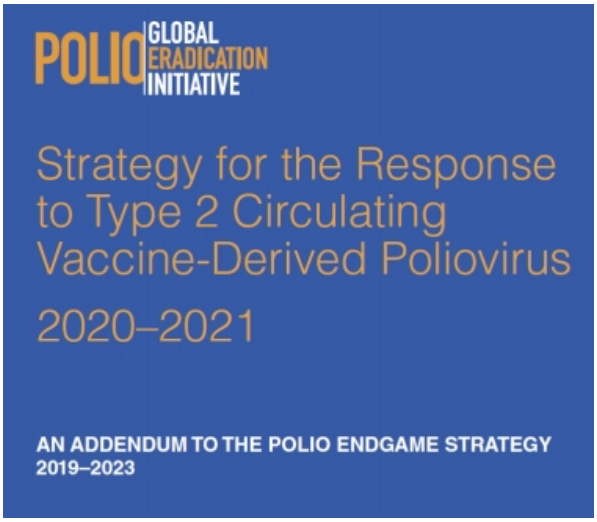
Interim Guidance on the use of Novel Oral Polio Vaccine Type 2 (nOPV2) for the response to Type 2 Circulating Vaccine-Derived Poliovirus (cVDPV2) during the Initial Use Period

(Addendum to the Standard Operating Procedures for Response to a Poliovirus Event or Outbreak, version 3. 1)

Context

Following the global certification of wild poliovirus type 2 (WPV2) eradication in 2015. the Global Polio Eradication Initiative (GPEI) planned and implemented a global withdrawal of trivalent oral polio vaccine (tOPV), replacing it with bivalent oral polio vaccine (bOPV) in April-May 2016. Termed 'the switch,' this global effort impacted both country essential immunization systems and supplementary immunization activities (SIAs). The GPEI anticipated a limited number of type 2 vaccine-derived poliovirus (VDPVs) outbreaks emerging in the post-switch period could be controlled through supplementary immunization activities (SIAs) using Sabin OPV (e.g. mOPV2). However, inconsistent pre-switch intensification efforts to boost immunity against poliovirus type 2, a global IPV shortage in 2016-2018, and an uneven quality of outbreak response activities have resulted in considerably more VDPV2 emergences and cVDPV2 outbreaks than predicted.



In early 2020, the GPEI finalized a new strategy to control circulating vaccine-derived poliovirus type 2 (cVDPV2) and address the evolving polio epidemiology. The Strategy for the Response to Type 2 Circulating Vaccine-Derived Poliovirus 2020–2021[1] is offered as an addendum to the existing Polio Endgame Strategy 2019-2023 launched in May 2019(2). The Polio Endgame Strategy 2019–2023 positioned the GPEI's current five-year strategic period in relation to the dual emergencies facing the polio eradication effort: the programme must interrupt WPV1 and stop cVDPV transmission. In consideration of the potential long-term implications for cVDPV outbreaks, the Endgame Strategy signaled the importance of a contingency plan to mitigate the risk of cVDPVs through near-term interventions, emergency protocols and policy changes. The cVDPV2 strategy entails strengthening the speed and quality of responses to cVDPV2 outbreaks, optimizing the management of available vaccine stocks and introducing an improved polio vaccine, novel oral polio vaccine type 2 (nOPV2). nOPV2 is a modified version of the existing type 2 monovalent OPV (mOPV2), that has been shown in clinical

[1] This strategy can be found at: http://polioeradication.org/wp-content/uploads/2020/04/Strategy-for-the-response-to-type-2-circulating-Vaccine-Derived-Poliovirus-20200406.pdf

trials to provide comparable protection against poliovirus while being more genetically stable and less likely to revert into a form which can cause paralysis. The vaccine's increased genetic stability means there is a reduced risk of seeding new cVDPV2 outbreaks compared to mOPV2.

Therefore, in April 2020, the Strategic Advisory Group of Experts on immunization (SAGE) endorsed the Initial Use Framework of nOPV2 under Emergency Use Listing (3,4). The initial use period is expected to last around three months after the first use of nOPV2 under the EUL.

. Purpose and scope of this document

The purpose of this Interim guidance on the use of Novel Oral Polio Vaccine type 2 (nOPV2) is to provide context and policy guidance on the use of nOPV2 in response to Type 2 Circulating Vaccine-Derived Poliovirus (cVDPV2) during the Initial Use Period. Guidance in this document is based on scientific evidence and expert consensus, with consideration of epidemiology and operational realities, including vaccine supply, vaccine acceptance and country context.

This guide is for national governments and public health decision-makers that coordinate responses to poliovirus events and outbreaks, and their global, regional and country-level partners.

This document is an addendum to the "Standard Operating Procedures: Responding to a poliovirus event or outbreak", Version 3.1' (SOPs) (5). It provides interim guidance for the use of nOPV2 in line with the 'Polio Endgame Strategy 2019 – 2023' (2) and the addendum 'Strategy for the Response to Type 2 Circulating Vaccine-Derived Poliovirus 2020 – 2021' (1).

Framework for Initial use of nOPV2 under Emergency Use Listing (4)

WHO Emergency Use Listing (EUL) would grant use of nOPV2 under specific guidance and with requirements for post-deployment monitoring. These requirements will be applicable for the duration that nOPV2 is used under EUL. As nOPV2 has not been used on a large scale or in outbreak response previously, there will be additional criteria for the initial uses of nOPV2 under EUL. These criteria will be important to ensure close monitoring for any unanticipated events and that such events can be quickly and effectively addressed to minimize risk and impact on broader immunization activities, including polio. The initial use period will begin with the first use of nOPV2 under the EUL. The initial use phase will last for approximately 3 months.

Essential criteria for first use under EUL:

1. VDPV2 detection (as per current Standard Operating Procedures).
2. Country capacity to acquire and distribute the vaccine in a timely manner (e.g. suitable country vaccine approval and import processes, non-restrictive pharmaceutical GMO legislation).
3. Country capacity to conduct post-deployment surveillance (in addition to any post-deployment monitoring requirements from EUL) including:
    a) AFP surveillance
    b) Environmental surveillance (established or the capacity to deploy before use)
    c) AEFI surveillance (and ability to determine if AEFIs are related to the vaccine)
4. Country capacity to respond to an unanticipated finding

5. A time-period of at least 12 weeks from last mOPV2 use in the area.

Rationale for the 12-week waiting period following last mOPV2 use

1. Accurately assess nOPV2 performance during outbreak response
2. Correctly attribute any safety signals/AEFIs to the corresponding vaccine
3. Evaluate nOPV2 effectiveness in stopping outbreaks and preventing cases
4. Minimize and assess the risk of recombination

Other considerations for first use under EUL:

- A time period of at least six weeks from OPV1/3 campaigns (to minimize the risk of recombination between nOPV2 and OPV1/3)
- An understanding of vaccine acceptance amongst the population in the country/area.
- Known access or security issues that would prevent adequate coverage.

Method for first use under EUL:

- The first uses under EUL should be an outbreak response with nOPV2 alone.
- There must be enough vaccine to conduct the full required number of rounds with nOPV2 alone.
- IPV use may be considered subsequently, after two initial rounds of nOPV2*.

(footnote: *The SAGE WG has recently recommended that IPV should not be used as part of outbreak response because evidence demonstrates that IPV campaigns are unlikely to reach children not reached with OPV campaigns, have limited impact on stopping transmission and high programmatic cost)

Response to cVDPV2 outbreaks – what did not change

Definitions, outbreak response standards, and protocols, including response timing and scale of campaigns required for high-quality SIAs, remain the same as detailed in the outbreak response SOPs v3.1 (5) except for the points mentioned in the next section.

Differences between the use of mOPV2 and nOPV2, during initial use period, in outbreak response – what did change

The following table summarizes the differences between the use of mOPV2 and nOPV2 in outbreak response during the nOPV2 initial use period. the details are explained in the appropriate references or the appropriate sections in this addendum

Topic	mOPV2	nOPV2 (during initial use period)
Readiness	General readiness activities for polio outbreak response for type 2 poliovirus	General readiness activities for polio outbreaks for type 2 poliovirus Special readiness activities for nOPV2 use as indicated in the Readiness Assessment tool/checklist Ref: nOPV2 vaccine deployment readiness checklist (6)

Readiness assessment	No special assessment of readiness. Any country affected by Outbreak/Event can respond	Assessment of readiness progress and readiness verification by multi-disciplinary GPEI team. Ref: section **Assessment of country readiness to use nOPV2** in this addendum
Approval of response and vaccine release	Submission of Risk Assessment to mOPV2 Advisory Group Authorization of vaccine release by the DG based of the mOPV2 Advisory Group decision	If country readiness is validated, the GPEI to review the risk assessment and proposed scope. Authorization of vaccine release by the DG based on the recommendation by the GPEI Ref: section **Authorization for the release of nOPV2** in this addendum
Timing and scale of immunization activities	A four-step vaccination strategy: The response consists of rapid response (R0), R1, R2, and a mandatory targeted mop-up round, with the option for further SIAs if justified by breakthrough isolates, cases or other evidence of ongoing transmission.	The nOPV2 Working Group has formally agreed that there should not be a rapid response round (R0) for nOPV2 responses during the initial use period All other elements of the response are the same as for mOPV2
Field use in relation to other OPV vaccines	Can be used concomitantly or in SIAD mode with bOPV. However, Co-administration of mOPV2 and bOPV is not recommended during campaigns for operational reasons	• There should be a 12-week interval between last use of mOPV2 or tOPV and first use of nOPV2 in the response area • There should be a 6-week interval between last use of OPV1/3 in campaigns and first use of nOPV2 in the response area. • There should be a 6-week interval between last use of nOPV2 and subsequent use of mOPV2 or tOPV or OPV1/3 in campaigns in the response area Ref: Framework for initial use of nOPV2 under EUL (4) and updated guidance from nOPV2 Working Group
Enhanced surveillance in response to outbreak	Is required as detailed in Chapter 8 in the SOPs v3.1	Higher requirement for surveillance enhancement and support to vaccine safety surveillance Ref: section **Enhanced AFP and environmental surveillance in response to Outbreaks** in this addendum
Vaccine safety	Standard AEFI surveillance that follows any mass immunization campaigns. No additional special activities required	In addition to standard AEFI surveillance that follow any mass immunization campaign, active surveillance for adverse events of special interest (AESI) to be carried out for 6 months following the initial use of nOPV2 in campaigns Ref: section **Vaccine Safety** in this addendum

A third option for vaccination response for cVDPV2 outbreaks is trivalent Oral Polio Vaccine (tOPV). SAGE has recommended that tOPV can be used for cVDPV2 outbreak response in subnational areas where there is co-circulation or high risk of co-circulation of cVDPV2 with cVDPV1, cVDPV3 or WPV1 in order to avoid the need to conduct dual mOPV2 and bOPV campaigns. When indicated, the usage of tOPV will follow the same procedures as mOPV2 with differences in vaccine management due to the different presentations.

Assessment of country readiness to use nOPV2

While many of the activities that countries will carry out to implement nOPV2 campaigns are the same as those required to implement an mOPV2/tOPV campaign, some additional activities are necessary because of:

- The need to meet the requirements for using the vaccine under an EUL recommendation for use
- The differences in vaccine presentation between nOPV2 and mOPV2 (50 vs 20 dose vials)
- Potential communications challenges affecting vaccine confidence

Countries that will opt for using nOPV2 for outbreak response during the initial use period will have to go through a rigorous readiness process to be approved for using nOPV2 (6,7). **It should be emphasized that countries should NOT wait for an outbreak to start the readiness process. The earlier the country starts the process, the better the chance they will be ready if an outbreak is confirmed.** Assessment of the country's readiness will be made by a multi-disciplinary GPEI team, convened by the nOPV2 working group. Membership will include the STT, OPRTT, Safety expert and regional colleagues. The nOPV2 Readiness Verification Team will assess and verify country readiness to use nOPV2, including the country's ability to meet all Emergency Use Listing (EUL) Requirements. This team will operate only until nOPV2 is licensed and pre-qualified, and the EUL requirements are no longer a pre-requisite for nOPV2 use.

Assessment of country readiness will go through two phases

- Readiness progress monitoring:
  The country will submit the readiness checklist with other supporting documents. The submission will start no later than one month after the country's decision to use nOPV2 in outbreak response. The country will continue monthly or more frequently submissions till readiness verification. The Readiness Verification Team will promptly review the submission and flag any concerns they might have on the nOPV2 preparations.
- Readiness verification:
  Once a country has completed all the actions outlined in the nOPV2 readiness checklist and has the required supporting documents available, a final readiness verification should be submitted to the Readiness Verification Team. This submission must include, in addition to the readiness checklist and supportive documents, the government authorization for importing and using nOPV2. The Readiness Verification Team will review the submission to decide if the country readiness is verified or there remain critical gaps that need to be addressed.

Authorization for the release of nOPV2

After the confirmation of a cVDPV2 outbreak, the country team would initiate the process of developing a detailed risk assessment with the support of the regional team and the Outbreak Preparedness and Response Task Team (OPRTT). The risk assessment should be finalized within 72 hours of outbreak confirmation and should outline options and vaccine requests as part of the proposed outbreak response activity. **Countries can save critical time by starting the investigation and developing the Risk Assessment following the detection of any type 2 poliovirus from any source without waiting for the sequencing results. This is particularly important in any area that has not used mOPV2/tOPV2 in the previous four months**.

Within 48 hours of the submission of the risk assessment, GPEI will review the vaccine request and response plan and risk assessment prepared by the requesting country and through the Director of the WHO Polio Department, advise the WHO Director General on the request and their recommendation. Thereafter, nOPV2 can be released to a country that has completed Readiness Verification.

In the event a country's readiness to use nOPV2 is not yet verified by the time the Risk Assessment is submitted for review, the country should be considered for mOPV2 use through the existing mechanism.

Vaccine management

Vaccine management is integral to ensuring a high-quality vaccination campaign and is of paramount importance at all levels and at all stages of the outbreak response. The movement of any vaccine used in outbreak response must be monitored. All vaccine received, distributed, and administered must be recorded. All vials will be returned to safe disposal sites (used, partially used, unused, vials discarded due to vaccine vial monitor changes or contamination).

For all mOPV2 or nOPV2 campaigns, it is of critical importance that every vial and dose of unused vaccine is accounted for and withdrawn to central storage in a safe and secure manner. Reporting on the status of vaccine used, retrieved and in storage is required after every SIA. All lost and missing vials must be reported (8,9).

Vaccine safety

To date, the safety of nOPV2 has been evaluated through phase 1 and phase 2 clinical trials. It has been well tolerated among adults, young children, and infants with no indication of any increase in general safety risk compared to mOPV2. There have also been no serious adverse events that have been identified to be causally related to vaccination with nOPV2. Still, countries will benefit from enhanced nOPV2 safety monitoring processes that will facilitate rapid identification and response to safety signals should they arise. In times of public health crises, such as during cVDPV outbreaks, enhanced vaccine safety surveillance processes can effectively and efficiently provide high quality data for public health decision-making in the setting of limited data from clinical trials, as well as timely response to the public about potential vaccine safety concerns.

Active surveillance for a focused list of adverse events of special interest (AESI) during the initial phase of use is an important complement to AFP and AEFI surveillance systems because it can assist with generating safety signals for complex conditions that may warrant timely further investigation to ensure public trust in the immunization program. For vaccine safety active AESI surveillance will take place for 6 months after the initial use of nOPV2 in campaigns. A national crisis communication

plan for nOPV2 must also foresee and mitigate the scenario of the potential AESI related to nOPV2 within 6 months of introduction.

Depending on the strength of the country's AFP surveillance infrastructure, AFP surveillance officers may be ideally positioned to fulfill the role of the AESI Surveillance Officers (SOs). If so, a process must be undertaken to integrate AESI surveillance into AFP surveillance, as well as separate processes to ensure AESI get identified, reported, investigated, and causally assessed (10). Alternately, if a country does not have a strong active AFP surveillance system, then a stand-alone AESI system, with dedicated AESI SOs can be established for the initial use period. The country may determine whether these SOs are managed by the AEFI surveillance system or another group.

Enhancing AFP and environmental surveillance in response to the outbreak

Enhancing AFP and environmental surveillance as well as AESI surveillance are essential elements of the readiness process for using nOPV2. These activities are detailed in **Implementation of nOPV2 for cVDPV2 outbreak response: Technical guidance for countries** (7) and **nOPV2 vaccine deployment readiness checklist (6)**. In addition, some activities will be added as part of the response to CVDPV2 outbreak. The following table summarizes some of the main activities expected to be implemented as part of the outbreak response using nOPV2.

Summary of field surveillance related activities in outbreak response using nOPV2 during the initial use period

Topic	Activity/Element	Description	Timeline
AFP Surveillance	Carry out retrospective AFP/AESI case search in all priority sites where nOPV2 was used, one month after first nOPV2 campaign	One-time retrospective case search one month after the first campaign reviewing previous 6-months	One month after the first nOPV2 SIAs round
	Systematic contact sampling of all AFP cases for 6 months after nOPV2 use	Systematic contact sampling of all AFP cases – 2 contacts per case	For the duration of nOPV2 use until 6 months after the last nOPV2 SIA round for campaigns during the initial use period only.
	Collect vaccination coverage data from age-matched, randomly selected community members around AFP VDPV2 cases	Collect additional data.	Implementation around any VDPV case for the duration of the EUL period
ES	Collect ES samples twice per month for 6 months after nOPV2 use (then monthly for additional 6 months)	Increased sampling frequency	Twice a month ES sampling for 6 months after last nOPV2 use for initial use countries

Support to Safety	Carry out active AESI surveillance with the support of the AFP network and possibly AESI retrospective case search	Active AESI surveillance is a complement to AEFI and aims to detect signals; the retrospective AESI search can be combined with the AFP retrospective case search (see above)	Active AESI surveillance is implemented for the duration of nOPV2 use and at least for 3 months following the last nOPV2 use Retrospective case search is a one-off activity one month after the first round of nOPV2 SIAs

More information and details are included in the ***Polio Field and Laboratory Surveillance requirements in the context of nOPV2 use (11)***

References

1. Global Polio Eradication Initiative. Strategy for the Response to Type 2 Circulating Vaccine-Derived Poliovirus 2020 – 2021: An Addendum to the polio Endgame Strategy 2019 – 2023. Geneva: World Health Organization: 2020 (http://polioeradication.org/wp-content/uploads/2020/04/Strategy-for-the-response-to-type-2-circulating-Vaccine-Derived-Poliovirus-20200406.pdf, accessed 15 September 2020)
2. Global Polio Eradication Initiative. Polio Endgame Strategy 2019 – 2023: Eradication, integration, certification and containment. Geneva: World Health Organization; 2019 (http://polioeradication.org/wp-content/uploads/2019/06/english-polio-endgame-strategy.pdf, accessed 15 September 2020)
3. Global Polio Eradication Initiative. Meeting of the Strategic Advisory Group of Experts on Immunization, 31 March–1 April 2020: Conclusions and Recommendations. Geneva: World Health Organization; 2020 (https://apps.who.int/iris/bitstream/handle/10665/332218/WER9522-eng-fre.pdf, accessed 15 September 2020)
4. Global Polio Eradication Initiative. Framework for initial use of nOPV2 under EUL. 2020. Geneva: World Health Organization; 2020 (http://polioeradication.org/wp-content/uploads/2020/04/GPEI-framework-for-use-of-nopv2-20200430.pdf, accessed 15 September 2020).
5. Global Polio Eradication Initiative. Standard Operating Procedures Responding to a poliovirus event or outbreak: Version 3.1. Geneva: World Health Organization; 2020 (http://polioeradication.org/tools-and-library/field-resources-for-polio-eradicators/gpei-tools-protocols-and-guidelines/, accessed 15 September 2020)
6. Global Polio Eradication Initiative. nOPV2 vaccine deployment readiness checklist. Geneva: World Health Organization; 2020 (http://polioeradication.org/wp-content/uploads/2020/08/nOPV2-Vaccine-Deployment-Readiness-Checklist-July-2020-FINAL.xlsx, accessed 15 September 2020)
7. Global Polio Eradication Initiative. Implementation of nOPV2 for cVDPV2 outbreak response: Technical guidance for countries. Geneva: World Health Organization; 2020 (https://apps.who.int/iris/bitstream/handle/10665/333520/9789240008588-eng.pdf , accessed 15 September 2020)
8. Global Polio Eradication Initiative. Technical Guidance for mOPV2 vaccine management, monitoring, removal and validation. Geneva: World Health Organization; 2020 (http://polioeradication.org/wp-content/uploads/2020/05/mOPV2-Technical-Guidance-20200525.pdf, accessed 27 September 2020)
9. Global Polio Eradication Initiative. Technical Guidance for nOPV2 vaccine management, monitoring, removal and validation. Geneva: World Health Organization; 2020 - draft
10. Global Polio Eradication Initiative. Guide to Surveillance for Adverse Events of Special Interest (AESI) during novel Oral Polio Vaccine type 2 (nOPV2) Introduction. Geneva: World Health Organization; 2020 - draft
11. Global Polio Eradication Initiative. Polio Field and Laboratory Surveillance requirements in the context of nOPV2 use. Geneva: World Health Organization; 2020 - draft