nOPV2 Frequently Asked Questions (FAQ)

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Contents

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). Circulating vaccine-derived polioviruses can occur when the weakened strain of the poliovirus contained in the 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 existing type 2 monovalent OPV (mOPV2) 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, making it less likely to be associated with emergence of cVDPV2 in low immunity settings. This means that nOPV2 has the potential to be a significant tool to help stop cVDPV2 outbreaks in a more sustainable way and achieve a polio-free world.

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 with the vaccine tested in adults, young children and infants. Additional studies including a Phase III trial in the Gambia are underway in order to enhance nOPV2's already strong evidence base and help achieve WHO prequalification.

Is the vaccine safe and does it provide immunity?

Clinical trials have demonstrated that nOPV2 is safe and effective. 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 type 2 polio. *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. For a full list of scientific publications, please see the nOPV2 web page of the GPEI website: http://polioeradication.org/nOPV2.

Following an initial use period for rollout of nOPV2 (March – October 2021), during which safety in largescale field administration was heavily scrutinized by WHO's independent Global Advisory Group on Vaccine Safety (GACVS), the Strategic Advisory Group of Experts on immunization (SAGE) endorsed the transition to the next use phase for the vaccine.

Where can I find further product information?

For more 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.

nOPV2 Rollout and Preparedness

When did rollout begin?

nOPV2 rollout began in March 2021. As at early October 2021, approximately 100 million doses of the vaccine had been administered in several countries fighting cVDPV2 outbreaks.

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 its recommendation for use in November 2020. 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 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 next use phase based on positive safety findings from the initial use period.

How are regional and country regulatory authorities involved?

WHO continues to engage 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 wanting to use the vaccine.

Which countries can access the vaccine?

The EUL recommendation for nOPV2 makes the vaccine available for use in countries affected by cVDPV2, provided they have:

- approved the importation and use of the vaccine through both their 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 requirements specified under EUL.

In the short term, given sharp increases in demand for nOPV2, the need for the polio programme to respond to multiple active cVDPV2 outbreaks, and COVID-19 associated challenges affecting supply, distribution of nOPV2 is being guided by a prioritization framework developed by GPEI. This will be in place until nOPV2 becomes more widely available. For countries unable to use nOPV2, mOPV2 remains available as a safe and effective vaccine with a proven track record of stopping cVDPV2 outbreaks.

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 wishing to use nOPV2 are detailed in the Preparing for nOPV2 use: an overview for countries and 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 the 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. The 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-level offices with any questions or requests related to nOPV2 implementation.

What kind of field monitoring is required?

Safety and surveillance monitoring requirements related to acute flaccid paralysis, as well as adverse events following immunization and adverse events of special interest, known as AEFI and AESI, are mandatory for the duration of nOPV2 use under EUL. These 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 examines reports on safety, effectiveness and other relevant data that may impact the validity of the EUL status.

How are nOPV2's effectiveness and genetics stability being assessed?

Outbreak control and case prevention are the key measures to gauge nOPV2's field effectiveness. While clinical trials already show strong evidence of nOPV2's immunogenicity, 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 and 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 will remain in place until the full course of clinical studies are complete and the vaccine achieves full licensing and WHO prequalification. This is currently estimated to happen in 2023.

Administration of nOPV2

How is nOPV2 administered? Is it used in routine immunization?

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 is conducted in the same way as that using mOPV2, and GPEI Standard Operating Procedures account for nOPV2 deployment and vaccine management.

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 nOPV2 campaigns?

As with other polio vaccines used for outbreak response, the target age group for immunization is 0-5 years. Depending on epidemiology, expanded age immunization may be warranted.

Can nOPV2 be used alongside other polio vaccines? What about in integrated campaigns?

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 continue 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 non-polio vaccines and other health interventions (e.g. vitamin A distribution).

Strategy and Finance

How much does 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 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 and getting 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, 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 polioviruses, 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, respectively. nOPV1 and nOPV3 are not expected to be ready for use under an EUL recommendation until 2024. There is no plan to replace currently used bOPV in routine immunization programmes.

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 outbreak 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 the ability to meet the post-deployment requirements under the EUL.

In the short term, given sharp increases in demand for nOPV2 and the need for the GPEI to respond to multiple active cVDPV2 outbreaks, distribution of the vaccine is being guided by a prioritization framework developed by GPEI, until it becomes more widely available. GPEI is working to ensure that production of nOPV2 continues as quickly as feasible.

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).

In the longer term, the polio programme aims to phase out use of mOPV2 in outbreak response prior to nOPV2 prequalification if nOPV2 proves successful in outbreak response and to carry a lower risk of cVDPV2 emergence, and if there is sufficient stockpile of the vaccine. However, mOPV2 supply will remain available for countries until the time when nOPV2 is prequalified and fully licensed.