

nOPV2 Frequently Asked Questions (FAQ)

October 2020

General

What is nOPV2 and why is it needed?

To better address the evolving risk of type 2 circulating vaccine-derived poliovirus (cVDPV2), GPEI partners are working to deploy an additional innovative tool – novel oral polio vaccine type 2 (nOPV2). The vaccine is a modified version of the existing type 2 monovalent OPV (mOPV2), that clinical trials have shown provides comparable protection against poliovirus while being more genetically stable and less likely to revert into a form which can cause paralysis. The vaccine's increased genetic stability means there is a reduced risk of seeding new cVDPV2 emergences compared to mOPV2.

How far along is nOPV2's development?

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

Is the vaccine safe?

The first in-human clinical trial was conducted in 2017 at the University of Antwerp and found nOPV2 to be safe and effective in providing immunity against polio. [The Lancet](#) published these findings in June 2019.

Key phase II trials are complete, and analysis of the data shows similarly encouraging results for safety, immunogenicity and genetic stability of nOPV2.

Collectively, the clinical trials provide a robust evidence base around the expected behaviour of the vaccine in humans.

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

nOPV2 has received an interim recommendation for use under WHO's [Emergency Use Listing procedure](#) (EUL) to enable rapid field availability, and potential wider rollout of the vaccine.

The EUL involves careful and rigorous analysis of existing data to enable early, targeted use of unlicensed products for a Public Health Emergency of International Concern – which polio has been since 2014. The mechanism has been used in the past to facilitate availability of diagnostic products for both Ebola and Zika virus.

WHO's Strategic Advisory Group of Experts on Immunization (SAGE) endorsed accelerated clinical development of nOPV2 and its assessment under EUL in October 2019.

When could nOPV2 be available?

Based on promising data from clinical trials, and the public health emergency that cVDPV2 constitutes, at-risk production of approximately 160 million doses of nOPV2 by quarter 4 2020 is currently underway to ensure it can be deployed immediately once relevant regulatory approvals for use are obtained.

Which countries will get the vaccine first?

The GPEI has developed [criteria for initial use](#) of nOPV2 and these plans were endorsed by SAGE in April 2020. Several epidemiological and logistical factors are considered to ensure an optimal system for supply of vaccine. These include ensuring nOPV2 is the only oral polio vaccine used in a geographic area where cVDPV2s are present and that the country in question has robust disease surveillance to ensure optimal analysis of the vaccine's performance.

What kind of monitoring will take place to make sure nOPV2 is safe and effective in large-scale settings?

Generating data on safety, immunogenicity, and genetic stability of nOPV2 are a top priority of the GPEI and the vaccine will be subject to continued benefit-risk analysis, guided by clear and established guidelines.

Even after meeting rigorous EUL criteria for safety and efficacy, nOPV2's performance in the field will be closely monitored in line with EUL standards.

Post-deployment monitoring is a requirement once a WHO EUL recommendation for use is granted. This is a risk-based process to track new product performance in the field. 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 listing status. The sources of such information will be primarily based on existing surveillance mechanisms in affected countries and on post-listing surveillance commitments of the manufacturer, set as conditions for the listing.

All countries using nOPV2 based on its WHO EUL recommendation for use will need to meet the post deployment monitoring requirements as outlined in the listing conditions.

How will the nOPV2's effectiveness be gauged?

Outbreak control and case prevention will be the measures to gauge nOPV2's effectiveness. In addition to outbreak control, as the vaccine has been designed to be more genetically stable than mOPV2, lower rates of new emergences of VDPV as a result of the vaccine's use is also expected.

Will nOPV2 be used alongside other polio vaccines?

Initial use of nOPV2 in countries affected by cVDPV2 will be limited to immunization with nOPV2 only. This is important to be able to adequately monitor the vaccine's performance.

After the initial use period, nOPV2 may be administered alongside other vaccines as appropriate to the country setting. Bivalent oral polio vaccine (bOPV) which protects against types 1 and 3 poliovirus, and inactivated polio vaccine (IPV) which provides immunity against all three strains but does not stop transmission of the virus will continue to be used in global routine immunization programmes and in mass supplementary immunization activities/campaigns in countries affected/at risk of type 1 wild poliovirus.

Having a number of vaccine options and use strategies gives us the best chance to achieve and sustain a polio-free world.

Will repeated doses be needed during an outbreak response?

Polio outbreak responses – for wild or vaccine-derived polioviruses – generally consist of multiple immunization rounds, needed to stop transmission. The quality of rounds determines how much vaccine is needed. It is possible to stop an outbreak with three to four high-quality rounds.

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 is US\$ 0.15 per dose. This means that over the long-term, prices 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.

How is GPEI working with health workers and communities to sensitize them on nOPV2?

GPEI has a history of successfully encouraging vaccine uptake and is committed to working across all levels of health systems and communities to ensure confidence in all polio vaccines.

The programme is working with countries where nOPV2 could be approved for use to ensure there is consensus among relevant in-country decision makers and health officials for use of the vaccine to stop cVDPV2 outbreaks. GPEI has also conducted research in focus countries to better understand potential challenges and barriers in communicating with communities about the new vaccine.

Health care providers are the main opinion leaders on health issues for parents and GPEI is raising awareness and working to garner support at all levels of the public health community for potential nOPV2 rollout.

The programme has a long-standing commitment to understanding the underlying reasons for non-vaccination – including misinformation that fuels doubts among parents, caregivers, and community leaders – to ensure its communications are tailored for local audiences in order to build trust.

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.

It is important to remember that vaccines are only as good as the number of people they reach - in order 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.

Who is funding nOPV2 development?

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 is funding at-risk production of 160 million doses of nOPV2 to ensure it can be deployed immediately following the issuance of WHO's interim Emergency Use Listing (EUL) recommendation for use.

Is nOPV being developed for other types of poliovirus?

nOPV for types 1 and 3 poliovirus, called nOPV1 and nOPV3, are in preclinical development and first in-human trials with these vaccines are expected to begin in late 2020 – early 2021.

Should 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; however, there is no plan to replace currently used bOPV in routine immunization programmes.

Additional questions

Regulatory

Are national regulatory authorities involved?

WHO is engaging its regional regulatory networks to sensitize National Regulatory Authorities (NRAs) on nOPV2 and its anticipated benefits based on data from clinical studies to date. Individual NRAs were invited to participate in the EUL review and are being engaged to help facilitate the necessary country-level decision process for authorization for use.

What specifically does post-deployment monitoring involve?

Post-deployment surveillance commitments are defined in a post-deployment monitoring plan, which the manufacturer of nOPV2 has developed together with the GPEI. The plan includes elements relating to general safety (adverse events following immunization – AEFI) monitoring, , acute flaccid paralysis (AFP) surveillance, environmental surveillance (where feasible) and vaccine effectiveness.

What will countries need to do in order to meet post-deployment surveillance requirements?

For many countries, the level and quality of data captured by existing surveillance systems, i.e. AFP surveillance, environmental surveillance and AEFI safety reporting systems, should be sufficient to meet requirements. However, for countries where these systems are weak, or are not yet in place, additional measures may need to be taken to enhance surveillance sensitivity. GPEI will be working with high risk countries in advance of nOPV2 rollout to assess their readiness to meet the post-deployment requirements and to identify plans to address any gaps.

What happens after post-deployment monitoring?

If no quality/safety issues are identified with nOPV2 post deployment, the EUL status of the vaccine may be maintained. If quality/safety issues are identified, WHO may revoke the EUL recommendation for use of nOPV2.

Generating data on safety, immunogenicity, and genetic stability of nOPV2 is a top priority for the GPEI. The ultimate goal is for the vaccine to pass through WHO prequalification.

Are further trials of nOPV2 planned before initial use?

Further nOPV2 trials will be conducted. Phase III clinical trials and additional nOPV2 studies are being planned and initiated, with the ultimate goal for nOPV2 to pass through WHO prequalification.

Operations

How will nOPV2 be administered?

nOPV2 is an oral vaccine. It is administered via two drops, given into the mouth of the child. This is the same as for other oral polio vaccines.

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 labeling as well as the size of the vaccine vial. Different labeling and packaging design is important to differentiate the two vaccines, although they will not be used together in the field during the initial use period. For vial size, nOPV2 will come in a larger 50-dose vial as opposed to the typical 20-dose vial.

Will campaigns for nOPV2 be conducted in the same manner as those for mOPV2?

Outbreak response with nOPV2 will be conducted in the same way as outbreak response using mOPV2. Relevant guidelines with necessary details have been prepared by GPEI.

What sort of cold chain differences will there be for nOPV2 use?

nOPV2 will come in 50-dose vials, which are larger in size than traditional 20-dose OPV vials. nOPV2's manufacturer, Bio Farma, has confirmed that nOPV2 is on track to have a vaccine vial monitor (VVM) type 2, like mOPV2.

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 for use. The decision to use mOPV2 is dependent on several factors including sufficient supply of nOPV2, evolving poliovirus epidemiology, and the ability of individual countries to authorize the use and import of nOPV2 in a timely manner and 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. This would mean that nOPV2 replaces mOPV2 for cVDPV2 response.

COVID-19

What are the implications of COVID-19 on the manufacturing and rollout of nOPV2?

The full impact of the global COVID-19 situation on nOPV2 manufacture and broad rollout remains to be seen. The program is preparing for additional delays, though nOPV2 continues to be a top priority and preparatory work will continue at full speed so that countries facing cVDPV2 outbreaks are able to respond with nOPV2, if desired and appropriate, once their national COVID-19 situation stabilizes.

About circulating vaccine-derived poliovirus

Circulating vaccine-derived polioviruses (cVDPVs) are rare and can occur if the weakened strain of the poliovirus contained in the oral polio vaccine (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. The best protection against all types of polio is ensuring all children are vaccinated in routine and supplementary immunization campaigns, and also maintaining strong disease surveillance. If a population is optimally immunized with polio vaccines, it will be protected from both wild poliovirus and cVDPVs.

cVDPV outbreaks are stopped using the same strategies that have enabled progress against polio – ensuring every child is reached with OPV through high quality immunization campaigns. In recent years, the polio programme has successfully stopped cVDPV outbreaks in several countries, including in war-torn Syria and across challenging terrains in Papua New Guinea.

Type 2 cVDPV (cVDPV2) is currently the most prevalent form of the vaccine-derived virus, and the vaccine currently used to combat it is type 2 monovalent oral polio vaccine (mOPV2).

To eradicate all forms of polio, countries must prioritize maintaining strong disease surveillance and improving immunization campaign quality to ensure all children are reached with polio vaccines.