

## 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 an innovative new tool that the GPEI is working closely with countries to deploy to better address [type 2 circulating vaccine-derived poliovirus \(cVDPV2\)](#). cVDPV can occur when the weakened strain of the poliovirus contained in oral polio vaccine (OPV) circulates in under-immunized communities for a long period of time and genetically reverts to a form that can cause paralysis. Type 2 cVDPV outbreaks have increased in scope and frequency in recent years.

nOPV2 is a next-generation version of the traditional type 2 monovalent oral polio vaccine (mOPV2) used to respond to cVDPV2 outbreaks. Data from both clinical trials and field use have shown that nOPV2 is safe and provides comparable protection against poliovirus while being more genetically stable than mOPV2, making it less likely to be associated with emergence of cVDPV2 in low immunity settings. This means that nOPV2 has the potential to play a significant role to stop cVDPV2 outbreaks in a more sustainable way and help achieve a polio-free world.

#### How far along is the vaccine’s development?

A dedicated consortium of experts has been working on nOPV2’s clinical development since 2011. Phase I, II and III clinical trials have been completed with the vaccine tested in adults, young children and infants, and

rollout of nOPV2 under a WHO Emergency Use Listing (EUL) recommendation began in March 2021 (see *Rollout and Preparedness*). Further field studies are being conducted in order to expand on nOPV2's already strong evidence base and help achieve WHO prequalification.

### **Is nOPV2 safe and effective?**

Clinical trials and extensive field use since March 2021 have demonstrated that nOPV2 is safe and effective in providing immunity against type 2 polio. The first in-human clinical trial was conducted in 2017 at the University of Antwerp and found nOPV2 to be safe and efficacious. *The Lancet* published these findings in June 2019. Key phase II trials carried out across sites in Belgium and Panama showed similarly encouraging results for safety, immunogenicity and genetic stability of nOPV2. *The Lancet* published findings from [these trials](#) in December 2020.

Throughout nOPV2's field use, GPEI and implementing countries have rigorously collected and analyzed data on its safety and effectiveness. In June 2022, WHO's Global Advisory Committee on Vaccine Safety (GACVS) nOPV2 sub-committee [met and reviewed safety data](#) from 13 countries that had administered over 253 million doses of nOPV2, including unanticipated events, and found no major safety concerns associated with the vaccine. As of August 2022, 18 out of 21 countries have successfully stopped cVDPV2 transmission following two rounds of mass vaccination activity. A further two countries did so after a third round.

### **How genetically stable is nOPV2?**

In addition to ongoing field data collection and analysis to continuously track nOPV2 safety and effectiveness, genetic stability of the vaccine is closely monitored by GPEI. As of August 2022, primary genetic enhancements made to the nOPV2 vaccine virus showed evidence of change due to a series of recombination events in only one out of thousands of environmental and clinical samples collected. This contrasts considerably to modeling estimates for mOPV2 use over the same scale and period.

### **Where can I find further product information?**

For product information, please see the official listing of nOPV2 on the WHO website:

<https://extranet.who.int/pqweb/vaccines/polio-vaccine-novel-oral-nopv-monovalent-type-2>. For a full list of scientific publications, please visit GPEI's [nOPV2 web page](#).

## **nOPV2 Rollout and Preparedness**

### **Where has nOPV2 been used and at what scale?**

nOPV2 rollout began in March 2021. At the beginning of August 2022, 21 countries across WHO's African, European and Eastern Mediterranean regions had rolled out the vaccine in response to cVDPV2 outbreaks, administering more than 450 million doses collectively, through mass vaccination campaigns.

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

nOPV2 is being deployed under [WHO's Emergency Use Listing \(EUL\) procedure, after having received a recommendation for use in November 2020](#). 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 in response to a Public Health Emergency of International Concern (PHEIC) – which polio has been since 2014. The EUL is used to enable the rapid availability of urgently needed health products for a number of diseases. WHO's Strategic Advisory Group of Experts on immunization (SAGE) endorsed accelerated clinical development of nOPV2 and its assessment under EUL in [October 2019](#) and in October 2021, a transition to vaccine's wider use phase based on positive safety findings from an initial use period.

### **How are regulatory authorities involved?**

WHO engages its regional regulatory networks and works directly with national regulatory authorities to share information about nOPV2 based on data from clinical studies as well as the assessment of nOPV2 by WHO and independent experts. To help streamline and facilitate the regulatory 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. Approval for use and import of nOPV2 by the national regulatory authority is a requirement for all countries planning to use the vaccine.

### **Can all countries access the vaccine?**

The EUL recommendation makes nOPV2 available for use in any country affected by cVDPV2, provided it has:

- approved the importation and use of the vaccine through both its 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 [specific requirements](#) for use under EUL.

nOPV2 is only available through a global stockpile, with the vaccine released by the WHO Director-General. Distribution of nOPV2 is guided by a prioritization framework developed by GPEI which factors in countries' readiness to use the vaccine (i.e. verification status), their unique epidemiological situations and vaccine usage history. Ample supply of effective type-2 containing OPV is available for countries not yet eligible to use nOPV2.

### **What are the special requirements for use of the vaccine under EUL?**

Special requirements including for cold chain and logistics, surveillance, safety, advocacy, communications and social mobilization are in place for use of the vaccine under EUL. All of the required activities for countries planning to use nOPV2 are detailed in [Preparing for nOPV2 use: an overview for countries](#) and the additional technical guidance documents featured on the GPEI's [nOPV2 web page](#).

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

All countries using nOPV2 under EUL will need to work with the GPEI to meet 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 guide [Preparing for nOPV2 use: an overview for countries](#), and supporting documents including [Polio Field and Laboratory Surveillance requirements in the context of nOPV2 use](#), [Safety Monitoring Requirements in the context of nOPV2 use](#), and [Vaccine Management Requirements in the context of nOPV2 use](#). A full set of nOPV2 supporting materials can be found on the GPEI's nOPV2 web page. GPEI will work with countries to prepare, and a country's readiness will ultimately be assessed prior to rollout by a multi-disciplinary GPEI team. Countries should contact their WHO and/or UNICEF regional or country offices with any questions or requests relating to nOPV2 implementation.

### **What kind of field monitoring is necessary?**

Safety and surveillance monitoring requirements related to acute flaccid paralysis (AFP), as well as adverse events following immunization (AEFI) are mandatory for the duration of nOPV2's use under EUL. Other field monitoring, such as implementation of adverse events of special interest (AESI) surveillance or environmental surveillance, are recommended but not mandatory. Requirements are referred to as the post-deployment monitoring requirements and will help ensure that nOPV2's performance remains closely monitored in line with EUL standards. WHO carefully and continually examines reports on safety, effectiveness and other relevant data that may impact the validity of the EUL status.

### **How is nOPV2 effectiveness and genetic stability being assessed?**

Outbreak control and case prevention are the key measures to gauge nOPV2's field effectiveness. As of August 2022, 18 out of 21 countries had successfully stopped cVDPV2 transmission following two rounds of mass vaccination activity, and a further two countries did so after a third round. Data has shown that nOPV2 effectiveness is on par with that of mOPV2, and while evidence of the vaccine's immunogenicity has already been well established, additional studies continue to be conducted throughout the EUL period to confirm protection against type 2 poliovirus in vaccinated individuals.

Similarly, genetic stability of the vaccine is being closely monitored by GPEI. A focused genetic characterization team under GPEI's nOPV2 Working Group conducts monthly evaluations of all nOPV2 isolates collected through AFP and environmental surveillance to identify any causes for concern. Further studies are being conducted to track the longer-term behavior of the vaccine in field settings. See the nOPV2 web page for a full list of scientific publications.

#### **When will special requirements for use of the vaccine cease to apply?**

Special requirements for nOPV2 use under EUL will remain in place until the vaccine achieves full licensing and WHO prequalification. This is currently estimated to happen in late 2023.

### **Administration of nOPV2**

#### **How and when is nOPV2 given?**

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 EUL and can only be used as part of an outbreak response strategy, like mOPV2. Outbreak response with nOPV2 is conducted in the same way as that using mOPV2, with GPEI Standard Operating Procedures governing its deployment, field handling and management.

nOPV2 is not for use in routine immunization. Inactivated polio vaccine (IPV) and bivalent oral polio vaccine (bOPV) continue to be the polio vaccines used in routine immunization programmes.

#### **What is the target age group for immunization with nOPV2?**

As with other polio vaccines used for outbreak response, the target age group for immunization is 0-5 years. However, depending on epidemiology, immunization of a wider age group may be warranted.

#### **Can nOPV2 be used alongside other vaccines?**

For use of nOPV2 under EUL, there is a waiting period of at least four weeks since last OPV campaign use in an area. This is to allow countries and GPEI to correctly attribute safety signals or environmental detections to nOPV2 and gather data on the vaccine's effectiveness. Use of OPV in routine immunization does not affect nOPV2 deployment timeframes. nOPV2 may be used alongside IPV or non-polio vaccines and other health interventions.

### **Strategy and Finance**

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

The production of nOPV2 is expected to be similar to production of monovalent type 2 oral polio vaccine (mOPV2), 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 the development 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 the promising data from clinical trials, and the public health emergency that cVDPV2 constitutes, the Foundation pre-funded the production of 200 million doses of nOPV2 to enable its rapid deployment upon receiving EUL.

#### **Is nOPV2 the silver bullet to stopping cVDPV2?**

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, and strong routine immunization programmes. 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 coverage to ensure all children are reached with polio vaccines.

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

nOPV for types 1 and 3 poliovirus, called nOPV1 and nOPV3, are in development and the first in-human trials with these vaccines began in 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. nOPV1 and nOPV3 are not expected to be ready for use under an EUL recommendation until 2025/2026. There is no current plan to replace bOPV in routine immunization programmes with nOPV.

**Now that nOPV2 is available, will mOPV2 be retired?**

mOPV2 is a safe and effective vaccine and continues to be used. Which vaccine is used for cVDPV2 response is dependent on several factors, including vaccine supply and evolving epidemiology, the ability of individual countries to authorize the import and use of nOPV2 in a timely manner, and their ability to meet the post-deployment requirements under EUL.

The key to any successful outbreak response remains achieving high levels of vaccination coverage and quickly. In line with SAGE guidance, GPEI strongly encourages swift response to cVDPV2 outbreaks with whichever vaccine is available (mOPV2/nOPV2).

The polio programme would aim to phase out use of mOPV2 in outbreak response prior to nOPV2 prequalification if nOPV2 continues to prove successful in outbreak response, and if there is sufficient stockpile of the vaccine. This would be to reduce risk of new cVDPV2 emergencies. However, mOPV2 supply will remain available for countries until the time when nOPV2 is prequalified and fully licensed.