carry increasing risks, the Cessation Risk Task Team (CRTT) requested the ESIWG to provide a concept note on the potential role of ES during a VDPV2 detection and response. This June 2020 version is an update of that note, originally published in May 2018, to include nOPV2.

4. Limitations of the Document:

The explicit breakdown of costs, personnel, and overall management have not been considered in detail at this stage.

Although important, the following scenarios are not covered by this document:

- I. Monitoring in hard-to-reach or security-compromised areas
- II. Monitoring in mass-gatherings
- III. Monitoring following a facility/laboratory breach

Furthermore, it will be necessary to build on the lessons learned through this approach, and extend the guidelines to detect OPV-1, and -3 with respect to bOPV cessation at a later date.

Note that this document is not a standard operating procedure.

5. General Guidelines

These guidelines should be implemented following a consensus by GPEI technical partners and national governments that ES would be appropriate and feasible for the given situation. It is envisioned that members of relevant GPEI groups, such as GPLN, OPRTT, STT, and ESIWG, in coordination with Country and Regional WHO staff and government counterparts, would be responsible for the feasibility assessment and implementation of the guidelines discussed here. The feasibility assessment should take into account both i) the ability to rapidly identify suitable sites for the collection of environmental samples; and ii) the capacity to rapidly train collectors and prepare laboratories in time (identifying existing labs that can receive additional specimens). Outside of an outbreak response, implementing i) and ii) can take months to set-up; therefore, pre-training an ES outbreak response team that could be deployed to work with local personnel in an outbreak area could be considered (i.e. this could be included within the surge

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of capacity at the start of the outbreak). Local personnel will be essential to provide local knowledge and not attract unwanted negative attention in high-risk settings.

The proposed enhanced ES is context-specific and refers to either enhancing the scope of existing ES in the country/region or initiating ES in a temporary manner for a defined time-period.

AFP surveillance will remain critical during type 2 events and outbreaks and the ES surveillance proposed here should not compromise the quality of AFP (and community) surveillance or the quality of any outbreak response campaigns.

5.1. Operational Framework for the Establishment of ES:

An overview of the decision process in determining the enhancement or deployment of ES is given in Figure 1 and is described in more detail below. The duration, frequency, and geographical scale of sampling, which are summarized by Figure 2 (with further details given in sections 5.4 and 5.5), will be determined by the type of VDPV2 isolated.

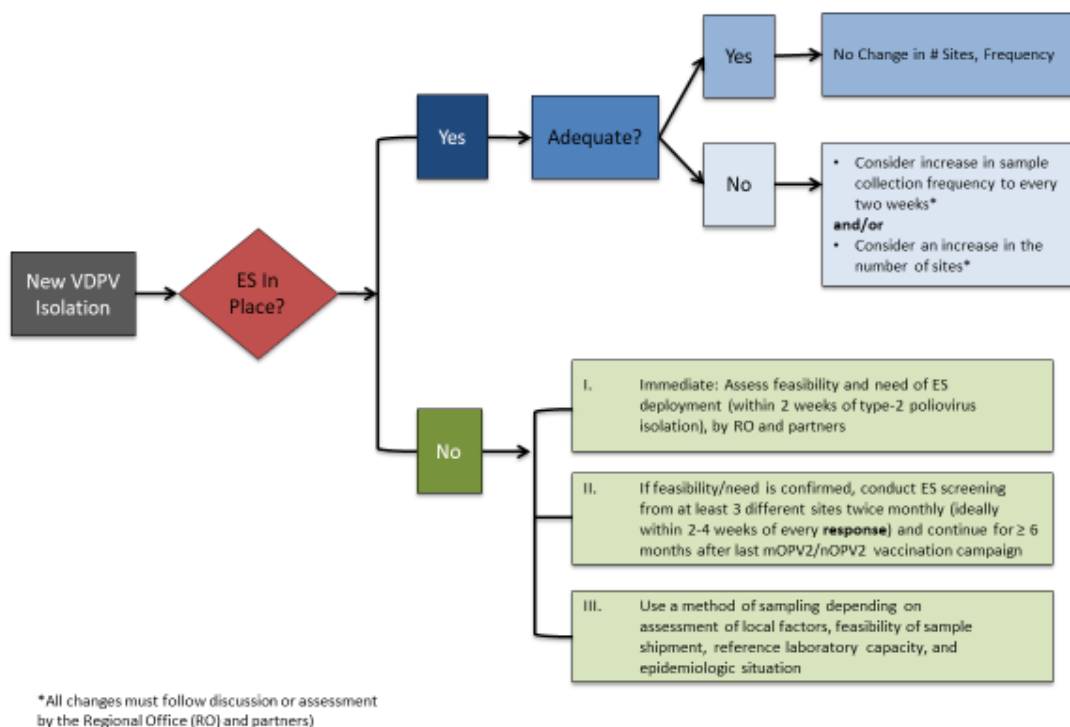
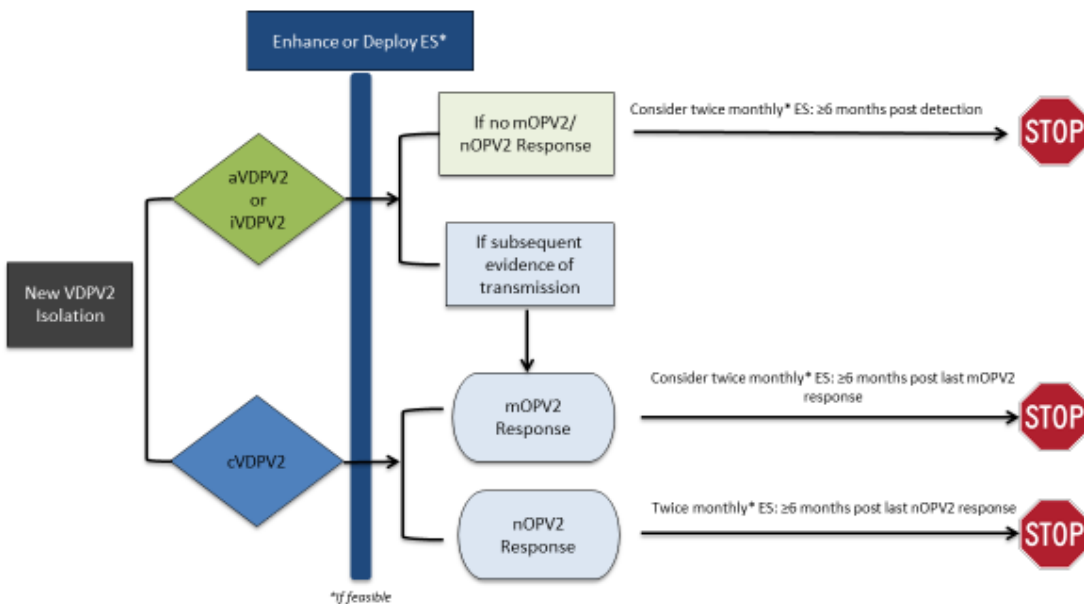


Figure 1 Overview of decision process to determine the enhancement or deployment of ES following a new VDPV isolation

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*Minimum sampling frequency is monthly; all changes must follow discussion or assessment by the Regional Office (RO) and partners)

Figure 2 Overview of timeline of enhanced environmental surveillance (ES) depending on the type of initial VDPV2 isolated

1. In areas **with** existing ES sites:
 - a. No change if existing number of sites and frequency of collection are assessed to be **adequate** (in terms of geographic scope and frequency, see sections 5.4 and 5.5) in the context of the outbreak and its response. The minimum recommended sampling frequency is monthly per ES site; however, this might not be adequate in the context of an outbreak.
 - b. If existing number of sites and frequency of collection are assessed to be **inadequate in an outbreak context**, consider:
 - i. Increasing sample collection frequency to twice monthly (or every two weeks), following discussion with Regional Office (RO) and partners
And / or,
 - ii. Increase the number of sites following assessment by the RO and partners:
 1. If the potential area of active outbreak, or the area of response is not well covered by existing ES sites. For example, the capital or major city of each administrative unit surrounding the initial detection location could be considered for sampling.
 2. If the population at risk is not adequately covered by current ES sites.

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- c. If the ES quality indicators (see section 5.2) are currently not being met, an investigation into the cause of the poor quality of sampling should be performed to identify how the quality can be improved.
- d. Any changes must be coordinated with the laboratory and regional office to ensure feasibility

Issues: 1) b (i and ii) should ideally be decided within two weeks of a VDPV isolation / outbreak confirmation; with implementation occurring 2 weeks later and / or within 2 weeks of an outbreak response vaccination campaign

2) Capacity of the reference laboratory/ies to process samples in a timely manner with optimum quality should be taken into consideration in finalizing the number of samples / sites in response to the outbreak. For reference labs that are outside the country, shipment and sample handling need to be coordinated based on any precedent or current feasibility.

2. In areas **without** existing ES:

- a. Immediate: Assess feasibility and need of ES deployment (within 2 weeks of type 2 poliovirus isolation), by RO and partners. Part of the feasibility assessment would include a site visit by an experienced ES person to identify whether potential locations to sample from exist.
- b. If feasibility/need is confirmed, conduct ES sampling from at least 3 different sites every two weeks (ideally within 2-4 weeks of every **response**) and continue for at least six months after last mOPV2 or nOPV2 vaccination campaign
- c. Use a method of sampling depending on assessment of local factors, feasibility of sample shipment, reference laboratory capacity, and epidemiologic situation.

Issues: 1) Capacity of the laboratory/ies to process samples in a timely manner with optimum quality should be taken into consideration in finalizing the number of samples / sites in response to the outbreak.

2) For countries/regions with limited/no lab capacity for prompt expansion, consideration for shipping samples or (BMFS) filters to a reference lab should be included in the initial assessment.

3) The feasibility assessment should consider the ability to train collectors, identify suitable sites, and prepare laboratories for a timely response.

The minimum recommended sampling frequency is **monthly** per ES site; any changes to the sampling frequency or adjustments in the overall ES network (i.e., opening new sites) should be discussed and coordinated with the GPEI partners in coordination with Country and Regional WHO staff and government counterparts, for feasibility.

5.2. Ensuring the Quality of ES:

- 1) **Site selection and validation:** New sites to be established on an ad-hoc basis need to be validated. Validation criteria (to be defined) should include the site selection process (standards to be followed).

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- 2) **Site quality indicators:** Sites should detect NPEV or poliovirus in at least 50% of samples in a six-month period to have a reasonable sensitivity. If virus isolation is less, possible reasons for this should be investigated and changing of sampling sites should be considered. In addition, the standard ES process indicators should be followed (e.g. $\geq 80\%$ of scheduled samples should be collected and $\geq 80\%$ of these should arrive in a lab in good condition).
- 3) **Tools:**
 - i. Existing grab sampling and standard WHO algorithm for poliovirus isolation where ES is established under the global ES expansion plan.
 - ii. In addition to the two-phase method, bag mediated filtration systems (BMFS) and other filtration methods may be considered where needed, and with necessary adaptations, if applicable (such as the “bucketing” protocol for areas with security concerns) i.e. i) in an area/country with no existing ES infrastructure; ii) where rapid, small-scale deployment is considered essential; or iii) in areas with special need such as sporadic access due to local factors, where enhanced sensitivity or collecting/testing larger volume of samples could be critical relative to other factors.

5.3. Limitations of “Ad Hoc” ES Approach

Per GPEI guidelines, ES sites are ideally placed in areas with convergent sewage networks, where sampling can be done at inlets to sewage treatment plants, pumping stations or other major sewage collectors, covering a population of approximately 100,000 to 300,000, with variations depending on the setting and epidemiological need. Given these standards and the conditions in the highest-risk areas, it is possible—even likely—that suitable sampling sites will not be available near a new VDPV2/SL2 detection. However, epidemiological or contextual need, such as high risk of undetected spread, may allow some compromise in site selection, so long as the expansion does not put unreasonable burden on the laboratory and program, and sites are closed if not useful.

Although the triggers for expanding the elective pattern of ES establishment to incorporate more reactive, “ad hoc” sampling is recognized in the current context, such an approach will have inherent limitations such as lack of standardization and comparability with a known baseline (i.e. the value of a negative result is unknown and unknowable), challenges related to prompt selection and deployment of ES sites and tools, and variance related to sensitivity dependent on timing, seasonality, and local factors.

5.4. Interpretation of results

Positive results will be informative to monitor VDPV2 circulation and the impact of a response, as outlined above. However negative results should not be interpreted as evidence for the absence of virus. In general, estimating the negative predictive value of such an approach is limited given the relatively small number of samples. Negative results should be cautiously used to avoid disturbance of established poliovirus surveillance systems.

5.5. Options for ES Following an Initial Ambiguous/Unclassified VDPV2 Isolation:

Objective(s): Monitor to determine whether there is evidence of transmission of a recently isolated aVDPV2 or iVDPV2 to inform whether a response is required. *(Although one-off VDPV2 isolations have been common in the past and have not led to outbreaks, there is a greater need, in the coming months to*

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years, to quickly determine if the virus is circulating given the increase in risk of potential transmission as the cohort of susceptible children grows. A response with mOPV2 may be more detrimental than beneficial if a VDPV2 is not circulating, hence the need to increase surveillance).

Guidelines:

- 1) **Duration:** Broadly, the enhancement or deployment plan should include monitoring for at least six months from the initial VDPV2 detection.
- 2) **Frequency:** Minimum recommended sampling frequency is monthly; where feasible and with consultation, consider sampling every two weeks
- 3) **Stopping / continuation trigger:**
 - i. No further VDPV2s are isolated throughout the six-month period from all types of surveillance and mOPV2 is not administered: stop
 - ii. Genetically linked VDPV2s are isolated from AFP cases, AFP case contact sampling, or ES samples and/or an mOPV2 or nOPV2 response is initiated: transition to protocol for ES following an outbreak response (see section 5.6).
- 4) **Geographic scope:** As a minimum the closest urban area of the first administrative level (ADM1) in which the VDPV occurred should be sampled (with a population >100,000 people). In addition, other large urban areas (>100,000 people) of adjacent ADM1s could be considered depending on the local epidemiology (note this may fall across neighboring countries). If these cities are not large enough, the closest feasible city with a population >100,000 should be considered, taking into account the feasibility to transport specimens to the lab. The 'closest' urban area should be defined by local knowledge of population movement as well as distance.

5.6. Options for ES Following Confirmation of a cVDPV2 Outbreak:

Objective(s): Monitor i) the geographical extent of cVDPV2 transmission to verify that the scale of the planned response is appropriate; ii) duration and geographic extent of SL2 excretion following mOPV2 or nOPV2 use (to confirm mOPV2/nOPV2 is used appropriately); iii) detect early evidence of the emergence and transmission of new VDPV2s that may result from mOPV2 or nOPV2 use; and iv) supplement AFP surveillance (and existing ES) to confirm interruption of the outbreak as needed.

Guidelines:

- 1) **Duration:** Broadly, the enhancement or deployment plan should (i) be started within 2-4 weeks of every response, and (ii) include monitoring for at least six months following the last use of mOPV2 or nOPV2 in the affected area.
- 2) **Frequency:** Minimum recommended sampling frequency is monthly; where feasible and with consultation with appropriate GPEI, WHO RO/CO, and national counterparts, consider sampling every two weeks until at least six months after last mOPV2 or nOPV2 use
- 3) **Stopping / continuation trigger:** Stop after at least six months from last mOPV2 or nOPV2 use
- 4) **Geographic scope:** This is difficult to pre-define and should be strategically defined, based on country context and knowledge of previous poliovirus circulation and population migration pattern. Nonetheless it should be broad in general, and consider the following:

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- a. The closest urban area (>100,000 people) within the ADM1 of outbreak case or ES site (where closest may be defined by distance or local knowledge of population movement)
- b. Major cities within the response zone and cities of ADM1 units adjacent to response zones (including areas in neighboring countries that fall within this definition). Major cities are defined as those >100,000 people.
- c. If new and genetically related cVDPV2 viruses are isolated from a geographically different location to the original outbreak location, new sites should be added given the change in the geography of transmission, if deemed feasible to implement. The location of new sites will be informed by the local knowledge of population movement.

6. Abbreviations

AFP	acute flaccid paralysis
ADM1	administrative level 1
aVDPV	ambiguous vaccine-derived poliovirus
CO	WHO country office
CRTT	Cessation Risk Task Team
cVDPV1/2/3	circulating vaccine-derived poliovirus type 1/type 2/type 3
ES	environmental surveillance
EOMG	Eradication and Outbreak Management Group
ESIWG	Environmental Surveillance and Implementation Working Group
GPEI	Global Polio Eradication Initiative
GPLN	Global Polio Laboratory Network
iVDPV	immunodeficiency-associated vaccine-derived poliovirus
NPEV	non-polio enterovirus
bOPV	bivalent OPV (contains Sabin types 1 and 3)
mOPV2	monovalent OPV (contains Sabin type 2)
nOPV2	novel OPV type 2
OPRTT	Outbreak Preparedness and Response Team
OPV	oral polio vaccine
RO	WHO regional office
SL2	sabin-like poliovirus type 2
SOP	standard operating procedure
STT	Surveillance Task Team
VDPV	vaccine-derived poliovirus