

**IMPLEMENTATION OF NOVEL
ORAL POLIO VACCINE TYPE 2
(nOPV2) FOR CIRCULATING
VACCINE-DERIVED POLIOVIRUS
TYPE 2 (cVDPV2) OUTBREAK
RESPONSE:**

**TECHNICAL GUIDANCE FOR COUNTRIES
December 2020 Version**



**IMPLEMENTATION OF NOVEL
ORAL POLIO VACCINE TYPE 2
(nOPV2) FOR CIRCULATING
VACCINE-DERIVED POLIOVIRUS
TYPE2 (cVDPV2) OUTBREAK
RESPONSE:**

**TECHNICAL GUIDANCE FOR COUNTRIES
December 2020 Version**

Contents

Acronyms and abbreviations	4
Introduction	5
Section 1: Rationale for using nOPV2 in cVDPV2 Outbreak Response	5
A new strategy for responding to cVDPV2 outbreaks	5
Scientific Research	6
Plans for vaccine rollout.....	7
The initial use period	7
Beyond the initial use period	8
Section 2: Preparing for nOPV2 use at the country level.....	10
Initiating the process: Key Steps and Resources for Consideration by National Immunization and Regulatory Decision-Makers.....	10
Engaging with the GPEI.....	11
Completing the nOPV2 Vaccine Deployment Readiness Checklist.....	11
Additional context on the requirements	12
More on nOPV2 monitoring and reporting	12
Country workplan.....	13
Timing and deadlines: Readiness tracking and verification	13
Outbreak detection and the decision to use nOPV2	14
Next Steps.....	14
Annex	15
Documentation Required for Readiness Verification	15
Table: Scientific Publications on nOPV2	17
nOPV2 Vaccine Deployment Readiness Checklist.....	18

Acronyms and abbreviations

ACSM Advocacy, communications, and social mobilization

AEFI Adverse event following immunization

AESI Adverse event of special interest

AFP Acute flaccid paralysis

bOPV Bivalent oral polio vaccine (containing OPV1 and OPV3)

C4D Communication for development

CCL&VM Cold chain, logistics and vaccine management

CDC US Centers for Disease Control and Prevention

cVDPV Circulating vaccine-derived poliovirus

cVDPV2 Circulating vaccine-derived poliovirus type 2

EPI Expanded Programme on Immunization

ES Environmental surveillance

EUL Emergency Use Listing

EVM Effective vaccine management

GPEI Global Polio Eradication Initiative

IPV Inactivated polio vaccine

ITD Intratypic differentiation

mOPV1 Monovalent oral polio vaccine type 1

mOPV2 Monovalent oral polio vaccine type 2

mOPV3 Monovalent oral polio vaccine type 3

NIBSC UK National Institute for Biological Standards and Control

NITAG National Immunization Technical Advisory Group

nOPV2 Novel oral polio vaccine type 2

NPAFP Non-polio acute flaccid paralysis

OPV Oral polio vaccine

OPV1 Oral polio vaccine type 1

OPV2 Oral polio vaccine type 2

OPV3 Oral polio vaccine type 3

PDM Post-deployment monitoring requirements

PHEIC Public Health Emergency of International Concern

SAGE Strategic Advisory Group of Experts on Immunization

SIA Supplementary immunization activity

SOP Standard operating procedure

STT Surveillance task team

UNICEF United Nations Children's Fund

VDPV2 Vaccine-derived poliovirus type 2

VVM Vaccine vial monitor

WHO World Health Organization

Introduction

Facilitating effective country-level decision-making on nOPV2 use

In 2020, the Global Polio Eradication Initiative (GPEI) launched a new strategy for circulating vaccine-derived poliovirus type 2 (cVDPV2) outbreak response as part of the Polio Eradication & Endgame Strategy. Included in this strategy is the implementation of a new tool for cVDPV2 outbreak response: novel oral polio vaccine type 2 (nOPV2), the next-generation version of the existing oral polio vaccine (OPV) type 2 (OPV2). Now that the vaccine has received its WHO Emergency Use Listing (EUL) recommendation for use, nOPV2 is anticipated to be available for use by January 2021.

Because the vaccine is being introduced under an EUL recommendation for use, implementing nOPV2 in outbreak response will require some additional mandatory preparation, including a national decision to use the vaccine and the authorization of its importation and use by the relevant regulatory authorities. Use of nOPV2 will also require some additional monitoring of activities during and after vaccination campaigns. It is therefore critical for any country interested in using nOPV2 to begin planning well in advance.

This document aims to support country-level decision-makers in preparing for nOPV2 implementation under an EUL recommendation for use and is specifically intended for those who will be involved in selecting nOPV2 for cVDPV2 outbreak response and preparing for its use. This includes but is not limited to: Expanded Programme on Immunization (EPI) managers, National Immunization Technical Advisory Groups (NITAGs) or other national immunization bodies that provide technical recommendations for vaccine introduction, appropriate actors in the national health and finance ministries, and relevant regulatory authorities at the country level. The document outlines core elements of the planning process to implement the vaccine and serves as a companion document to the GPEI nOPV2 Vaccine Deployment Readiness Checklist, featured in the Annex. The Annex also details the nOPV2 readiness verification process as well as and scientific publications that are relevant to nOPV2 implementation.

This resource is being updated so that decision-makers have access to the most up-to-date guidance. The next update is currently planned to take place after the conclusion of the initial use period. This version replaces the first (July 2020) edition.¹

Section 1: Rationale for using nOPV2 in cVDPV2 Outbreak Response

A new strategy for responding to cVDPV2 outbreaks

Circulating vaccine-derived poliovirus (cVDPV) events and outbreaks can emerge when the weakened strain of the poliovirus contained in the OPV circulates in under-immunized populations for a long period of time. If not enough children are immunized against polio, the weakened vaccine virus can pass between individuals and, over time, genetically revert into a form that can cause paralysis. In recent years, an increase in cVDPV type 2 (cVDPV2) outbreaks has posed a major challenge to eradication efforts.

To better address existing cVDPV2 transmission and help prevent future outbreaks, the GPEI has finalized a strategy for the control of cVDPV2. The Strategy for the Response to Type 2 Circulating Vaccine-Derived Poliovirus 2020-2021 is an addendum to the Polio Endgame Strategy 2019-2023 that was launched in May 2019. The strategy provides a plan to mitigate the risk of cVDPV and involves the following core elements:

- Strengthening the speed and quality of responses to cVDPV2 outbreaks
- Optimizing the management of available vaccine stocks
- Implementing nOPV2, an improved version of the existing monovalent oral polio vaccine type 2

¹ The first edition of the document is available online for historical reference, at <https://apps.who.int/iris/handle/10665/333520>.

- (mOPV2), for cVDPV2 outbreak response
- Creating an enabling environment for sustained vaccine uptake and trust in the programme.²

The implementation of nOPV2 is therefore one of the key elements of the GPEI's strategy for successfully responding to cVDPV2 outbreaks.

nOPV2 AT A GLANCE

SAFETY: Data to date indicate that the safety profile is similar to mOPV2, but with decreased risk of reverting to a form that could cause paralysis in areas with low immunization coverage.

PRESENTATION: It will come in 50-dose vials. The liquid will be similar in colour to mOPV2. Like mOPV2, the vaccine will also feature a vaccine vial monitor type 2 (VVM2).

ADMINISTRATION: Individuals receive two drops in the mouth.

USE: While it is under EUL, nOPV2 will be used in outbreak response only (like mOPV2), not in routine immunization or in preventive campaigns. Specific guidance for nOPV2 use is provided through updated GPEI standard operating procedures (SOPs) for outbreak response.

Scientific Research

nOPV2 is a modified version of the existing OPV2 vaccine (also known as the Sabin OPV type 2 vaccine, or mOPV2) that provides comparable protection against poliovirus type 2. The vaccine is more genetically stable than OPV2, which makes it less likely to revert into a form that could cause paralysis in areas where children have not been sufficiently immunized. Development on nOPV2 started in 2011, and the first in-human clinical trial with nOPV2 was conducted in 2017 at the University of Antwerp, in Belgium. Data from this phase I study were published in *The Lancet* in 2019.³ Two phase II trials are now complete, and the analysis of these data shows promising results for both the effectiveness and safety of the vaccine.

Data from the clinical studies⁴ show nOPV2 to be well tolerated in adults, young children, and infants, with a similar safety profile compared to mOPV2. No serious adverse events have been identified that are considered to be related to vaccination with nOPV2. Immunogenicity of nOPV2 was also found to be non-inferior to mOPV2 in infants, which means that it is expected to be as effective in preventing paralytic disease as the current vaccine. Most importantly, it was established that nOPV2 is significantly more genetically stable and therefore less likely to revert to neurovirulence compared to mOPV2. Collectively, the clinical trials provide solid evidence of the safety and effectiveness of the vaccine, and accelerated clinical development of nOPV2 was endorsed by the WHO Strategic Advisory Group of Experts on Immunization (SAGE) in October 2019.⁵ **Relevant scientific publications on nOPV2, as well as the nOPV2 clinical development summary, which provides a concise summary of the scientific data, are located on the nOPV2 web page of the GPEI website (<http://polioeradication.org/nOPV2>).**

² More background is provided in the GPEI programme strategy documents. Global Polio Eradication Initiative. Polio Endgame Strategy 2019–2023. Geneva: World Health Organization; 2020 (<http://polioeradication.org/wp-content/uploads/2019/06/english-polio-endgame-strategy.pdf>, accessed 25 May 2020). See also: Global Polio Eradication Initiative. Strategy for the Response to Type 2 Circulating Vaccine-Derived Poliovirus, 2020–2021. 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 25 May 2020).

³ Van Damme P, De Coster I, Bandyopadhyay A, Revets H, Withanage K, De Smedt P et al. The safety and immunogenicity of two novel live attenuated monovalent (serotype 2) oral poliovirus vaccines in healthy adults: a double-blind, single-centre phase 1 study. *Lancet*. 2019; 394(10193):148–158. doi:10.1016/S0140-6736(19)31279-6.

⁴ Please refer to the nOPV2 publications table, featured in the Annex.

⁵ World Health Organization. Weekly Epidemiol Rec. 22 November 2019; 94(47):541–560 (<https://www.who.int/wer/2019/wer9447/en/>, accessed 25 May 2020).

Plans for vaccine rollout

nOPV2 is being introduced for outbreak response through the WHO EUL procedure.⁶ The EUL (Emergency Use Listing) procedure is a regulatory pathway that is available for use in Public Health Emergencies of International Concern (PHEIC) such as polio, so that vaccines and medicines can be made available as soon as possible in these emergency circumstances. The EUL assessment process involves the rigorous examination of all available data on the product by the WHO Vaccines Prequalification (PQ) Team and a team of independent experts.

The EUL assessment process has concluded and a recommendation for the use of the vaccine has been officially granted by the WHO PQ team.⁷ Additionally, the manufacturer of nOPV2, PT BioFarma, is ensuring that vaccine supply will be available and ready for shipment by the end of 2020. This means that outbreak response with nOPV2 can take place as early as January 2021.

The initial use period

What is the initial use period? The initial use period refers to the period of time spanning the first uses of nOPV2 in outbreak response, when additional criteria for monitoring the vaccine's safety and effectiveness are in place. The GPEI established a set of essential criteria for the initial uses of nOPV2, which have been endorsed by the SAGE to ensure ability to conduct close monitoring of vaccine performance.⁸ Given that cVDPV2 outbreaks disproportionately affect areas with weaker healthcare systems and inaccessible areas, the enhanced monitoring outlined in the initial use framework is essential to detect any unanticipated events and be able to respond to these quickly and effectively to minimize risk and impact on broader immunization activities. The initial use period under an EUL will also present an opportunity to collect additional data and conduct operational studies to inform our understanding of how to best utilize nOPV2.

How long will the initial use period last? The initial use period will conclude upon a thorough review of the following:

- That there are no safety red flags seen during nOPV2 field use. This assessment will be based on the advice and recommendations of the SAGE⁹ and the newly established nOPV2 Subcommittee of the Global Advisory Committee on Vaccine Safety (GACVS)
- Supporting data on nOPV2's continuing genetic stability, as determined by the newly established Genetic Characterization Subgroup of the GPEI nOPV2 Working Group

Because the conclusion of the initial use period depends primarily on the amount and quality of data available to analyse, the primary factor in the length of the initial use period is not a set length of time, but rather the amount of doses administered in the outbreak responses and the data collected. The initial use period is therefore expected to last at least 3-6 months. This is why any country interested in using nOPV2 in the first half of 2021 should begin preparing for nOPV2 use now – and should anticipate needing to meet the initial use criteria.

What are the criteria for the use of nOPV2 during the initial use period? The criteria for the initial use of nOPV2 are listed in Table 1:

⁶ Roadmap for assessment of nOPV2 manufactured by PT BioFarma under the EUL procedure. Geneva: World Health Organization; 2020 (<https://www.who.int/medicines/news/2020/roadmap-assessment-nOPV2.pdf?ua=1>, accessed 25 May 2020). See also: Emergency Use Listing Procedure Version 9, January 2020. Geneva: World Health Organization; 2020 (https://extranet.who.int/prequal/sites/default/files/documents/EUL_Procedure_Jan2020.pdf, accessed 25 May 2020).

⁷ World Health Organization. Recommendation for an Emergency Use Listing (EUL) of novel Oral Polio Vaccine Type 2 (nOPV2) submitted by PT BioFarma (Persero). Geneva: World Health Organization, 2020 (https://extranet.who.int/pqweb/sites/default/files/documents/nOPV2_EUL_recommendation_0.pdf, accessed 3 December 2020). For additional product information on nOPV2, please consult:

<https://extranet.who.int/pqweb/vaccines/polio-vaccine-novel-oral-nopv-monovalent-type-2>

⁸ World Health Organization. Weekly Epidem Rec. 29 May 2020; 95(22):241-256 (<https://www.who.int/wer/2020/wer9522/en>, accessed 30 May 2020). See also: Global Polio Eradication Initiative. Framework for initial use of nOPV2 under EUL. 2020 (<http://polioeradication.org/wp-content/uploads/2020/12/Framework-for-Initial-Use-of-nOPV2-20201202.pdf>, accessed 3 December 2020).

⁹ SAGE has endorsed in principle that nOPV2 becomes the vaccine of choice for cVDPV2 outbreak response after review of the initial use period is completed and all requirements are met. Weekly Epidem Rec. 27 Nov 2020; 95(48):585-608 (<https://apps.who.int/iris/bitstream/handle/10665/337100/WER9548-eng-fre.pdf?ua=1>, accessed 7 December 2020).

Table 1. Criteria and additional considerations for nOPV2 use during the initial use period

Essential Criteria for the nOPV2 Initial Use Period	
<ul style="list-style-type: none"> The detection of vaccine-derived poliovirus type 2 (VDPV2) (as per GPEI standard operating procedures) The capacity to acquire/distribute vaccine in a timely manner (e.g. suitable country vaccine approval/ importation processes) The capacity to respond to unanticipated findings 	<ul style="list-style-type: none"> The capacity to conduct post-deployment surveillance (acute flaccid paralysis (AFP) surveillance, environmental surveillance (ES), adverse event following immunization (AEFI) surveillance) A waiting period of 12 weeks after the last mOPV2 use in the area
Additional Considerations for nOPV2 Use in Outbreak Response	
<ul style="list-style-type: none"> A waiting period of six weeks after bOPV outbreak response campaigns (to minimize the risk of recombination between nOPV2 and mOPV1/mOPV3) 	<ul style="list-style-type: none"> Access or security issues Vaccine acceptance
Rationale for the 12-Week Waiting Period Following mOPV2 Use	
<ul style="list-style-type: none"> Accurately assess nOPV2 performance during outbreak response Correctly attribute any safety signals/AEFIs to the corresponding vaccine Evaluate nOPV2 effectiveness in stopping outbreaks and preventing cases Minimize and assess the risk of recombination¹⁰ 12 weeks was chosen to balance the need for a time interval to evaluate safety and effectiveness against feasibility given existing mOPV2 use, particularly on the African continent. This time period will be re-evaluated following the initial use period. 	

Beyond the initial use period

Once sufficient data is generated to support vaccine safety, the requirement to meet initial use criteria will be lifted based on a recommendation by the SAGE, and nOPV2 use will continue under the EUL. The ultimate goal is to achieve licensure and WHO prequalification of nOPV2, which is expected to occur in 2023. Countries would still need to meet the EUL requirements for safety and surveillance monitoring, also referred to as post-deployment monitoring (PDM) requirements, until the vaccine is fully licensed.¹¹

Table 2 provides a high-level overview of the timelines and requirements that can be anticipated for the use of nOPV2 under an EUL recommendation for use. The country-level activities that need to be implemented to meet these requirements are described in Section 2.

¹⁰ Recombination with other viruses, which can lead to reversion, cannot be ruled out; however, the modifications made to the vaccine have made reversion much less likely in comparison to mOPV2.

¹¹ All post-deployment monitoring requirements are fully detailed in documents including the Risk Management and Pharmacovigilance Plan (RMPVP), which was created by nOPV2's manufacturer, PT BioFarma, in conjunction with the GPEI. The relevant requirements that pertain to country implementation are included in the nOPV2 Vaccine Deployment Readiness Checklist and the Additional Technical Guidance Documents, which are listed in the Annex.

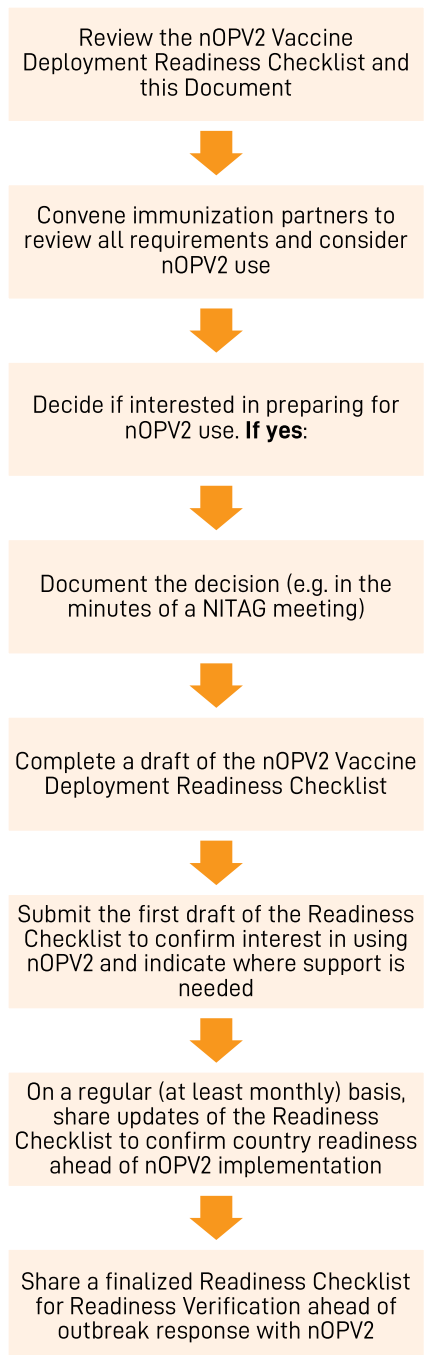
Table 2. Process overview and timeline: nOPV2 rollout under an EUL recommendation for use

	Initial use period following the initial EUL recommendation for use	Continued use of nOPV2 under EUL	nOPV2 receives WHO prequalification (end of EUL recommendation and listing period)
Timing	The first outbreak responses with nOPV2 under an EUL recommendation for use	Following the conclusion of the Initial Use Period and review of the data generated, SAGE will be asked to endorse wider use of nOPV2 under the EUL recommendation through 2022	To be determined, but not before 2023. Some necessary activities (e.g. studies) have been delayed due to COVID-19
Applicable criteria	<p>Essential criteria for initial use</p> <p>Safety and surveillance monitoring requirements following vaccine deployment (sometimes called post-deployment monitoring, or PDM requirements), which are required for use of the vaccine under EUL (note that these may evolve over time, based on data and learnings)</p>	Safety and surveillance monitoring requirements following vaccine deployment (sometimes called post-deployment monitoring, or PDM requirements), which are required for use of the vaccine under EUL (note that these may evolve over time, based on data and learnings)	Standard conditions of vaccine use; no specific requirements are foreseen
Country-level implementation considerations	<p>Rapidly approving the importation and use of nOPV2 under an EUL recommendation for use</p> <p>Setting/scaling up surveillance systems, particularly safety surveillance systems, to meet the EUL requirements</p> <p>Preparing cold-chain and logistics systems to accommodate nOPV2</p> <p>Establishing communications plans, including crisis communications plans, to support nOPV2 implementation</p> <p>Training staff and front-line workers on nOPV2 implementation</p> <p>Additional surveillance and safety monitoring activities to meet the essential criteria for initial use</p>	<p>Rapidly approving the importation and use of nOPV2 under an EUL recommendation for use</p> <p>Setting/scaling up surveillance systems, particularly safety surveillance systems, to meet the EUL requirements</p> <p>Preparing cold-chain and logistics systems to accommodate nOPV2</p> <p>Establishing communications plans, including crisis communications plans, to support nOPV2 implementation</p> <p>Training staff and front-line workers on nOPV2 implementation</p>	Standard conditions for vaccine use, informed by lessons learned from the implementation of nOPV2 under the EUL recommendation for use

Section 2: Preparing for nOPV2 use at the country level

This section outlines the country-level decision-making and preparation process for the potential use of nOPV2 for cVDPV2 outbreak response. It describes the activities involved in addressing implementation considerations and preparing for nOPV2 use.

Figure 1. Overview of the national nOPV2 decision-making and implementation process



Which countries should prepare for nOPV2 use?

Because outbreaks often occur with little warning and because the requirements for using nOPV2 under EUL take time to implement, particularly during the initial use period, all countries at risk of a cVDPV2 outbreak are encouraged to start planning for nOPV2 implementation as soon as possible.

Countries considered at high risk for cVDPV2 are:

- Countries with VDPV2 detections in the past 6 months through AFP surveillance or ES
- Countries that have had a cVDPV2 detection in the past 6-12 months
- Countries that border countries that meet the above criteria.

Other countries in regions where cVDPV2 has been detected that do not meet these criteria but would like to be prepared for a possible VDPV2 detection and subsequent response with nOPV2 may also wish to start preparations now.

Initiating the process: Key Steps and Resources for Consideration by National Immunization and Regulatory Decision-Makers

The first step in the decision-making process is to convene the relevant national immunization partners (i.e., a NITAG, or other immunization technical group, EPI managers and representatives, and policy-makers from the ministries of health and finance) to review this document and other key resources on nOPV2, consider the requirements for implementation, and ultimately decide whether to begin planning for nOPV2 use.¹² Alignment of the NRA or relevant national regulatory body for the importation, use and monitoring of nOPV2 is also essential for implementation. Engagement with regulatory authorities should take place as soon as possible because national regulatory approval processes can take time.

¹² Countries are also encouraged to visit the NITAG Resource Centre (<https://www.nitag-resource.org>), which

The Key Resources for these national groups to review and consider are listed below and can be found at www.polioeradication.org/nOPV2:

- [This technical guidance document and the nOPV2 vaccine deployment readiness checklist](#)
- [The scientific research and data on nOPV2](#), which includes scientific publications on nOPV2 as well as the nOPV2 clinical development summary. The publications are featured in the Scientific Research and data section of the nOPV2 web page of the GPEI website. An updated relevant publications list as of the time of this writing is also provided in the Annex of this document.
- [The SAGE and WHO Executive Board Recommendations on nOPV2](#), also featured in their own section of the nOPV2 web page
- [The official WHO Vaccine Prequalification Team recommendation and assessment report on nOPV2](#), which details the WHO PQ team's assessment of the vaccine and rationale for the EUL recommendation
- [Strategy for the Response to Type 2 Circulating Vaccine-Derived Poliovirus 2020–2021](#), which explains the GPEI's overall strategy for addressing cVDPV and includes more information on risk-benefit analysis and contingency planning
- [The nOPV2 Regulatory Considerations Document](#), an internal document which describes how the WHO PQ team will coordinate with the GPEI and with country regulatory authorities to facilitate the introduction of nOPV2. It also describes the roles and responsibilities of different stakeholders as well as the use of AVAREF as a platform for the development of recommendations of the candidate vaccine for its authorization for emergency use in the target countries. The document is available through each WHO Regional Office.

Engaging with the GPEI

Engaging with the GPEI will enable decision-makers to better understand the global and regional planning that is underway for nOPV2 implementation as well as the GPEI resources available to support nOPV2 implementation in countries. Because of their role in coordinating nOPV2 implementation and in developing regional implementation strategies, countries are encouraged to engage with both WHO and UNICEF regional offices, in addition to their country-level offices. To help facilitate engagement with the GPEI and overall coordination throughout the readiness process, countries interested in preparing for nOPV2 use are encouraged to designate a **national nOPV2 focal point**.

Completing the nOPV2 Vaccine Deployment Readiness Checklist

Many of the activities that countries will carry out to implement nOPV2 campaigns are the same as those required to conduct an mOPV2 campaign. However, some additional activities are required, given the requirements for implementation under an EUL recommendation for use and given the differences in nOPV2's presentation (e.g. vial size). This is why the Readiness Checklist was created: **to outline the special EUL requirements and help countries track progress towards the requirements and overall nOPV2 preparedness**. The Readiness Checklist applies to all countries interested in using nOPV2 under EUL at any point, and countries can begin completing items on the checklist as soon as they are ready to start preparing for possible nOPV2 use.

Each checklist item has a corresponding category and number (e.g. A1, D3) for easy reference, but items can be completed in any order. The checklist is part of an Excel document that also contains an introductory tab and four tabs with additional considerations pertaining to four categories: safety; surveillance; advocacy, communications and social mobilization (ACSM); and cold chain, logistics and vaccine management (CCL&VM).

Table 3. Snapshot of the nOPV2 Vaccine Deployment Readiness Checklist

Category	Additional Technical Guidance Documents (available on the nOPV2 web page and/or through WHO/UNICEF regional offices)	Ref. Number	Requirement	Req. for using nOPV2 under EUL <i>All countries to complete</i>	Additional req. for initial use period <i>Only required during the initial use period</i>	Date completed	Status update for incomplete items and/or any additional information/details (include date of update)
Environmental Surveillance	Polio Field and Laboratory Surveillance requirements in the context of nOPV2 use	E1	The country has at least one functional ES site in areas where nOPV2 will be used (i.e. enterovirus detection rate of $\geq 50\%$)		<input type="checkbox"/>		
		E2	A plan has been developed to collect ES samples twice per month for 6 months after nOPV2 use		<input type="checkbox"/>		

- The “additional technical guidance documents” column lists any additional documents related to the category which are important for countries to consult as part of their implementation planning. These documents provide more explicit implementation details and/or instructions on implementing the requirements and working with the GPEI to complete any necessary reporting requirements. A list of these documents, with hyperlinks, is also provided on the nOPV2 web page.
- Activities in the column entitled “Requirements for using nOPV2 under EUL” must be completed by any country planning to use nOPV2 at any point when the vaccine is under an EUL recommendation for use.
- Activities in the “Additional requirements for initial use period” column must be completed if the country is implementing nOPV2 during the initial use period under an EUL recommendation for use. The activities in this column must be completed in addition to, not instead of, the activities in the “Requirements for using nOPV2 under EUL” column.
- The additional considerations tabs for cold chain logistics and vaccine management, surveillance, safety monitoring, and ACSM provide additional context, in the form of specific questions and indicators, that will help countries identify gaps and develop concrete plans for completing the readiness requirements. Addressing each consideration is not required but can help ensure optimal preparedness for nOPV2 implementation. Countries are encouraged to analyse and discuss the considerations and implement those that are feasible and appropriate.

Additional context on the requirements

The checklist requirements are specifically related to nOPV2's implementation under an EUL recommendation for use. **The requirements for AFP surveillance, environmental surveillance, and safety monitoring (categories D, E and F) include PDM requirements. These are especially critical to maintaining nOPV2's EUL authorization and eventually completing the submission for licensure and WHO prequalification of nOPV2.** There are also additional requirements in these categories that pertain exclusively to the initial use period; these requirements are essential to assessing the vaccine's safety and/or effectiveness and moving out of the initial use period.

More on nOPV2 monitoring and reporting

While the focus of this document is nOPV2 readiness, countries and the GPEI will need to work together, in conjunction with nOPV2's manufacturer, to report on all PDM requirements. These reporting requirements are detailed in:

- **The additional technical guidance documents** now featured in column B of the checklist (where appropriate)
- **Additional GPEI guidance documents, training tools and activities** that pertain to specific technical areas. These additional documents pertain less to individual countries and their readiness and more to particular working groups and reporting activities at the global level. They are therefore not referenced within the checklist or this guidance document. However, these documents will be discussed with countries as necessary and appropriate throughout the

implementation process.

Country workplan

Another important tool to help determine feasible and appropriate activities is the country workplan. Following a review of the requirements and an assessment of the country's current capacity to meet them, a workplan should be developed to capture the activities that the country will need to carry out to meet the requirements. The items should then be costed out and a plan should be developed to identify and allocate both the financial and human resources that will be needed. Because each country's context is different, each workplan will be different, which is why countries should develop their own individual plans and discuss any gaps in resources or support with the GPEI early in the readiness process.

Timing and deadlines: Readiness tracking and verification

Given that the Readiness Checklist provides not only the list of requirements but also a way to track progress (by recording completed items and status updates), it can also serve as a point-in-time indicator of country readiness status. For this reason, the checklist is also used to communicate readiness status.

Because the timing of future country-level outbreak events is unknown, there is no calendar-based due date for the checklist. Rather, countries should begin completing items on the checklist as soon as they have decided to start preparing for nOPV2 use and update the checklist as they continue their preparations. Country nOPV2 focal points are asked to submit the Readiness Checklist to their WHO and UNICEF regional offices based on the timing indicated in Table 4, as part of an overall readiness tracking process. The goal of this process is to ensure close communication with GPEI partners about country readiness status and needs so that any support needs can be addressed, and country readiness can be verified ahead of outbreak response with nOPV2.

Country readiness is assessed by the GPEI, through a dedicated Readiness Verification Team. The primary factors that will be considered in the assessment include country interest in using nOPV2, country-level regulatory approval for the importation and use of nOPV2, and the completion and evaluation of the final Readiness Checklist and any documentation needed to demonstrate country readiness (please see the complete list of readiness verification documents in the Annex).

Table 4. Snapshot of the readiness tracking process

Timing	Activity	Purpose
As soon as the country confirms interest in using nOPV2 and completes a first draft of the Readiness Checklist	First checklist submission for initial readiness assessment Items to submit: <ul style="list-style-type: none"> The Readiness Checklist Evidence of the country's decision to implement nOPV2 (e.g. minutes of a NITAG meeting), if available 	To confirm and communicate country interest in preparing for nOPV2 use To indicate areas where support is needed
At least once per month following initial submission	Monthly checklist updates for readiness progress tracking Items to share: <ul style="list-style-type: none"> Updated Readiness Checklist Other documentation for readiness verification as it becomes available 	To ensure the continued communication and assessment of readiness progress To enable countries to leverage GPEI support and resources when available and appropriate
Once the Readiness Checklist is completed, or after outbreak detection and submission of a request for nOPV2 (whichever comes first)	Final Readiness Update and Readiness Verification Items to submit: <ul style="list-style-type: none"> Updated Readiness Checklist Evidence of the country's decision to implement nOPV2, if not submitted previously Evidence of country approval of the importation and use of nOPV2 All remaining documents for readiness verification 	To confirm country readiness ahead of nOPV2 use in cVDPV2 outbreak response

Outbreak detection and the decision to use nOPV2

When an outbreak is detected, a country that has completed the preparation process may wish to use nOPV2 during the outbreak. nOPV2 will be released through a two-phase process:

1. **Verification of country readiness**, as described above
2. **Release of the vaccine and establishment of any additional specifications for outbreak response (e.g. target age)**: Factors will include available supply, country-level and regional poliovirus epidemiology, and other potential considerations relevant to the specific context of the outbreak. The release of the vaccine is done on approval of the WHO Director-General.

The individual country and the GPEI will work together throughout this process. Once the process is complete, the country is prepared to carry out cVDPV2 outbreak responses with nOPV2 under the EUL and will not need to complete the readiness process again.

The procedures and critical activities necessary to plan for and implement a high-quality nOPV2 outbreak response are not part of the Readiness Checklist, but instead are detailed in the GPEI Standard Operating Procedures (SOPs) for Outbreak Response. The SOPs have been updated to provide specific details and guidance that will be important for nOPV2 deployment. Training modules and other materials for front-line workers are also being developed and should be implemented in coordination with the GPEI. The latest resources are available at <http://polioeradication.org/nOPV2>.

Next Steps

WHO and UNICEF regional and country offices, together with the GPEI, are available to support countries in their assessment of whether nOPV2 is the right vaccine for them at this time and in planning for successful implementation.

The GPEI will coordinate with countries regularly through all relevant national and regional bodies, and will continue to share resources, updates, and information as they become available. This document will be updated again following the conclusion of the initial use period.

Global and country-level nOPV2 resources, from FAQs to scientific publications and technical resources for countries, will be made accessible as they become available via <http://polioeradication.org/nOPV2>. This will ensure that all relevant nOPV2 resources are available in one place. Country-level decision-makers are encouraged to consult the available resources, the nOPV2 Vaccine Deployment Readiness Checklist, and all relevant GPEI offices and teams as they begin – and throughout – the process.

Annex

Documentation Required for Readiness Verification

Category	Requirement	Guidance notes	Supports req. #
Approvals	Confirmation of national decision to use nOPV2	Confirmation by NITAG (or other national immunization or polio coordination body, if no NITAG is in place) Option 1: Meeting minutes which should include: <ul style="list-style-type: none"> Signature by chair List of members Date Option 2: Formal letter	B1
	Approval from NRA for the import and use of nOPV2	Formal letter/written authorization which should include all official forms required for the import of the vaccine into the country. Where there is no NRA in country, this can come from the Ministry of Health.	B2
Cold Chain and Vaccine Management	nOPV2 vaccine management and logistics plan	Vaccine Management Plan which includes <ul style="list-style-type: none"> Outline of how containment requirements will be met, including plans for: <ul style="list-style-type: none"> Reverse logistics requirement Vial disposal Confirmation that impact of 50 dose vial presentation has been factored into tools and capacity estimates 	C1
	Cold Chain Equipment Inventory and Gap Analysis for estimated campaign scope	Short summary of cold chain capacity which should include: <ul style="list-style-type: none"> Date of last inventory Assumptions of gap analysis, along with confirmation it looked at freezer, cold box and vaccine carrier capacities and that they are sufficient for nOPV2 campaign needs 	C2
Surveillance	Country's updated surveillance guidelines and supporting documents	Country's updated surveillance guidelines and supporting documents, which include details on: <ul style="list-style-type: none"> How active case searches will be carried out in all priority sites in each geographic area where nOPV2 was used, one month following nOPV2 use in that area How vaccination coverage data from age-matched, randomly selected community members around AFP VDPV2 cases will be collected How systematic contact sampling of all AFP cases for 6 months after an nOPV2 outbreak response will be done Written confirmation that the lab has been informed that ES samples will be collected twice per month for 6 months after nOPV2 use (can be provided as an email, note verbale, letter, meeting minutes, etc.). <p>Further details can be found in the <i>Polio Field and Laboratory Surveillance requirements in the context of nOPV2 use</i></p>	D1/D2/D5
	Case Investigation Form (CIF) for last 3 AFP cases in country	Revised CIF clearly noting: <ul style="list-style-type: none"> Routine and SIA OPV doses Date of last IPV/OPV dose received 	D3
	*Surveillance desk review and plan	<ul style="list-style-type: none"> Desk review Surveillance strengthening plan PID checklist completed 	D4
	*Country's Situation report (SitRep) or	SitRep or equivalent report which includes:	D6/D7

Category	Requirement	Guidance notes	Supports req. #
	equivalent report showing the country data (past 12 months)	<ul style="list-style-type: none"> NPAFP rate ≥ 2 at national and 80% of all districts with < 15-year-old population more than 100,000 over the past 12 months Stool adequacy $\geq 80\%$ at national level and in at least 80% of districts expected to report AFP cases over past 12 months 	
	* Country Environmental Surveillance (ES) dashboard	ES Dashboard includes: <ul style="list-style-type: none"> Geocodes Location/char of ES site Collection frequency ES indicators for at least 1 functional ES site where nOPV2 will be used (EV detection $\geq 50\%$) 	E1/E2
Safety	Safety monitoring plan	Country should adapt the global guide into their own country specific guide. At a minimum, the country-specific guide should include: <ul style="list-style-type: none"> Case definitions Country-specific surveillance processes (flow) – This should include an adaptation of Figure 2 from the global guide Data flow Country-specific forms Roles and responsibilities table The submission should also include a budget for this work with an indication that there are sufficient resources available to cover the costs.	F1
	Safety training plan for nOPV2 roll out	List of planned trainings, including details on: <ul style="list-style-type: none"> Dates of trainings Facilitator for each session Designation of participants 	F2
	TORs for causality committee	Meeting minutes from a recent meeting confirming the committee exists (note: if committee is new or not yet established, the training needs for its establishment should be included in the training plan)	F3
	VRE plan	VRE must show evidence of collaboration across safety, comms, and surveillance teams in country in its development	F4
Advocacy, Communications and Social Mobilization	Integrated communications plan (including advocacy, C4D, and crisis comms)	<ul style="list-style-type: none"> Description of types and details of the stakeholders that are identified to support OBR. Description of at-risk population and analysis of missed children, refusals, and reasons from previous campaigns. Front Line Worker (FLW) training plan which clarifies plans for both training of trainers and cascade training reach all vaccinators Crisis Communication Committee SOP for crisis response SOP for misinformation management system. 	G1/G2/G3
<ul style="list-style-type: none"> Regional/global lab coordinators will be asked to confirm the readiness of the laboratory serving this country; no supporting documents will be required as part of the readiness verification process. Outbreak operations and national coordination status should be indicated on the readiness checklist; no additional supporting documents are required *denotes documents/considerations that are only required during the initial use phase			

Table: Scientific Publications on nOPV2

Type of Publication	Publication and link
Summary of clinical results and research to date	Clinical Development Summary for nOPV2
WHO Vaccines Prequalification Team assessment of clinical and manufacturing data on nOPV2	Recommendation for an Emergency Use Listing (EUL) of novel Oral Polio Vaccine Type 2 (nOPV2) Submitted by PT BioFarma (Persero)
Data on Phase I trial	The safety and immunogenicity of two novel live attenuated monovalent (serotype 2) oral poliovirus vaccines in healthy adults: a double-blind, single-centre phase 1 study (The Lancet, 2019); also summarized in the Clinical Development Summary for nOPV2
Data on Phase II trials	Safety and immunogenicity of two novel type 2 oral poliovirus vaccine candidates compared with monovalent type 2 oral poliovirus vaccine in healthy adults: two clinical trials (The Lancet, 2020) and Safety and immunogenicity of two novel type 2 oral poliovirus vaccine candidates compared with a monovalent type 2 oral poliovirus vaccine in children and infants: two clinical trials (The Lancet, 2020); also summarized in the Clinical Development Summary for nOPV2 and in SAGE presentations (October 2019 and April 2020); also summarized in the Clinical Development Summary for nOPV2 and in SAGE presentations (October 2019 and April 2020)
How nOPV2 was developed/what modifications were made to mOPV2 and why	Engineering the Live-Attenuated Polio Vaccine to Prevent Reversion to Virulence (Cell Host & Microbe, 2020) Development of a new oral poliovirus vaccine for the eradication end game using codon deoptimization (npj Vaccines, 2020)
Overall programme vaccination strategy and why nOPV2 is important to eradication	<ul style="list-style-type: none"> • Polio endgame options: will we have the vaccines needed? (2019 Lancet commentary) • Poliopolis (2019 correspondence in The Lancet) • Poliopolis: pushing boundaries of scientific innovations for disease eradication (2019 Future Microbiology publication) • Polio vaccination: past, present, and future (2015 Future Microbiology publication)

nOPV2 Vaccine Deployment Readiness Checklist

Note: The Readiness Checklist in Excel format is available on the nOPV2 web page at <http://polioeradication.org/nOPV2>.

Introduction to the Readiness Checklist

This checklist and accompanying guidance focus on items unique to nOPV2 as required under the Emergency Use Listing (EUL). Other campaign preparations are outlined in other guidance documents.

Requirements are divided into two lists: "Requirements for using nOPV2 under EUL" (column E) and "Additional requirements for initial use period" (column F); only countries planning to use nOPV2 during the initial use period need to complete column F.

Objectives of the Readiness Checklist

- To summarize the requirements for nOPV2 use under EUL and the additional requirements during the initial use period under EUL.
- To provide a tool to identify gaps and monitor progress towards nOPV2 readiness.
- To serve as part of the verification of a country's readiness for nOPV2 for a vaccination response.

Structure and methodology

The Readiness Checklist and its requirements are featured on the "Checklist" tab. Reference numbers (e.g. A1, D3, etc.) are provided for ease of reference, not for an explicit order or sequence of steps to follow. Countries may choose to perform activities in parallel if possible.

The "CCL&VM", "Surveillance", "Safety" and "ACSM" tabs contain additional information and considerations that some countries may find useful during preparations.

Initial use period

Note: For the first few months where nOPV2 is used, countries will need to prepare to meet the initial use requirements in column F, in addition to the checklist requirements in column E. For more details on the Framework for initial use of nOPV2 under EUL, please ask your local WHO or UNICEF office for more information or refer to the Framework document available at: <http://polioeradication.org/wp-content/uploads/2020/12/Framework-for-Initial-Use-of-nOPV2-20201202.pdf>

Upon completion of the initial use period, the additional criteria are lifted and only the requirements in column E of the Readiness Checklist apply.

Readiness tracking and verification

Countries are asked to submit the Readiness Checklist ("Checklist" tab) to their WHO and UNICEF regional offices as part of the nOPV2 readiness process, to ensure close communication with GPEI partners on their readiness status and needs.

STEP 1: ONGOING PROGRESS MONITORING

Under this step, the following will take place:

- Country provides periodic updates on progress in nOPV2 readiness planning. Countries are encouraged to update on progress regularly so that it does not impede potential future release of vaccine should there be notification of an outbreak.
- Regional and global colleagues review and flag any concerns they may have proactively—i.e. while nOPV2 preparations are ongoing.
- Any requirement that is met can be signed off as soon as it is completed.

STEP 2: READINESS VERIFICATION

Once the Readiness Checklist is completed, or after outbreak detection and submission of a request for nOPV2 (whichever comes first), the following steps will take place to confirm readiness for nOPV2 use:

- The final Readiness Checklist and any supporting documentation for readiness verification will be submitted to the relevant WHO and UNICEF regional offices (please refer to the nOPV2 technical guidance document and/or the relevant regional office for more details)
- Once it has been confirmed that all requirements have been met, a country receives its nOPV2 readiness verification and is eligible for the dose release process.
- The readiness verification step can take place before an nOPV2 response is planned, or in conjunction with planning a specific nOPV2 response. If done in advance of a specific response, especially during the initial use phase, some elements (for example, Environmental Surveillance presence in outbreak response area) may need to be verified again prior to sign-off.

nOPV2 Vaccine Deployment Readiness Checklist – National Level

December 2020 Version

National nOPV2 Focal Point:
Date of Submission:
Contact Name:
Contact Phone:
Contact Email:

Category	Additional Technical Guidance Documents (available on the nOPV2 web page and/or through WHO/UNICEF regional offices)	Ref. Number	Requirement	Req. for using nOPV2 under EUL All countries to complete	Additional req. for initial use period Only required during the initial use period	Date completed	Status update for incomplete items and/or any additional information/details (include date of update)
Coordination		A1	A national coordinating mechanism/body has been created and technical committees have been established to oversee preparations for nOPV2 across the following critical areas: 1) cold chain, logistics and vaccine management; 2) safety/causality; 3) advocacy, communications, and social mobilization; 4) surveillance; and 5) laboratory	<input type="checkbox"/>			
nOPV2 Approvals	Internal tools and documents to support decision-making (regulatory considerations document, NRA approval letter template, etc.)	B1	An official national decision to implement nOPV2 for outbreak response is confirmed and documented by national immunization partners	<input type="checkbox"/>			
		B2	Approval for the importation and use of nOPV2 has been secured from the NRA or other relevant national authority and documented for reference	<input type="checkbox"/>			
Cold Chain, Logistics & Vaccine Management (see "CCL&VM" tab for further details/activities to consider)	Novel OPV2 (nOPV2) Management, Monitoring, Removal and Disposal (in 50 dose vials with VVM type 2)	C1	Logistics processes, vaccine management protocols and other relevant tools for outbreak response have been adapted to reflect the characteristics of nOPV2 (i.e. containment, reverse logistics requirements and 50-dose vial presentation)	<input type="checkbox"/>			
	nOPV2 Vaccine Request Form	C2	A cold-chain inventory assessment has been conducted or updated; freeze capacity and pre-qualified vaccine carrier availability are well documented	<input type="checkbox"/>			
AFP Surveillance (see "Surveillance" tab for further details/activities to consider)	Polio Field and Laboratory Surveillance requirements in the context of nOPV2 use	D1	A plan has been developed to carry out active case searches in all priority sites in each geographic area where nOPV2 was used, one month following nOPV2 use in that area	<input type="checkbox"/>			
		D2	A plan has been developed to collect vaccination coverage data from age-matched, randomly selected community members around AFP VDPV2 cases	<input type="checkbox"/>			
		D3	An AFP Case Investigation Form has been adapted to record routine and SIA OPV doses	<input type="checkbox"/>			
		D4	A Desk Surveillance Review has been completed and a plan has been developed to address identified weaknesses relevant to nOPV2 use (may be performed with support from the GPEI Surveillance Task Team; see "Surveillance" tab)		<input type="checkbox"/>		
		D5	A plan has been developed for systematic contact sampling of all AFP cases for 6 months after an nOPV2 outbreak response		<input type="checkbox"/>		
		D6	The country achieves a NPAFP rate 2 at the national level and in at least 80% of all districts with more than 100 000 people aged under 15 years		<input type="checkbox"/>		
		D7	The country meets stool adequacy of ≥80% at the national level and in at least 80% of all districts reporting AFP cases		<input type="checkbox"/>		
		E1	The country has at least one functional ES site in areas where nOPV2 will be used (i.e. enterovirus detection rate of ≥50%)		<input type="checkbox"/>		
Environmental Surveillance (see "Surveillance" tab for further details/activities to consider)		E2	A plan has been developed to collect ES		<input type="checkbox"/>		

Category	Additional Technical Guidance Documents (available on the nOPV2 web page and/or through WHO/UNICEF regional offices)	Ref. Number	Requirement	Req. for using nOPV2 under EUL All countries to complete	Additional req. for initial use period Only required during the initial use period	Date completed	Status update for incomplete items and/or any additional information/details (include date of update)
details/activities to consider)			samples twice per month for 6 months after nOPV2 use				
Safety Monitoring (see "Safety" tab for further details/activities to consider)	Global AESI surveillance guide Novel oral polio vaccine type 2 (nOPV2) Vaccine-Related Event (VRE) Response Plan	F1	An active AESI safety monitoring protocol has been developed and materials and resources at all levels are available for AEFI surveillance and AESI active case search	<input type="checkbox"/>			
		F2	All disease surveillance officers have been trained on AEFI surveillance and AESI active case search	<input type="checkbox"/>			
		F3	The causality assessment committee has been trained to conduct AEFI/AESI causality assessment and has been oriented on nOPV2 AESI case definitions	<input type="checkbox"/>			
		F4	The nOPV2 vaccine-related event (VRE) response plan has been adapted to the country context, with stakeholder roles/responsibilities outlined and relevant trainings conducted	<input type="checkbox"/>			
Advocacy, Communications & Social Mobilization (see "ACSM" tab for further activities to consider)	Strategic Communications Guidance for cVDPV Outbreak Response including nOPV2 Introduction of nOPV2 for Polio Outbreak Response: A Training Manual for Supervisors Novel oral polio vaccine type 2 (nOPV2) Vaccine-Related Event (VRE) Response Plan Additional internal GPEI planning tools and templates	G1	Advocacy strategy for key in-country stakeholders (e.g. medical practitioners, religious and community leaders) has been finalized	<input type="checkbox"/>			
		G2	The C4D action plan has been developed. Key components: nOPV2 communications and messaging have been adapted to the local context; key actors including front-line workers have been trained; all stakeholders have been mapped and sensitized; concrete plans for digital platforms have been developed; all necessary messaging, tools and products have been developed	<input type="checkbox"/>			
		G3	A crisis communications plan has been developed and the plan addresses the needs identified in the nOPV2 VRE response plan for AEFI and possible public controversy (including tailored content to respond to misinformation on social media)	<input type="checkbox"/>			
Laboratory	Polio Field and Laboratory Surveillance requirements in the context of nOPV2 use	H1	A plan has been developed to prepare the national lab for nOPV2 use, including updating the isolation algorithms and stocking/ training on the ITD testing kits for both AFP and ES along with modifications to the reporting mechanism	<input type="checkbox"/>			
		H2	Relevant laboratories are prepared to ship samples to CDC or NIBSC for complete genome sequencing for post-response monitoring	<input type="checkbox"/>			
Campaign Operations	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)	I1	SIA guidelines have been updated to include nOPV2 (including microplanning tools and the SIA preparedness dashboard)	<input type="checkbox"/>			
		I2	An nOPV2 SIA training plan and materials are developed	<input type="checkbox"/>			



[HTTP://WWW.POLIOERADICATION.ORG/](http://www.polioeradication.org/)