

## nOPV2 Frequently Asked Questions (FAQ)

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### The Vaccine

#### What is nOPV2 and why is it needed?

The novel oral polio vaccine type 2 (nOPV2) is a new tool that GPEI partners are deploying to better address type 2 circulating vaccine-derived polioviruses (cVDPV2).

Circulating [vaccine-derived polioviruses](#) (cVDPV) can occur when the weakened strain of the poliovirus contained in the oral polio vaccine (OPV) circulates in communities with low immunization coverage for a long period of time and genetically reverts to a form that can cause paralysis. cVDPV2 outbreaks have increased in scope and frequency in recent years. nOPV2 is a modified version of the existing type 2 monovalent OPV (mOPV2) vaccine currently used to respond to cVDPV2 outbreaks. Clinical trials have shown that nOPV2 is safe and provides comparable protection against poliovirus while being more genetically stable than mOPV2 and therefore less likely to revert into a form which can cause paralysis in under-immunized communities. This means that nOPV2 could help stop the spread of cVDPV2 outbreaks.

#### How far along is nOPV2’s clinical development?

A dedicated consortium of experts has been working on nOPV2 development since 2011. One phase I and two phase II trials have been completed, and the vaccine has been tested in adults, young children, and infants. Additional studies are underway, and results and publications are updated as they become available on the nOPV2 web page of the GPEI website: <http://polioeradication.org/nOPV2>.

#### Is the vaccine safe and does it provide immunity?

Clinical trials have demonstrated that nOPV2 is safe and efficacious. The first in-human clinical trial was conducted in 2017 at the University of Antwerp and found nOPV2 to be safe and efficacious in providing immunity against polio. [The Lancet](#) published these findings in June 2019. Key phase II trials carried out across sites in Belgium and Panama are complete, and analysis of the data shows similarly encouraging

results for safety, immunogenicity and genetic stability of nOPV2. *The Lancet* published findings from [these trials](#) in December 2020.

#### **Will the vaccine look the same as mOPV2?**

nOPV2 will look similar to mOPV2. The liquid will be similar in colour and the same type of dropper dispensers will be used. Differences will include the packaging and vaccine vial labelling as well as the size of the vaccine vial: nOPV2 will come in a larger 50-dose vial as opposed to the typical 20-dose vial. The different labelling and packaging design are important to differentiate the two vaccines, although they will not be used together in the field during the initial use period. nOPV2 will also feature the same type of vaccine vial monitor (VVM) as mOPV2. For more product information, please visit the official listing of nOPV2 on the WHO Prequalification Department's website:

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

#### **nOPV2 Rollout**

##### **What is the regulatory pathway to use nOPV2 in cVDPV2 outbreak response?**

On 13 November 2020, nOPV2 received a recommendation for use under [WHO's Emergency Use Listing \(EUL\) procedure](#). The EUL is a WHO regulatory mechanism that involves careful and rigorous analysis of existing data to enable the early and targeted use of yet to be licensed vaccines, diagnostic tests and treatments for Public Health Emergencies of International Concern (PHEIC) – which polio has been since 2014. The EUL has been used to enable the rapid availability of multiple products in the past. WHO's Strategic Advisory Group of Experts on Immunization (SAGE) endorsed accelerated clinical development of nOPV2 and its assessment under EUL in [October 2019](#).

##### **How are country-level regulatory authorities involved in the regulatory process?**

The EUL recommendation for nOPV2 makes the vaccine available for use in cVDPV2 outbreak response. For nOPV2 to be used in-country, the National Regulatory Authority (NRA) or other country-level regulatory authority must provide authorization for the importation and use of nOPV2. To help streamline and facilitate this process, [the WHO Executive Board issued a decision in February 2020](#) encouraging Member States to authorize the expedited importation of nOPV2 on the basis of its EUL recommendation for use. WHO is also engaging its regional regulatory networks and working directly with national regulatory authorities to share information about nOPV2 and its anticipated benefits based on data from clinical studies to date as well as the assessment of nOPV2 by WHO and independent experts.

##### **When will nOPV2 be available for use in a country?**

Now that the EUL recommendation for use has been issued, nOPV2 may be used in cVDPV2 outbreak response in countries that have:

- Approved the importation and use of nOPV2 through both the National Immunization Technical Advisory Group (NITAG) or equivalent technical immunization advisory group and the National Regulatory Authority (NRA) or equivalent authority in countries without an NRA
- Prepared to meet the EUL requirements as well as the [criteria for the initial use of nOPV2](#) under the EUL.

The first response with nOPV2 could take place as early as January 2021.

##### **How will nOPV2 be administered? Can it be used in routine immunization to boost immunity?**

nOPV2 is an oral vaccine. It is administered via two drops, given into the mouth of the child, as with other oral polio vaccines. nOPV2 is only recommended for outbreak response under its Emergency Use Listing and can only be used as part of an outbreak response strategy, like mOPV2. Outbreak response with nOPV2 will be conducted in the same way as outbreak response using mOPV2, and the GPEI Standard Operating Procedures for cVDPV2 Outbreak Response have been updated to account for nOPV2 deployment. IPV and bivalent oral polio vaccine (bOPV) will continue to be used in routine immunization.

##### **Will nOPV2 be used alongside other polio vaccines?**

When nOPV2 is deployed during the initial use period in countries affected by cVDPV2, it will be the only polio vaccine used for outbreak response. Before using nOPV2, there is a required waiting period of 12

weeks after the last mOPV2 use in an area. This will allow countries and the GPEI to correctly attribute any safety signals or environmental detections to nOPV2 and gather data on nOPV2's effectiveness in stopping outbreaks and preventing cases.

### **What are the special requirements for the initial use of nOPV2?**

Countries wishing to use nOPV2 must meet [specific requirements for use of the vaccine under the EUL](#). Additionally, countries aiming to use nOPV2 within the first half of 2021 will likely be using the vaccine during the initial use period—the period spanning the first uses of the vaccine, during which specific criteria apply. [Initial use criteria](#) have been established by the GPEI and endorsed by the SAGE to ensure ability to conduct close monitoring of the vaccine's performance. 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 respond to these quickly and effectively to minimize risk and impact on broader immunization activities. All of the required activities to prepare to meet the criteria are detailed in the [nOPV2 Vaccine Deployment Readiness Checklist](#) and the additional technical guidance documents featured on the GPEI's nOPV2 web page.

### **How long will the initial use period last?**

It is expected the initial use period will last for a minimum of 15 weeks following the first use of the vaccine in a country. This will allow for sufficient time to observe nOPV2's performance in the field and to collect and rigorously analyse data generated from the vaccine's use. The actual duration of the initial use period will depend on the quantity and quality of data collected during the initial use phase. WHO's Global Advisory Committee on Vaccine Safety (GACVS) nOPV2 sub-committee will conduct a final review of data from the initial use period, after which SAGE will then decide whether to endorse the end of the period to enable broader rollout of nOPV2. As the vaccine will continue to be used under EUL, countries will still need to meet certain requirements for its use, however, these will not be as comprehensive as those in place during the initial use period.

### **What kind of monitoring will be required after the initial use period?**

After the initial use period concludes, special safety and surveillance monitoring requirements (related to acute flaccid paralysis and environmental surveillance, as well as adverse events following immunization, and adverse events of special interest, known as AEFI and AESI) will continue to be in place while nOPV2 continues to be used under the EUL recommendation for use. These requirements are sometimes referred to as the post-deployment monitoring requirements and will help ensure that nOPV2's performance in the field is closely monitored in line with EUL standards. WHO's Regulation and Prequalification Department (RPQ) will carefully examine reports on safety, effectiveness and other relevant data that may impact the validity of the EUL status.

### **How does a country prepare to meet the requirements for nOPV2 use under the EUL?**

All countries using nOPV2 based on its WHO EUL recommendation will need to work with the GPEI to meet the relevant post deployment monitoring requirements. To help facilitate this process, the GPEI has developed a readiness process for countries to prepare to meet the requirements, as well as instructions for monitoring once the vaccine has been deployed. These are outlined in the [nOPV2 technical guidance document](#), the [nOPV2 Vaccine Deployment Readiness Checklist](#), and the relevant supporting documents, including [Polio Field and Laboratory Surveillance requirements in the context of nOPV2 use](#), the [Global AESI surveillance guide](#), and the [Novel oral polio vaccine type 2 \(nOPV2\) Vaccine-Related Event \(VRE\) Response Plan](#). A full set of nOPV2 supporting materials can be found on the GPEI's [nOPV2 web page](#). The GPEI will work with countries to prepare, and a country's readiness will ultimately be assessed prior to nOPV2 introduction by a multi-disciplinary global and regional GPEI team. Countries should contact their WHO and/or UNICEF regional or country-level offices with any questions or requests related to nOPV2 implementation.

### **When will nOPV2 stop being used under an EUL recommendation and receive WHO prequalification?**

Following a successful initial use period, nOPV2 will continue to be used under the EUL recommendation for use and full clinical development of nOPV2 will continue, with the goal of achieving WHO prequalification. It is currently estimated that nOPV2 will achieve prequalification in 2023.

### **How will nOPV2's effectiveness be gauged?**

Outbreak control and case prevention will be the key measures to gauge nOPV2's effectiveness. Genetic stability of the vaccine will be monitored by the Genetic Characterization Subgroup of GPEI's nOPV2 Working Group. Further, while clinical trials already show strong evidence of nOPV2's immunogenicity, additional studies will be conducted after campaign rounds throughout the EUL period to confirm protection against type 2 poliovirus in vaccinated individuals.

### **Strategy and Finance**

#### **How much will nOPV2 cost per dose?**

The production of nOPV2 is expected to be similar to production of the existing type 2 oral polio vaccine, which costs US\$ 0.15 per dose. This means that over the long-term, prices for nOPV2 could approach those for mOPV2, once investments in research, facilities and testing have been recouped. Details need to be finalized based on experience from commercial production and release, and scale of use of the vaccine, among other factors.

#### **Who is funding nOPV2 development and production?**

The Bill & Melinda Gates Foundation has funded all development and clinical trials of nOPV2 to date, working closely with GPEI partners throughout the process to ensure resources are going toward a tool that could prove critical to helping end all forms of polio. Based on promising data from clinical trials, and the public health emergency that cVDPV2 constitutes, the Foundation has already funded the production of 200 million doses of nOPV2 to ensure it will be ready and can be deployed quickly in affected countries meeting initial use requirements and requesting the vaccine.

#### **If nOPV2 works, is it the silver bullet to eradication?**

If nOPV2 proves to be as effective as anticipated at stopping cVDPV2 outbreaks, it would be a significant development for eradication efforts; however, this alone will not achieve a polio-free world. Other core strategic components remain essential, including campaign quality and heightened surveillance in polio-affected and at-risk countries. Finally, it is important to remember that vaccines are only as good as the number of people they reach. To eradicate all forms of polio, and maintain eradication, countries must prioritize maintaining strong disease surveillance and improving immunization campaign quality to ensure all children are reached with polio vaccines.

#### **Is nOPV being developed for other types of poliovirus?**

nOPV for types 1 and 3 polioviruses, called nOPV1 and nOPV3, are in preclinical development and the first in-human trials with these vaccines are expected to begin in early 2021. If clinical trials with these vaccines prove successful, nOPV1 and nOPV3 could be kept in stockpiles and used in case of future cVDPV1 and cVDPV3 outbreaks respectively. nOPV1 and nOPV3 are not expected to be ready for use under an EUL until 2024. There is no plan to replace currently used bOPV in routine immunization programmes.

#### **If nOPV2 is successful, will mOPV2 then be retired?**

mOPV2 will continue to be used in some countries even though nOPV2 has received a WHO EUL recommendation. The use of mOPV2 is dependent on several factors, including the ability of individual countries to authorize the use and import of nOPV2 in a timely manner, the sufficient supply of nOPV2, evolving poliovirus epidemiology, and the ability of countries to meet the post-deployment requirements under the EUL. The polio programme would likely stop using mOPV2 in outbreak response prior to nOPV2 prequalification if nOPV2 proves successful in outbreak response and to carry a lower risk of seeding outbreaks, as anticipated, and if there is sufficient stockpile of the vaccine. [The 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 for use are met. This would mean that nOPV2 replaces mOPV2 for cVDPV2 response in all countries where it is feasible to do so. However, mOPV2 supply will remain available for countries until the time when nOPV2 is pre-qualified and fully licensed.