Consultation between the GPEI and Polio Vaccine Manufacturers, National Authorities for Containment and National Regulatory Authorities

11 October 2022 | Geneva, Switzerland (and online)

Contents

Foreword

This year marks the start of the new 2022–2026 Global Polio Eradication Initiative (GPEI) strategy, which aims to achieve global poliovirus eradication and maintain a polio-free world. The goal of eradicating poliovirus transmission by 2023 is within reach but achieving it necessitates consolidation to ensure that all components of the GPEI strategy are fully implemented. One of these critical components is attaining polio vaccine security, which is defined as the timely, sustained, and uninterrupted supply of affordable polio vaccines of assured quality. Another issue is poliovirus containment, which is one of the core requirements for global certification of poliovirus eradication and is inextricably linked to polio vaccine production.

The World Health Organization (WHO) estimates that approximately 140 million doses of inactivated polio vaccine (IPV)[1] and approximately 1.2 billion doses of bivalent oral polio vaccine (bOPV)[1] are required in the coming year to stop wild poliovirus type 1 endemic transmission in Afghanistan and Pakistan, respond to poliovirus outbreaks, and reduce polio transmission risks. To date, 1.58 billion doses of OPV2, which was withdrawn from routine immunization in 2016, have been deployed via the Global OPV Stockpile to respond to outbreaks of circulating vaccine-derived poliovirus type 2 (cVDPV2); and more will be provided in 2023.

The success of the GPEI depends on the collective work of the vaccine industry and national authorities to ensure vaccine security, and on progress towards poliovirus containment. You are critical stakeholders in our shared journey to polio eradication, and our annual meeting provides an important forum for us to share knowledge and experience, voice concerns, and work together to finally rid the world of polio.

We have four years left to deliver our eradication strategy. Vaccines remain our main tool and supporting their forecasting, development, manufacturing and regulation is as important now as it has ever been. We are committed to continuing to collaborate, both during and after this meeting, to improve polio vaccine forecasting, facilitate research into new products and technologies, and strengthen frameworks for product regulation and poliovirus containment to support your work on planning and implementing uninterrupted vaccine supply.

Your dedication to the cause of polio eradication is essential to its success, and we – all the GPEI partners – very much look forward to working with you as we continue to drive towards our shared goal of a polio-free world.

Aidan O'Leary

Director of Polio Eradication, WHO; Chair, GPEI Strategy Committee

[1] World Health Organization (WHO) Market Information for Access to Vaccines (MI4A) initiative.
This is an estimate of the total IPV and bOPV quantities to be purchased in 2023 by countries, Gavi, the Vaccine Alliance, and GPEI.

List of abbreviations

bOPV	bivalent oral polio vaccine
CAG	WHO Containment Advisory Group
CCS	Containment Certification Scheme
CP	certificate of participation
cVDPV	circulating vaccine-derived poliovirus
CWG	Containment Working Group
dPEF	designated poliovirus-essential facility
EMA	European Medicines Agency
ES+	positive environmental sample
EUL	Emergency Use Listing
GAP-III	WHO Global Action Plan for Poliovirus Containment, 2015
GAP-IV	Global Action Plan for Poliovirus Containment, fourth edition, 2022
GCC	Global Commission for the Certification of the Eradication of Poliomyelitis
GMP	good manufacturing practices
GPEI	Global Polio Eradication Initiative
ICC	interim certificate of containment
IPV	inactivated polio vaccine
IPV1	first dose of inactivated polio vaccine
KP	Khyber Pakhtunkhwa
mOPV	monovalent oral polio vaccine
NAC	national authority for containment
NRA	national regulatory authority
NID	national immunization day
nOPV	novel oral polio vaccine
nOPV2	novel oral polio vaccine for poliovirus type 2
NRA	national regulatory authority
OBRA	outbreak response assessment
OPV	oral polio vaccine
PEF	poliovirus-essential facility
PHEIC	public health emergency of international concern
PQ	WHO Prequalification Programme
PV	poliovirus
SAGE	Strategic Advisory Group of Experts on Immunization
SIA	supplementary immunization activity
tOPV	trivalent oral polio vaccine
VLP	virus-like particle
WHO	World Health Organization
WPV	wild poliovirus
WPV1	wild poliovirus type 1

Executive summary

The development of effective polio vaccines was one of the major medical breakthroughs of the 20th century. Polio vaccines have saved millions from paralytic polio, and they are the reason why the polio map has shrunk from 125 countries to just two.

On 11 October 2022, the GPEI held its annual consultation with polio vaccine manufacturers, national regulatory authorities, and national authorities of containment to discuss these vital tools and ensure their optimal use to support the goal of eradicating polio by 2026.

More than 250 participants, from 26 countries, attended the consultation, either in person or online. Together, they explored the opportunities and obstacles in polio vaccine development and production and discussed the plans and processes that are being established in preparation for a polio-free world by 2026. Their deliberations covered four key areas of discussion: the status of polio today, vaccine supply and demand, new products and innovations, and containment.

This report presents a summary of the presentations and discussions held during the consultation. Key messages to emerge from these are highlighted in Table 1.

Table 1. Key messages to emerge from the GPEI consultation.

Polio today	Vaccine needs and supplies
• Both endemic countries have seen a significant reduction in WPV1 this year. • An outbreak of WPV1 in southeastern Africa in 2022 prompted a rapid multi-country emergency response but remains of concern. • Outbreaks of cVDPVs have fallen in number and are largely limited to four highly localized geographies outside endemic countries: northern Nigeria, eastern Democratic Republic of Congo, northern Yemen, and south-central Somalia. • Eradication remains a feasible goal and GPEI still aims to stop transmission of polioviruses (both wild and vaccine-derived) by the end of 2023.	• A quarter of the world, including some high-risk countries, continues to use a single dose of IPV, and coverage in these countries is often low. • Because of the need to deal with unexpected cVDPV2 outbreaks in southeastern Africa, there were no preventive polio campaigns in 2022. • Novel OPV2 (nOPV2) is produced by a single supplier and is used in line with WHO's Emergency Use Listing. It has become the vaccine of choice for the Global OPV Stockpile, with Sabin OPVs remaining on hand as a backup. • Accurate forecasting is critical to match supply and demand, and ongoing efforts are required to reduce the significant variability in current forecasts and make demand projections as realistic as possible, particularly in the long term.
New products and innovations	**Containment**
• 500 million doses of nOPV2 have been administered in 23 countries. To date, the WHO Director-General has approved the release of more than 700 million doses of this vaccine to countries. The new vaccine is performing as expected, with full licensing and WHO prequalification expected by the end of 2023. • nOPV1 and nOPV3 development continues, with Phase II results expected in 2024. • Treatments for chronic excretors, including antivirals and monoclonal antibodies remain under investigation and on track for use in the post-certification era. • Non-infectious virus-like particles are being developed as promising alternatives to IPVs.	• Poliovirus containment is a requirement for global certification of poliovirus eradication. • The award of the first interim certificate of containment marks a major milestone in preparing for the post-certification era. • There are significant gaps in compliance with containment timelines, and there is a clear need to accelerate progress. • To help achieve global poliovirus containment, WHO developed and published a suite of new strategic, technical, and policy documents in 2022, including the *WHO Global Action Plan for Poliovirus Containment, 4th edition*, 2022 (GAPIV), the *Strategy for Global Poliovirus Containment*, and the *Global Poliovirus Containment Action Plan 2022–2024*.

1. Polio today

1.1. Introduction

Since launching in 1988 the GPEI has helped countries drive the incidence of polio down by 99.9%, saving an estimated 18 million people from paralysis and preventing 1.5 million childhood deaths. But even though polio now only affects a handful of countries, it still poses a global threat and remains a public health emergency of international concern (PHEIC). Disruptions to routine immunization caused by the COVID-19 pandemic caused a surge in cases in 2020; and uneven vaccination coverage across the world has led to polio being spotted in unexpected places, from Malawi and Mozambique to Israel, the United Kingdom of Great Britain and Northern Ireland and the United States of America.

Polio's ability to re-emerge suddenly proves the need to continue striving towards a polio-free world. Vaccines provide the foundation for polio eradication and with the end of polio in sight, it is more important than ever for vaccine manufacturers, national authorities and global partners to work together to secure access to a steady and affordable supply of safe and effective polio vaccines that can be used for both routine immunization and outbreak response. This requires a strategic approach to polio vaccine production that includes efforts to expand vaccine manufacturing, build viable markets, and develop new technologies in line with achieving and sustaining safe and secure poliovirus containment.

In October 2022, the GPEI held its annual consultation with poliovirus vaccine manufacturers, national authorities for containment (NACs) and national regulatory authorities (NRAs) to explore opportunities and obstacles in polio vaccine production and to enable optimal planning to support polio eradication goals.

The consultation had four key objectives:

- feedback on the outcomes of last year's consultation and the Mid-Term Update;
- provide an update on progress towards wild poliovirus (WPV) type 1 eradication;
- discuss projected demand for polio vaccines in the GPEI strategy period 2022–2026; and
- identify key issues around manufacturing, research and development, and containment.

Around 250 participants from 26 countries – including representatives of 33 manufacturers, 15 NACs and 5 NRAs – attended the consultation, in person or online.

1.2. Update on progress and epidemiology

Speaker: Aidan O'Leary, WHO, GPEI

For decades the GPEI has steadily progressed towards eradication. In 1988, WPV was endemic in 125 countries. Wild poliovirus types 2 and 3 (WPV2 and WPV3) were declared eradicated in 2015 and 2019 respectively. In 2022, WPV1 was endemic in just a few districts of two countries – Afghanistan and Pakistan – and outbreaks of circulating vaccine-derived polioviruses (cVDPVs) were similarly localized and limited to just a handful of sub-national geographies.

Over the next 15 months, GPEI plans to target its efforts at these limited geographies to eradicate polio from its last remaining strongholds. By cutting outbreak response times, increasing vaccine demand, improving campaign effectiveness and increasing reach in inaccessible areas, the

programme aims to deliver on the two main goals of its *Polio eradication strategy (2022–2026)*: to stop WPV and cVDPV transmission by the end of 2023, with certification and validation of absence by no later than the end of 2026.

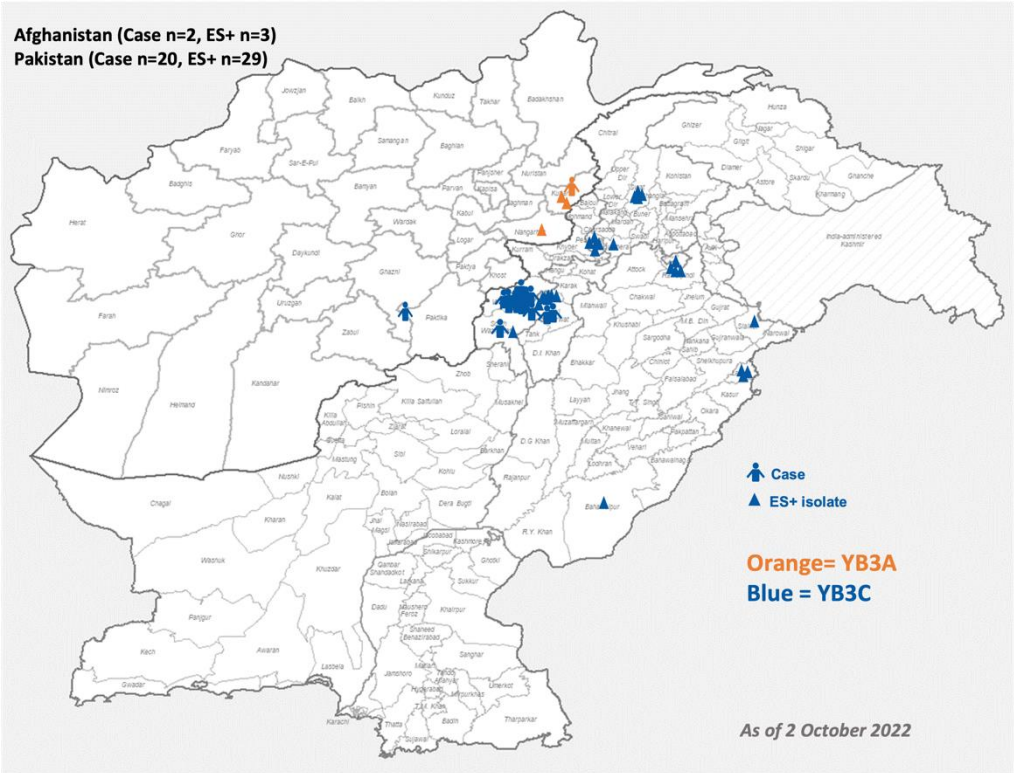
Goal 1: interrupt endemic WPV transmission

Both endemic countries have seen a significant reduction in WPV1 circulation over the past year.

In Afghanistan, an intense immunization response, comprising seven national campaigns and multiple sub-national campaigns and case responses, has progressively reduced the number of unreached children from more than three million in early 2021 to around half a million (mostly in the southern region) in late 2022. The overall increase in reach has translated into a rapid rise in immunity. cVDPV2 has not been detected for more than 14 months; and in 2022 there were only two cases of WPV1 detected, in the eastern region (see Fig. 1). Of the eight genetic clusters seen in 2020, only two (YB3A and YB3C) have survived to 2022.

In Pakistan, there has been a similar downturn in WPV1 circulation, with no cVDPV2 detected for more than a year and fewer than 50 WPV1 cases and positive environmental samples (ES+) reported in 2022 (see Fig. 1). All these detections come from a common source and were found in small and highly localized concentrations. For the first time ever, endemic transmission here is limited to a single genetic cluster (YB3C) found in just three districts in South Khyber Pakhtunkhwa (KP). This marks a major shift in the epidemiology of polio in Pakistan and presents a critical window of opportunity for achieving eradication.

Fig. 1. WPV1 cases and environmental samples in 2022.



In both endemic countries, GPEI is seizing the eradication opportunity through an aggressive response targeted at those limited geographies with highest risk. In Afghanistan, mass immunization

campaigns will be used to interrupt endemic transmission in the eastern region, close the immunity gap in the southern region and prevent WPV1 importation from neighbouring South KP. In Pakistan, campaigns will similarly be used to interrupt endemic transmission in South KP, stop any outbreaks in districts with new detections of WPV1, and reduce the risk of transmission in high risk/consequence districts next to infected areas or with historic reservoirs.

The end of polio has never been closer. But this is no time for complacency. Transmission anywhere threatens children everywhere. An outbreak of WPV1 in south-east Africa that was genetically linked to WPV1 in Pakistan showed the enduring risk of international spread however limited endemic zones are (see Box 1).

Box 1. WPV1 in south-east Africa

In 2022, WHO's Africa Region saw its first outbreak of WPV1 for more than five years, around the Zambezi Basin. In total, six cases were reported from Malawi and Mozambique. All were genetically linked to a WPV1 strain detected in Pakistan in 2019. Mozambique was also affected by a concurrent outbreak of cVDPV2.

The outbreak prompted a rapid multi-country emergency response that was underway within 30 days of notification. By October 2022, four rounds of immunization campaigns had been completed in Malawi and Mozambique, while neighbouring countries of Tanzania, Zambia and Zimbabwe had stepped up their disease surveillance and were undertaking, or preparing for, immunization campaigns themselves.

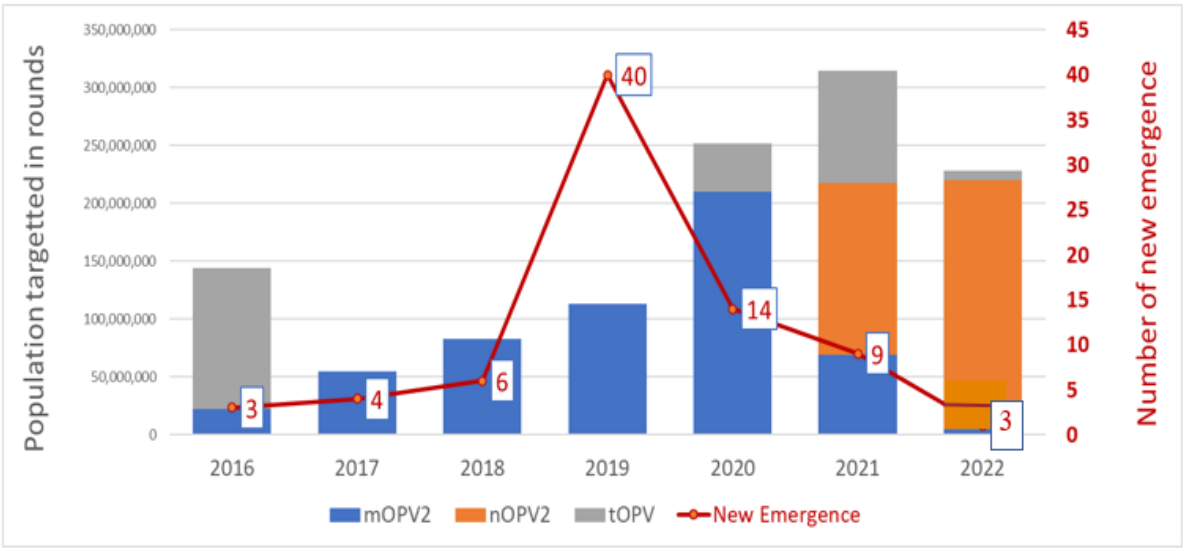
The quality of campaigns was initially problematic due to lack of experience, but lot quality assurance sampling show it has significantly improved. And in October 2022 poliovirus outbreak response assessments (OBRAs) were initiated to identify gaps in the response and inform further improvements.

Goal 2: interrupt cVDPV transmission

COVID-19 disruptions to more than 60 immunization campaigns during 2020 caused a trebling of cVDPV2 cases reported around the world. Since then, the number of countries reporting cVDPV2 outbreaks has fallen sharply and outbreak response has been swift and effective (see Fig. 2). The novel oral polio vaccine type 2 (nOPV2) is the vaccine of choice for outbreak response to cVDPV2 and is proving as safe and effective as monovalent OPV type 2 (mOPV2) but much more genetically stable (see section *3.1 Novel OPVs*).

In 2022 there were just three new emergences of cVDPV2: in Jerusalem, Israel; London, United Kingdom; and New York, United States of America. All detections in Jerusalem and London have been in environmental samples; in New York there has also been one human case reported. All the cVDPV2 viruses detected have been genetically linked. The reasons for these emergences are unclear, but they are particularly concerning because they show that VDPVs can emerge in high-income settings with good sanitation where live vaccines are not in use. In each country, the rates of routine immunization are very high; but there are pockets of un- or under-immunization that pose a potential risk of transmission. Each country is responding with enhanced surveillance and targeted immunization campaigns using the immediately available inactivated polio vaccine (IPV). Further genetic and epidemiological investigations are ongoing to determine the possible spread of the virus and the potential risk associated with it.

Fig. 2. Rapid decline in new emergences of cVDPV since 2019.



More than 90% of cVDPV detections in 2022 were restricted to four sub-national geographies (outside WPV1 endemic countries):

- northern Nigeria, which was the largest exporter of cases (27% of all detections);
- eastern Democratic Republic of Congo, which had seven unique emergences across three provinces;
- northern Yemen, which saw more than 200 children paralysed in the last 12 months; and
- south-central Somalia, which continues to have the longest-lasting infection (1,642 days).

In all four areas, immunization rates are low because access is hampered by insecurity and conflict. GPEI continues to work to increase its reach in these last major zones of transmission and boost immunization coverage.

2. Vaccine needs and supplies

2.1. Routine immunization and IPV

Speakers: Alejandro Ramirez Gonzalez, WHO; Ian Lewis, UNICEF Supply Division; Stephen Sosler, Gavi, the Vaccine Alliance

Rolling out IPV2

WHO's Strategic Advisory Group of Experts on Immunization (SAGE) first recommended using at least one dose of IPV in their routine immunization schedule in 2013. This milestone was achieved in 2019. In 2020, SAGE recommended adding a second dose of IPV (IPV2) to the polio immunization schedule and in 2022, WHO updated its position paper on polio vaccination to reflect this decision.[2] For all countries using OPV in their routine immunization programmes, WHO recommends three doses of bOPV and two doses of IPV, with IPV1 administered from a minimum of 14 weeks of age and IPV2 given at least four months later (using a full or fractional dose) to achieve the highest immunogenicity. For countries using IPV-only schedules, WHO recommends

[2] Polio vaccines: WHO position paper – June 2022. Weekly Epi Record. 2022;97(25):277–300.

three doses of IPV, beginning at six to eight weeks of age, with at least four-week intervals between each dose.

Since SAGE's recommendation to add IPV2, 47 (out of 99) countries have introduced a second dose, bringing the number of countries using a two or more-dose schedule to 142. That is equivalent to 73% of WHO Member States, representing 84% of live births in the world. Around a quarter of the world's countries remain on a one-dose schedule of IPV, mostly in WHO's African and Western Pacific Regions, including some high-risk countries such as Democratic Republic of Congo. More worryingly, immunization coverage with IPV1 in these countries is often also low. Disruptions to immunization programmes caused by COVID-19 and conflict are also contributing to a decline in coverage in some countries. For example, Brazil, the Democratic People's Republic of Korea, Guinea-Bissau and Myanmar all saw a significant drop in IPV1 coverage in 2021.

IPV supply

The standalone IPV supply market has improved over the past 18 months to the point where there is now sufficient supply for all countries to introduce the second dose of IPV into their routine schedules. The demand through UNICEF for standalone IPV is 100–110 million doses annually. As a result, this mechanism accounts for most of the global standalone IPV supply. The PAHO Revolving Fund does not expect any shortages in 2022–2023; UNICEF expects to have some doses left over.

UNICEF's latest tender for IPV runs from 2023–2025, with an option of a one-year extension. It is based on a maximum annual demand scenario of around 115–120 million doses and assumes that: all countries will have introduced IPV2 by 2023, no countries will have moved to a hexavalent product or a fractional dose schedule, and there will be no changes to the funding policies of Gavi, the Vaccine Alliance. The volume of supply offered was three times higher than the demand forecast. The outcome of the tender was a reduction in the cost of IPV. The weighted average price for 2023 will be less than US$ 2 per dose and is expected to drop further over the tender period. Awards were made to five manufacturers, including a second manufacturer for ten-dose presentations, which improves supply security.

Overall, the IPV market is now considered to be healthy but with some overcapacity, which may be a challenge moving forward.

Supporting low-income countries

Gavi, the Vaccine Alliance supports the roll-out of IPV in routine immunization by offering to provide IPV1 and IPV2 doses in 73 Gavi-eligible countries, with exceptions to Gavi's usual co-financing and eligibility policies.[3] In total, 42 Gavi-eligible countries have introduced IPV; 28 of those have done so using the SAGE-recommended schedule for maximum immunogenicity. Some of the 18 Gavi-eligible countries without plans to introduce IPV2 are at high risk under the current epidemiological situation, especially in south-east Africa. These include Malawi, Tanzania and Zambia.

Gavi also provides IPVs to conduct catchup vaccination activities, targeted at the 43 million children who missed out on routine immunization because of global supply constraints in 2016–2019. COVID-19 delayed the implementation of catchups but these have now been implemented and 95% of the missed cohort have now been reached. Six countries have yet to vaccinate their missed cohorts (two million children); five of these have yet to request Gavi for support to do so. The older these children get, the harder it becomes to catch them up. In answer to a query, Mr Sosler clarified that

[3] Excluding Ukraine (self-financed), Armenia and Georgia (aP-Hexavalent) and India (separate decision).

different countries use different approaches to do their catchup activities, including through routine screening and nonselective campaigns.

Prioritizing polio

Participants discussed how to support countries to prioritize routine immunization for polio against a backdrop of concurrent vaccine-preventable disease outbreaks and diverse emergencies that impact resource availability and stretch response capacities. They highlighted the fact that immunization coverage data for IPV1 is national and belie the situation at sub-national levels, where coverage can be much lower.

Speakers highlighted three ways in which GPEI is working to ensure polio remains a country priority:

- ensure positive externalities for outbreak response to polio, for example by combining it with vaccinating against measles or by integrating it with other primary health care interventions;
- secure high-level political engagement, for example as done during the recent WPV1 outbreak in south-east Africa when the WHO Director-General met with the President of Malawi within five days;
- run workshops for countries on how to prioritize and implement routine immunization for polio, as was recently done in WHO Regional Office for Africa.

2.2. Global OPV Stockpile

Speaker: Vachagan Harutyunyan, WHO

The Global OPV Stockpile is a long-term supply mechanism that aims to build preparedness for contingencies after OPV cessation. It was established in 2015 following a request by WHO Member States at the 68th World Health Assembly. It is governed by WHO and managed with UNICEF support. To date, 1.58 billion doses of OPV2, which was withdrawn from routine immunization in 2016, have been deployed through the Global OPV Stockpile. It has proven to be a very effective and valuable mechanism for responding to cVDPV2 outbreaks all over the world.

Stockpile strategy

Plans and priorities for the Global OPV Stockpile are closely aligned to GPEI goals and will necessarily evolve over time, as the world progresses from eradication to post-certification. For the next three to five years (2022–2026), over the lifespan of the current GPEI strategy, the stockpile aims to remain responsive to polio epidemiology and programmatic context while allowing enough lead time to adapt vaccine production. It has three specific objectives:

- ensure uninterrupted supply of OPV2 to combat ongoing cVDPV2 outbreaks;
- prepare for potentially catastrophic contingencies (such as a failure to deploy nOPV2 or outbreaks that exceed GPEI response capacity); and
- establish a stockpile of OPV1, OPV3 and new products to prepare for OPV cessation.

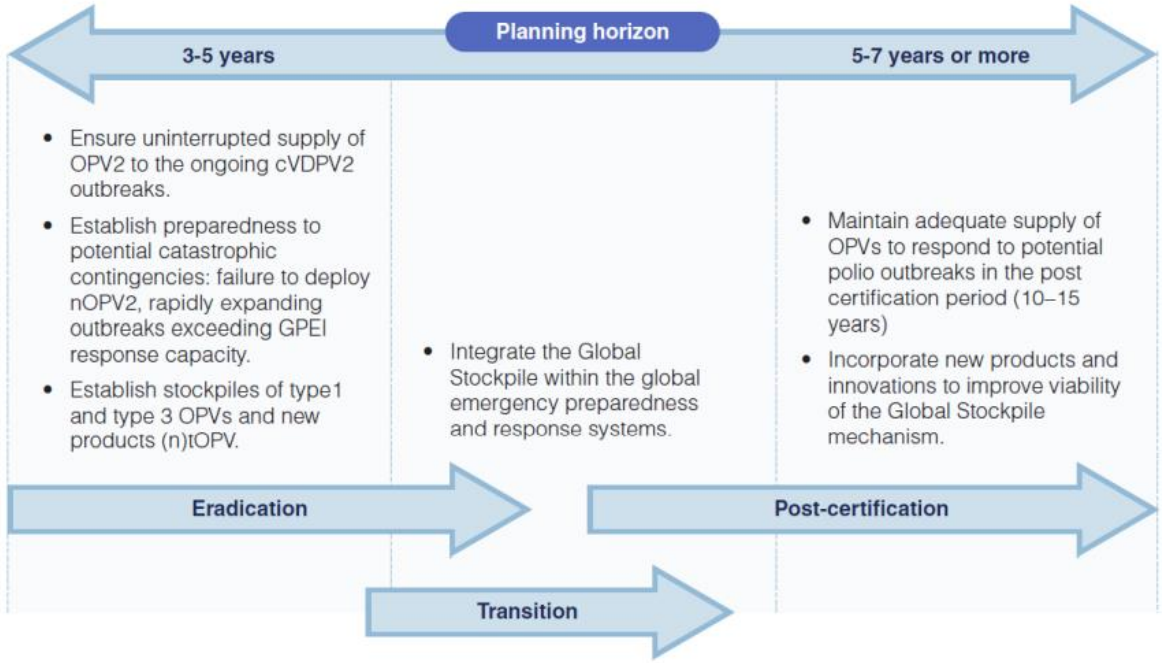
During this pre-cessation timeframe, nOPV2 that is currently deployed under the WHO Emergency Use Listing will be the vaccine of choice for the stockpile, although Sabin OPV2 will continue to be prepositioned as a backup measure, for use in line with SAGE recommendations (see Table 2).

Table. 2. Global OPV Stockpile, 2022–2027 demand forecast.

		Number of doses forecasted (million)					
	Vaccine	2022	2023	2024	2025	2026	2027
Before bOPV cessation	nOPV2	750	433	623	481	502	494
	Sabin OPV2	200	–	–	–	–	–
After bOPV cessation	OPV2 (bulk)	–	–	250	250	250	250
	OPV2 (finished)*	–	–	–	–	100	–
	OPV1 (bulk)	–	–	–	500	500	–
	OPV1 (finished)*	–	–	–	–	100	–
	OPV3 (bulk)	–	–	–	250	250	–
	OPV1 (finished)*	–	–	–	–	50	–

After certification, the Global OPV Stockpile will be integrated within global emergency preparedness and response systems and will focus on maintaining adequate supplies of OPVs and any new relevant products and innovations to respond to potential poliovirus outbreaks and maintain a polio-free world (see Fig. 3). In response to a query about stockpile vaccine choices post-cessation, Dr Harutyunyan clarified that the scope and scale of the stockpile, and decisions on how far to diversify stocks, would be guided by the evolving epidemiology. He emphasized the importance of close collaboration with manufacturers, NRAs and NACs to facilitate any transition and committed to continuing to update and share GPEI forecasts to help stakeholders manage their production schedules.

Fig. 3. Global OPV Stockpile, planning horizon.



Risk mitigation

Dr Harutyunyan identified some of the major risks to implementing the *Global OPV Stockpile Strategy (2022–2026)*, from insufficient financing, limited production capacity and long lead-times

to uncertain epidemiology and limited uptake. He highlighted the measures being used to mitigate these, for example:

- forward planning and taking a proactive approach to fundraising;
- working with manufacturers to improve long-term forecasting, diversify the manufacturing base and expand production capacities, for example through technology transfer;
- extending OPV supply lead times for vaccine production;
- regularly reviewing annual demand forecasts and ensuring contingency and redundancy planning; and
- advocating for optimal Sabin OPV2 uptake and planning for OPV2 stock maintenance.

2.3. bOPV needs and supplies

Speakers: William Mbabazi, WHO; Ann Ottosen, UNICEF

bOPV mass immunization campaigns, also called supplementary immunization activities (SIAs) or national immunization days (NIDs), complement routine immunization programmes. They aim to interrupt circulation of poliovirus by immunizing every child under five years of age with two drops of OPV, regardless of previous immunization status. In particular, bOPV SIAs are used to interrupt endemic circulation of WPV1 (endemic SIAs), mitigate the risk of importation and VDPV emergence (preventive SIAs), or stop any new outbreaks of WPV or cVDPVs (outbreak response SIAs). The number of bOPV SIAs that are required each year varies according to ongoing polio epidemiology and programmatic priorities.

Projected bOPV needs for SIAs

The GPEI uses two planning tools to help plan for bOPV SIAs in the medium and short term:

- a five-year placeholder calendar that forecasts SIA resource requirements (both vaccines and funding) in the medium term, based on the best available risk and immunization projections at the start of the strategy period; and
- an annual calendar to prioritize SIA options for the coming year, based on addressing highest risks within the approved annual budget.

The placeholder calendar does not distinguish between different types of bOPV SIAs much. Rather it assumes that any low demand for preventive campaigns will likely be offset by increased demand for outbreak response campaigns. This was the case in 2022, when the cancellation of preventive campaigns was offset by the need for several unforeseen outbreak response campaigns in south-east Africa.

The annual calendar is primarily used for planning preventive campaigns to fill gaps in routine immunization to achieve optimal immunity levels for eradication. This includes campaigns to boost coverage among new birth cohorts to at least 80% DPT3 by age 2; as well as catchup campaigns to reach 80%–90% OPV3 coverage among historical cohorts.

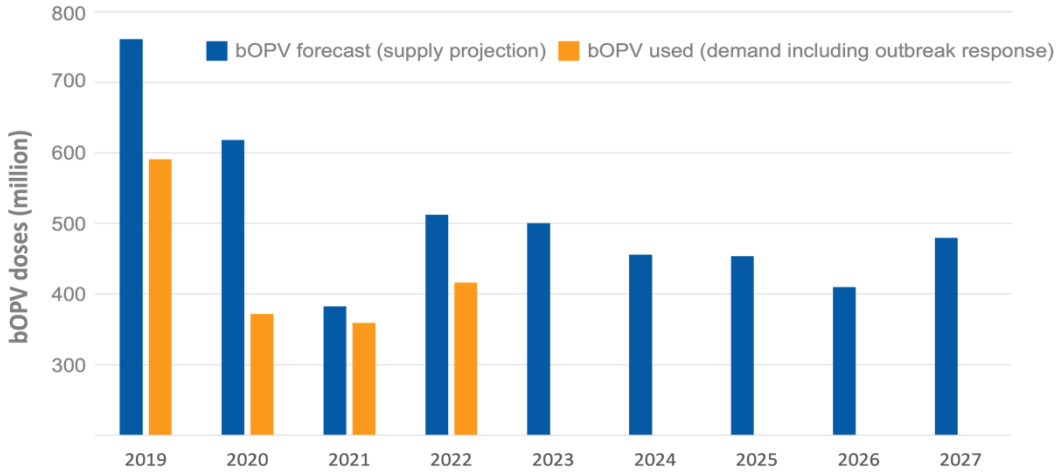
The annual calendar is developed using a risk-based approach, based on best- and worst-case scenarios of existing coverage rates as well as other factors. The incidence of measles over the previous 12 months is taken into account as a tracer for unvaccinated populations that risk importing WPV1; and the presence of highly disruptive measles outbreaks is similarly considered as a tracer for areas where the risk of transmission and VDPV emergence is likely to be high.

The SIA calendar approved by GPEI for 2023 projects a need for nearly 420 million doses of bOPV, excluding bOPV requirements for routine immunization or for outbreak response in self-procuring

countries such as China or India (see Fig. 4). In response to a query about plans for preventive SIAs, Dr Mbabazi confirmed that GPEI would continue to plan preventive SIAs using a risk-based approach, prioritizing campaigns in high- and medium-high-risk geographies.

Fig. 4. bOPV SIAs vaccine supply and demand forecasts.[a]

[a] *Excludes bOPV demand for routine immunization and SIAs in self-procuring countries.*



The GPEI continues to explore options for increasing the reach of bOPV SIAs, for example by integrating them into scheduled campaigns for other vaccine-preventable diseases, or by codelivering them as part of measles outbreak responses. As the deadline for eradication approaches, the GPEI is also planning for the post-OPV cessation era, building on lessons learnt during the switch from tOPV to bOPV in 2016.

bOPV supply

The last bOPV tender issued for 2018–2022 remains relevant and the procurement objectives are unchanged: to sustain sufficient supply of OPV to meet demand for polio eradication and to withdraw OPV from the market in a responsible way that maintains affordability.

In 2022, there was considerable volatility in demand throughout the year with annual projections varying from 680 million doses to 870 million doses (a difference of nearly 190 million doses). Several factors contributed to the wide variation in demand, for example: the outbreak in south-east Africa (which increased demand by 150 million doses); cancellation of preventive SIAs in non-endemic countries due to GPEI funding constraints (which decreased demand below awarded volumes); and higher-than-expected demand in Pakistan (which increased demand in the second half of the year).

The large variability in forecasts underscores the need for manufacturers to remain flexible to meet evolving GPEI requirements and manage cases of over- or under-supply. This means for example being able to scale up quickly and at short notice to tackle unexpected outbreaks. At the same time, being flexible also means being able to adjust for delayed or cancelled campaigns, for example by ensuring sufficient cold chain capacity to store unused supplies or postponing production to avoid aging stocks.

For 2023, the demand for bOPV to implement the approved SIA calendar (option 3) and meet all requirements for routine immunization is projected to be around 623 million doses. To meet this

demand, UNICEF has contracts with seven manufacturers, which combined ensure the supply of 785 million doses (excluding any potential carry over from 2022, which could potentially be as much as 175 million doses subject to demand materialization in Q4 2022).

Based on these forecasts, bOPV supply is sufficient to meet the projected demand for 2023. UNICEF continues to work with GPEI, countries and manufacturers to ensure an uninterrupted supply of bOPV to meet eradication goals. This includes updating its risk assessment following the COVID-19 pandemic to develop an updated placeholder calendar.

During the discussion on bOPV supplies, participants asked for some consideration to be given to vaccine packaging and labelling, which they said should be easily distinguishable from mOPV2 or nOPV2 to ensure containment. All OPVs are easy to identify before use because they use different colour caps. The problem lies in reverse logistics, as stocks that return from the field with droppers rather than caps on and the readability of labels is often very poor, making it difficult to identify which vaccine has been returned.

3. New products and innovations

3.1. Novel OPVs

Speakers: Ananda S Bandyopadhyay, Bill and Melinda Gates Foundation (BMGF); Simona Zipursky, WHO

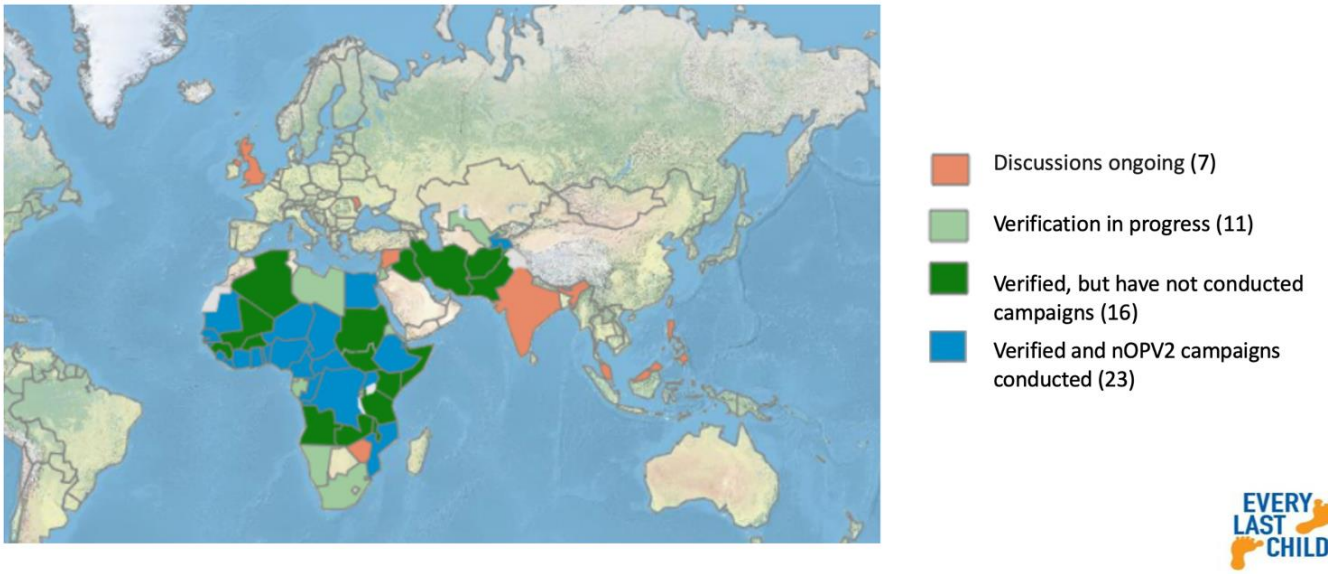
nOPV2 rollout

nOPV2 has been in development since 2011. On 13 November 2020, nOPV2 became the first vaccine to be issued an Emergency Use Listing (EUL) recommendation by WHO's Prequalification programme (PQ); and rollout under the EUL procedure began in March 2021. By 2022 it had become the de-facto vaccine of choice for responding to cVDPV2 outbreaks.

EUL is a special, rigorous and independent regulatory pathway that is available for use in PHEICs. It ensures that vaccines and other medical products can be made available as soon as possible in emergency public health situations such as cVDPV2 outbreaks. To use nOPV2 under EUL, countries must complete a verification process and show that they can meet a set of 15 readiness requirements, including for cold chain and logistics, surveillance, safety monitoring, laboratories, advocacy, communications and social mobilization.

By October 2022, 500 million doses of nOPV2 had been administered in response to cVDPV2 outbreaks, across 23 countries (see Fig. 5), over 700 million doses of nOPV2 had been released from the stockpile during that period. A further 16 countries had already met the readiness requirements but are yet to use nOPV2 in the field; 18 countries were considering or conducting the verification process but had yet to complete it.

Fig. 5. Status of nOPV rollout in October 2022.



nOPV2 performance in the field

Throughout nOPV2's field use, GPEI and implementing countries have rigorously collected and analysed data on the vaccine's safety, genetic stability and effectiveness. These data confirm that nOPV2 is performing as expected.

nOPV2 has a similar safety profile to Sabin mOPV2. To date, WHO's Global Advisory Committee on Vaccine Safety sub-committee on nOPV2 has reviewed safety data from more than 253 million doses of nOPV2 administered across 13 countries and found no major safety concerns associated with the vaccine. The committee noted that the detection rate for adverse events of special interest is lower than background rates from the literature; and the number of cases of suspected vaccine-associated paralytic poliomyelitis (VAPP) is much lower than that expected for Sabin OPVs.

Molecular epidemiology data from field use over 18 months show that nOPV2 is also much more genetically stable than Sabin OPV2 and much less likely to revert to a virulent form that can cause paralysis in under-immunized communities. Other parameters of genetic stability – including recombination rates and VP1 nucleotide changes show nOPV2 to outperform Sabin mOPV2.

A look at epidemiological data from nOPV2 and Sabin mOPV2 campaigns reveals the two vaccines have similar immunogenicity and confirm that nOPV2 provides comparable protection against poliovirus type 2 to Sabin mOPV2. Both vaccines have similar risk ratios for cVDPV2 incidence and prevalence in environmental surveillance. More than 80% of countries that used nOPV2 show no evidence of breakthrough transmission after two rounds of SIAs. Northern Nigeria provides a prominent exception with breakthrough transmission continuing to occur despite multiple nOPV2 campaigns; Sabin mOPV2 has had similar challenges in this region.

The overall number of new cVDPV2 emergences seen across the world also continues to fall since the introduction of nOPV2 in the field. In 2022 there were just three new emergences detected (see Fig. 2 above), all of which have been linked to prior use of Sabin OPVs rather than nOPV2.

Development plans

nOPV2 remains in clinical development and will continue to be used under the EUL throughout 2023. The dossier for prequalification and licensure is expected to be submitted to the Indonesian

NRA (Badan POM) and WHO PQ in the first quarter of 2023, with the aim of achieving full licensing and WHO prequalification by the end of 2023.

Participants discussed plans for product presentations after licensing, noting that nOPV2 is currently the only OPV that is presented in 50 dose vials (all other OPVs come in 20 dose vials). A change to 20 dose presentation has been considered for nOPV2, to align with other product presentations used by GPEI and to reduce wastage. It has not yet been implemented. Ms Zipursky added that the move to 20 dose vials relies on gathering enough stability data to ensure a shelf life of 24 months to match the current shelf life. Ms Ottosen confirmed that the tender for nOPV2 will ask for both 20 and 50 dose vials. Asked what the maximum shelf life might be expected to be by the end of 2026 (for stockpiling purposes), Ms Zipursky said there was no target shelf life for nOPV2 (in vial or bulk form) at present but that this could be something for GPEI and the manufacturers to further discuss and work on.

In addition to the ongoing development of nOPV2, clinical development is ongoing for nOPV1, nOPV3 and multivalent nOPV. nOPV1 and nOPV3 are in Phase I of development; multivalent nOPV is in pre-clinical development. All three remain on track, with Phase II results for the monovalents expected in 2024. Asked about the need for multivalent nOPV given that it will not be available until 2026, Dr Bandyopadhyay confirmed that this was a contingency measure and that the strategy for outbreak response post-certification would be to use monovalent nOPVs. Multivalent nOPV would only be used in the unlikely event that there was co-circulation or accidental spill over of multiple viruses at once.

Asked whether there are any lessons learnt from COVID-19 to shorten the timeline for getting nOPV1, nOPV3 and multivalent nOPVs into use, Dr Bandyopadhyay reminded participants that the development timeline for the new nOPVs is already expected to be shorter than that for nOPV2 – between three and five years. He agreed that there was some scope to further accelerate the timeline, both in terms of clinical development as well as regulatory readiness and approval processes.

3.2. New polio products

Speaker: Martin Eisenhawer, WHO

Traditional polio products (IPVs and OPVs) have many strengths: they are safe, effective and easy to use, and they have a secure supply. But there is definite room for improvement: IPVs provide poor mucosal immunity and OPV use can give rise to VDPVs. Both types of vaccine also require the use of live virus during manufacturing, which poses a containment issue. And while polio vaccines are well developed, there are still no treatments for immunocompromised individuals who shed poliovirus for extended periods of time (also known as chronic excretors) who will still serve as a reservoir of virus after eradication and OPV cessation into the post-certification era.

The development of nOPVs will resolve some of the enduring issues associated with Sabin OPVs (see section *3.1 Novel OPVs*). Several other new products are also under development as potential alternatives to IPVs and treatments for chronic poliovirus excretors.

Polio virus-like particles (VLPs)

VLPs work by mimicking a virus to induce an immune response. Unlike live-attenuated or inactivated vaccines, VLPs are not infectious and so reduce the biosafety risk associated with current polio vaccines. The overall goal of polio VLP research and development is to find a replacement product for IPV after eradication.

Since 2011, a research consortium established by WHO and led by the University of Leeds (United Kingdom) has been researching and developing recombinant VLPs, based on a yeast expression system with baculovirus as a back-up. Yields are improving and stabilities are similar or superior to IPV. The immunogenicity of VLPs in transgenic mice is also comparable to or better than IPV; in rats, the immunogenicity is only comparable with the use of a simple AI-based adjuvant.

Following a 2019 call for expressions of interest in commercialization, contracts have been made with three pre-manufacturers. Discussions with all three are ongoing and VLPs have already been sent to one pre-manufacturer for immunogenicity testing in rats to look for reproducibility. Full development proposals (for clinical development and GMP manufacturing) from each pre-manufacturer are still pending and will form the basis for selecting a candidate manufacturer for VLPs. Dr Eisenhawer estimated that VLPs were still five to six years away from regulatory approval.

Responding to a query, Dr Eisenhawer confirmed that no market analysis had yet been done for VLPs. He said those interested in commercializing VLPs see them as a replacement for IPV or as part of a hexavalent vaccine, but he emphasized that the incentive for manufacturers to switch to VLPs will depend on the evolving containment environment, including any constraints on continuing with Sabin IPV that follow from that. Participants highlighted another potential use for VLPs in neutralizing assays to support diagnosis. Dr Eisenhawer reminded participants that VLPs remain in the pre-clinical phase of development and while several publications have demonstrated the proof of principle, these products still need to be proved in practice.

Treatments

Since 2006, the Polio Antivirals Initiative has worked to find safe and effective antiviral treatments to stop poliovirus shedding in immune deficient adults given the oral polio vaccine. In particular, the initiative is working to develop two antiviral agents with independent, direct mechanisms of action in order to maximize antiviral activity and reduce potential for drug resistance development.

- Pocapavir is a viral capsid inhibitor that has been shown to stop excretion in a mOPV challenge study and in compassionate use, although some drug resistance development was observed.
- V-7404 is an irreversible viral protease inhibitor that has been successfully used with pocapavir to boost antiviral activity.

Good manufacturing practices (GMP) batches of drug substance and drug product have been produced for both pocapavir and V-7404. A submission to the European Medicines Agency (EMA) is being prepared as the first step to defining the path to regulatory approval. A meeting with WHO PQ to discuss the potential for getting an EUL recommendation is also scheduled.

In addition to working on pocapavir and V-7404, the Polio Antivirals Initiative is also investigating monoclonal antibodies that could be used after bOPV cessation to clear VDPVs, including those shed by immunocompromised individuals. To that end, one antibody – huMAb 92 – shows some promise against all three serotypes VDPVs but development remains in its early stages. Engineering is ongoing to improve the antibody's half-life, after which GMP batches can be produced. First-in-human studies are currently planned for early 2024.

3.3. Polio vaccines and prequalification (PQ)

Speaker: Mathias Janssen, WHO

WHO PQ's goal is to ensure that polio vaccines used in immunization programs are of high quality, safe, and effective. During a WHO PQ assessment, WHO independent experts review extensive quality, safety, and efficacy data. PQ is distinct from EUL, the latter is a risk-based procedure that provides a time-limited recommendation for use during a PHEIC and necessitates ongoing efforts toward both WHO PQ and full market approval by NRAs.

Several polio vaccines have been prequalified to date; in November 2020, nOPV2 was the first vaccine to receive an EUL (see Table 3).

Table 3. Number and type of prequalified polio vaccines, vaccines that received EUL.

	Vaccine	Current	Under evaluation
PQ	combinations	1 (1 presentation)	1
	wIPV	8 (17 presentations)	–
	sIPV	3 (4 presentations)	1
	mOPV1	4 (5 presentations)	2
	mOPV2	3 (4 presentations)	–
	mOPV3	2 (3 presentations)	1
	bOPV	8 (13 presentations)	–
	tOPV	1 (1 presentation)	–
EUL	nOPV2	1 (1 presentation)	–

Post-PQ activities

All vaccines are subject to post-PQ/EUL activities after PQ is granted or listed to ensure their continued acceptability. Manufacturers must submit annual reports, retain sample lots for WHO targeted testing, and notify WHO of any changes to products, labels, or inserts in order to maintain their products' approval status. They must also report any product complaints or adverse events that occur as a result of immunization.

Following PQ/EUL, the WHO vaccine prequalification team performs specific activities to support GPEI goals, such as assessing OPV batches for inclusion in the Global OPV Stockpile, performing technical reviews of vaccine tenders for UNICEF, and providing technical assistance to countries.

nOPVs and PQ

Since nOPV2 received EUL, WHO and Bio Farma, the nOPV2 manufacturer, have supported countries around the world to authorize its use by sharing the product dossier, generating additional data and running readiness workshops. As a result of these activities, nOPV2 has already been authorized for use in 39 countries.

The next step for nOPV2 is to transition from EUL to PQ, which is expected to be completed during 2023. WHO confirmed that all efforts will be made to provide a PQ decision in the shortest possible time. WHO is also reviewing options to facilitate assessment and registration for other nOPVs as they progress through the development pipeline.

To ensure success, WHO emphasized the value of involving NRAs and WHO PQT/VAX as early as possible – to anticipate regulatory requirements and timelines, evaluate the need for new WHO guidance and explore options for joint review (for example through African Vaccine Regulatory Forum). Participants also emphasized the need for regulators to involve NACs in the development process for nOPVs to ensure these adequately addresses containment issues.

4. Containment and certification

4.1. WHO Global Action Plan for Poliovirus Containment, Fourth Edition, 2022 (GAPIV)

Speaker: Harpal Singh, WHO

Following polio eradication certification, facilities that retain polioviruses pose the greatest threat to maintaining a polio-free world so strong containment is required to certify global poliovirus eradication. The *WHO Global Action Plan for Poliovirus Containment, 4th edition, 2022* (GAPIV) describes the global strategy for reducing facility-associated risk of poliovirus release after eradication. This is achieved through (1) risk elimination by destroying poliovirus materials or transferring them to a poliovirus-essential facility (PEF) and (2) risk mitigation by complying with GAPIV facility, immunization coverage and environmental control safeguards to manage biorisk, as described in GAPIV. The GAPIV biorisk management standard provides a framework for verifying facility compliance and containment certification in accordance with the Containment Certification Scheme (CCS), as well as the requirements of other relevant standards and documents.

GAPIV was developed following a 2021 recommendation from WHO's Poliovirus Containment Advisory Group (CAG) to update GAPIII to: reflect developments in polio eradication strategy and improved understanding of biorisk and biorisk management; and to better align with other relevant global standards. The revision process was largely driven by stakeholders, with multiple rounds of discussions and input solicitation, including a period of public consultation. CAG provided close supervision and guidance throughout the process. CAG approved GAPIV on June 30 2022, and it was published on July 1 2022, taking effect immediately. In response to a question, Dr Singh confirmed that GAPIV will be available in the United Nations' six official languages (Arabic, Chinese, English, French, Russian and Spanish).

Major changes from GAPIII to GAPIV

The change from GAPIII to GAPIV has resulted in several changes to the structure and content of the standard.[4]

- GAPIII annexes 2 and 3[5] have been merged and converted from tables to prose to eliminate redundancy, improve clarity and make it easier to read.
- The biorisk management system elements have been reorganized – elements of similar content have been merged, reducing the number of biorisk management elements from 16 to 14.
- Terminology has changed to align with other standards, including renaming primary, secondary and tertiary safeguards as facility, immunization coverage and environmental safeguards.
- New guidance on emerging issues has been included, especially around the safe handling of novel poliovirus strains.
- There has been a shift away from prescriptive requirements for facility safeguards lacking evidence towards a risk-based approach, for example around the requirements for exit showers and dedicated effluent decontamination systems.

[4] See WHO Global Action Plan for poliovirus, fourth edition (GAP-IV) for a summary of all changes made during the 2021–2022 revision process.

[5] Annex 2: Biorisk management standard for poliovirus-essential facilities holding wild poliovirus materials and Annex 3: Biorisk management standard for poliovirus-essential facilities holding only OPV/Sabin poliovirus materials (no WPV) of GAPIII

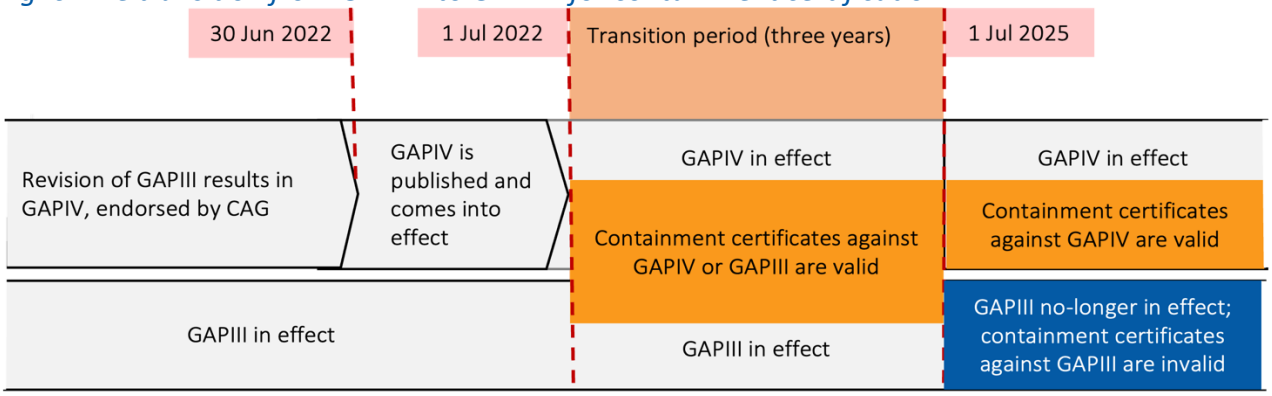
The requirements in GAPIV are now fully aligned with other relevant global standards, including *Guidelines for the safe production and quality control of poliomyelitis vaccines* and WHO *Laboratory biosafety manual* and associated monographs.

Containment certification

Countries that retain polioviruses have agreed to put in place all necessary safeguards for PEFs. They accomplish this by certifying each PEF in accordance with GAPIV requirements using the containment certification scheme (CCS).

The allowable transition period from GAPIII to GAPIV is three years, beginning with the publication of the new GAP in July 2022. Both GAPIII 2015 and GAPIV 2022 will remain valid during the transition period, and facilities retaining polioviruses will use it to plan and implement the full transition to GAPIV. During the transition period, facilities will collaborate with their NAC to approve any changes made to comply with GAPIV requirements. (Fig. 6).

Fig. 6. The transition from GAP-III to GAP-IV for containment certification.



4.2. Global containment update

Speaker: Arlene King, Global Certification Commission (GCC)

The global strategy (2022–2026) and action plan (2022–2024) for poliovirus containment are built around three strategic goals that need to be achieved by all poliovirus containment stakeholders in parallel to eradication and beyond, into the post-certification era.

1. **Complete inventories**: reduce to a minimum the number of facilities retaining poliovirus materials.
2. **Certify PEFs**: ensure that all eradicated poliovirus materials in PEFs are stored and handled according to international standards to maintain long-term containment.
3. **Sustain containment**: strengthen and support national and international programmes to ensure sustainability and continuity of poliovirus containment in the post-certification era.

Activities and deadlines to meet these goals are aligned with eradication milestones and in 2018, all Member States committed to meeting them through World Health Assembly Resolution 71.16. The deadline for completing inventories of all facilities that currently have poliovirus type 2 (PV2) materials and destroying or transferring infectious materials was 2016; the deadline for designating all NACs was the end of 2018. Planned PV2 PEFs should have obtained a certificate of participation (CP) by the end of 2019; those retaining PV2 wishing to proceed with obtaining an interim certificate of containment (ICC) should declare their intention before the end of 2022. The deadline for completing initial inventories for WPV1 and WPV3 materials is the end of 2022. PEFs retaining

WPV1 or WPV3 poliovirus materials should have their CPs by the end of 2023, when all WPV and cVDPV transmission is expected to have successfully been interrupted.

Progress in containment

A look at the current status of the containment goals shows some significant gaps and underlines the need to accelerate progress to align with eradication goals (see Table 4).

There have however been some encouraging trends and significant achievements for containment over the past few years. For example, the overall number of PEFs planned has dropped from 89 to 61 since 2018, with further reductions expected once ICC audits are planned or completed (i.e. where progress with obtaining ICC certificates is not successful). And in October 2022, Canada became the first country in the world to advance to the second stage of containment certification, with one of its PEFs being awarded an ICC.

Table 4. Current status of activities to achieve containment goals and objectives.

	Activity	Deadline	Progress
Goal 1	Complete PV2 inventories	end 2016	6 countries pending
	Complete WPV1 and WPV3 inventories	end 2022	28 countries pending
Goal 2	Establish NACs	end 2018	22/25 (3 countries declaring PV2 retention with no NAC)
	Obtain CPs for all PV2 PEFs	end 2019	14/24[a] (10 countries with no or incomplete CPs)
	Declare intent to apply for PV2 ICCs	end 2022	19/24[a] (5 countries have not declared their intentions)

[a] Brazil has a NAC but is not included in the denominator here because it is no longer planning to have a PEF

GCC conclusions and recommendations

In June 2022, the GCC, which oversees the certification process for polio eradication, held its 22nd meeting and reviewed the status of containment activities. It endorsed the global strategy and action plan and expressed concern that compliance with the timelines for containment as set out in WHA 71.16 is off track. It also acknowledged that VDPV (all serotypes) inventories may need to be updated.

To accelerate progress and get containment back on track, the GCC recommended that:

- WHA 71.16 noncompliant countries be reminded of their commitment and strongly urged to act;
- WHO maintains an inventory of facilities retaining novel poliovirus strains that includes the same information as that provided in the CP; and
- NACs begin the containment of WPV1 and WPV3, with the aim of getting CPs for all new PEFs by the end of 2023.

A series of strategic resources, practical tools and technical and policy guidance are also being developed to support the achievement of containment goals. The new strategy, action plan and GAPIV have already been published, along with guidance for laboratories. Other resources under development include a new M&E framework and renewed post-certification strategy, as well as an updated version of the Containment Certification Scheme that sets out expectations, mechanisms, roles, responsibilities and timelines for certification and a revision to the PIM Guidance is also expected following recommendations made by CAG.

Dr King emphasized the importance of in-country collaboration – between NRAs, NACs and PEFs (including manufacturers) – to achieve containment goals.

5. Breakout discussions

During the breakout session, participants joined one of three groups to discuss key topics at the interface of polio vaccine production and polio eradication and containment. Each group discussion was facilitated by a member of the GPEI.

5.1. GAPIV implementation and compliance

Facilitator: Derek Ehrhardt, WHO

The containment breakout session focused on the biorisk management requirements and implementation approach, as well as the recently published GAPIV conformity assessment activities. They focused on two main topics, as detailed below.

Implementing biorisk management requirements in GAPIV

a. Evidence for facility, immunization coverage and environmental control safeguards
Dr Singh confirmed that the reference used for the inclusion of new facility safeguard requirements in GAPIV, such as handwashing, was already cited in the bibliography section of GAPIV. The more frequently encountered issue was a lack of evidence for including polio-prescriptive requirements, and in such cases, these were shifted to a risk-based approach to determine the mitigation measure that should be implemented. This also allows facilities to ensure that the measures implemented as a result of a risk assessment are locally relevant, proportionate to risk, and long-term. The shift to a risk-based approach is in line with the *WHO Laboratory biosafety manual*, considered to be the global biosafety standard. There is a general lack of evidence for safeguards that aim to minimize the consequences of a facility-associated release of poliovirus (immunization coverage and environmental control safeguards), which CAG will address at its next meeting scheduled for the end of 2022.

b. Containment requirements for handling novel poliovirus strains
CAG developed a set of criteria for evaluating improved 'safety' of novel poliovirus strains to determine the containment requirements for their storage and handling that should be used by facilities handling novel poliovirus strains. Any 'temporary waiver' (exempt from the containment requirements of GAPIV) granted by CAG:

- is interim in nature and will be reviewed periodically;
- only applies to specific novel poliovirus strains and uses and cannot be generalized; and
- is not an exemption from the requirement to report to the respective NPCC for inclusion in national poliovirus inventories.

Although the discussions focused on nOPV2 and S-19 poliovirus strains, participants were asked to take note of the GCC recommendation for WHO to maintain an inventory of all facilities retaining any kind of novel poliovirus strains. This should be reported to WHO with information in the CP application form submitted by the NAC, if it exists, or by NPCCs. Presently these facilities will not be required to have a GCC-countersigned CP in place.

Containment certification

a. Audit teams. Several questions were raised about the qualifications and composition of the audit team required to certify PEFs against the GAP standard. The CWG Secretariat confirmed that countries are no longer required to use formally qualified CCS auditors, but all other CCS requirements remain in effect. Individuals and experts with relevant backgrounds, competencies and skills should be included on national audit teams. Before proceeding with their audits, countries should submit to CWG complete documentation detailing the timeframe, audit team composition and experience (as per CCS recommendations), and a detailed audit plan.

b. ICC applications. Participants raised concerns about the process for standardising the evaluation of ICC applications, which is subject to variation. Dr. King of the CWG confirmed that applying for an ICC is a multi-step process that begins with submitting an audit plan and, once approved, continues with conducting the audit and submitting the audit report and supporting documents to the GCC for review and approval. To support ICC applications, various tools and templates have been developed; these are available online, and all countries are encouraged to use them to standardize the information received.

Participants noted that all the containment issues raised during the breakout session (and more) would be discussed in depth at the annual polio containment meeting planned for the next day. The outcomes of that meeting, along with all other relevant information, guidance and tools for containment certification are available on the GPEI containment webpage.

5.2. Research and development priorities

Facilitator: Martin Eisenhawer, WHO

Participants reexamined the product pipeline for polio vaccines and treatments – which includes nOPVs, VLPs, S19, antivirals and monoclonal antibodies (see section 3 above) – and reflected on three critical questions.

What are industry's key priorities for vaccine research?

Participants agreed that the biggest priority is to develop a new generation of polio vaccines that avoid the use of live virus in vaccine manufacturing without adversely impacting the cost of goods. To that end, the development of VLPs and s19 is very encouraging.

Participants noted that both expression systems being used in VLP development (yeast and baculovirus) can be used to produce human vaccines at affordable costs. Indeed, ongoing research suggests that the best yields are obtained in the least expensive media, and the cost-of-goods for VLPs is not expected to be higher than that associated with IPV.

Both VLPs and S19 were identified as potential replacement products for use in hexavalent or other combination vaccines. VLPs do require an adjuvant but both adjuvants under investigation (aluminium hydroxide and phosphate) have been specifically chosen because they are already present in combination vaccines. Research into S19 is further developed and suggests that by using a capsid that mimics what is in IPV today it might be even easier to integrate S19 into a multivalent formulation than it is with VLP.

Beyond product development, participants identified surveillance as another key priority for research, especially when certification comes into play. They noted the need for tools and techniques that can successfully scale up surveillance and enable its implementation in multiple environments.

Participants suggested that methods for analysis are advancing rapidly and that the largest gap in surveillance lies in sample collection.

What other areas of research are important beyond the existing product pipeline?

Participants identified three key areas where further investigation is warranted.

Mucosal immunity. In terms of prevalence, duration, and excretion, IPV causes lower intestinal mucosal immunity than OPV. However, historical evidence suggests that this is not always the case for other types of mucosal immunity, including nasopharyngeal mucosal immunity. This suggests that in some communities where poliovirus transmission is solely oral, the role and value of IPV may be much greater than previously thought. More research in this area is required.

Vectored vaccines. Noting the comments on mucosal immunity, participants suggested that research into vectored vaccines based on viruses that produce VLPs in situ in the mucosal surface (for example the Newcastle disease virus) could be valuable and impactful. These types of vaccines can be used orally and have great potential.

S19 infectious status. S19 strains are considered live viruses from a containment perspective. But all the evidence to date suggests that they shouldn't replicate in humans and participants called for a body of research to be compiled that collates this evidence to convince containment stakeholders that S19 strains should not be considered live viruses. They pointed to some of the mRNA virus vectors used in COVID-19 vaccines as a precedent for this: these viruses can infect a cell but are not capable of replicating and as such are not considered to be live viruses.

What can WHO and GPEI do to facilitate polio-related research?

Participants made three recommendations for WHO and GPEI partners.

- Continue research and development into VLPs, S19 and other promising products.
- Provide more information about timelines for developing S19 and VLP in the context of timelines for eradication and certification.
- Work with regulatory networks and NRAs in low- and middle-income countries to develop or strengthen regulatory pathways for antivirals and monoclonal antibodies.

5.3. Securing bOPV supply

Facilitator: Ian Lewis, UNICEF

GPEI plans to phase out the use of bOPV everywhere by 2027. It is vital that until that happens, a secure supply of bOPV is maintained. But with the end of demand for bOPV in sight, some manufacturers (Sanofi and GSK) have already left, or are planning to leave, the market. And with the rapidly evolving epidemiology of polio, predicting demand remains a huge challenge, with estimates often liable to vary by more than 100 million doses within a single year.

In the face of these market complexities and demand uncertainties, participants considered how best to maintain an affordable, reliable and agile supply of bOPV over the next five years to bOPV cessation. They identified three key strategies that could be used to help secure bOPV supplies.

Better forecasting. Manufacturers were very clear about the need for better forecasts of bOPV demand so that they can effectively procure raw materials and plan production schedules to ensure sufficient vaccines are available when they're needed. They noted that lead times for raw materials are getting longer, rising from six months to eight months for bulk production, meaning it now takes around 24 months to go from raw material to finished product. The price of raw materials is relatively stable, but energy costs are rising, which is also something of concern. Manufacturers

remain committed to supplying bOPV and are willing to stay in the market through to bOPV cessation, but it is important for them to know how much to produce to align supply and demand. GPEI, countries and other procurement agencies and buyers need to improve their long-term forecasting, not only at the aggregate level but also for individual manufacturers. Overall annual requirements based on the GPEI placeholder calendar through to 2027 are projected to be between 600 million doses and 700 million doses annually.

Shorter shelf-life. As a way of coping with uncertain forecasts and fluctuating demand, manufacturers asked for more flexibility in accepting products with a shorter shelf-life, especially as the deadline for bOPV cessation approaches. This would help avoid situations in which planned immunization campaigns are delayed or cancelled so the predicted demand does not materialize, and manufacturers are left holding large volumes of aging stocks. During the COVID-19 pandemic many manufacturers faced this very situation and WHO and UNICEF developed a guideline to encourage countries to accept vaccine stocks with a shorter-than-usual shelf life. Countries were largely receptive to the approach for COVID-19 vaccines; although participants noted that adopting the same approach for routine polio immunization activities may be more challenging.

Risk-sharing. Manufacturers asked whether GPEI would be willing to share some of the risk associated with producing bOPV supplies to forecast through to bOPV cessation, specifically to help cover costs in the event of surplus supply. They recalled that at the time of tOPV cessation, there was some compensation for manufacturers that had been left with surplus supply but noted that this is not currently in the GPEI budget.

6. Conclusion

Before closing the 2022 consultation, Aidan O'Leary, Director of Polio Eradication at WHO, offered some concluding remarks. The goal of interrupting polio transmission by the end of 2023 is feasible. The strategies for polio eradication work when they are fully implemented, as evidenced by the incredible progress in eradication achieved over the past 30 years. Over the next 15 months, to overcome the final hurdles to eradication, the priority must be to focus on those last few pockets of the world where polio still lingers and where access remains difficult.

Mr O'Leary informed participants of a pledging event in October 2022 that will be the first step in securing the more than US$ 4 billion required to implement the 2022–2026 GPEI strategy. He underscored the finite nature of support for eradication and stressed the need to reach the strategy's eradication milestones without delay. There is also growing pressure to accelerate progress in containment to better align with the eradication timeline. WHO Member States should expect more visibility in public reporting about what the requirements for containment are, and where the gaps in meeting those lie.

Eradicating polio requires collaboration and cooperation on a global scale and this is the GPEI's strongest asset. Mr O'Leary emphasized the continued value of working in partnership with vaccine manufacturers, regulators and containment authorities. He thanked all participants for their active involvement in this year's consultation and for the high level of deliberations, which he described as useful, insightful and informative. He also thanked all speakers and facilitators for their contributions, and the organizing team.

Annexes

Annex A. Agenda

Consultation between the GPEI and Polio Vaccine Manufacturers, National Authorities for Containment and National Regulatory Authorities

11 October 2022 | Geneva, Switzerland (and online)

Chair: Aidan O'Leary, Director of Polio Eradication, WHO; Chair, GPEI Strategy Committee.

09.00–09.20 Introduction	
Welcome and opening remarks	Aidan O'Leary, WHO
Feedback on the outcomes of last year's consultation and the mid-term update, and expectations for this year's consultation	David Woods, WHO
09.20–10.20 Session I. Status update on eradication, stopping outbreaks and epidemiology	
Status of the programme: Current epidemiology, progress towards eradication and stopping outbreaks, and plans for cessation of OPV use	Aidan O'Leary, WHO
10.30–12.30 Session II. Vaccine forecasts and timeframes	
Update on the supply of IPV and demand forecast	Ian Lewis, UNICEF Alejandro Ramirez Gonzalez, WHO Stephen Sosler, Gavi
Global OPV stockpile: detailing the new strategy and projected dose requirements	Rissa Durham, BMGF Ann Ottosen, UNICEF, Vachagan Harutyunyan, WHO David Woods, WHO
bOPV supply and demand forecast	William Mbabazi, WHO Jason Thompson, UNICEF Arie Voorman, BMGF
13.30–14.30 Session III. New product developments and innovations with potential to impact supply	
nOPV: Rollout of nOPV2 and future plans for nOPV1 and 3	Simona Zipursky, WHO Ananda Bandyopadhyay, BMGF
Update on development of polio VLPs, antivirals and monoclonal antibodies	Martin Eisenhawer, WHO
Update on prequalification-related activities to facilitate access of polio vaccines for routine and emergency response	Carmen Rodriguez Hernandez, WHO
14.30–15.30 Session IV. Containment and certification	
GAP: Update on revised changes, transitioning to GAP-IV and compliance verification	Harpal Singh, WHO
Update on global Containment certification	Arlene King, GCC
15.45–17.00 Session V. Interactive breakout groups *(in parallel)*	
Group 1: Implementation of GAPIV: issues & solutions	Harpal Singh, WHO
Group 2: Research: research and R&D priorities	Martin Eisenhawer, WHO
Group 3: bOPV supply: Short- and long-term	Ian Lewis, UNICEF
17.00–17.10 Wrap-up	
Concluding remarks	Aidan O'Leary, WHO

Annex B. List of participating organizations

Participating Organization	Country
ADM Consulting	Switzerland
AIM Vaccine Group	China
AJ Vaccines	Denmark
ANSM	France
Australia NAC	Australia
Batavia biosciences	The Netherlands
Beijing Bio-Institute Biological Products Co. Ltd.	China
Beijing Minhai Biotechnology Company	China
Belgium NAC	Belgium
Bharat Biotech International Limited	India
BIKEN	Japan
Bill & Melinda Gates Foundation	USA
Bilthoven Biologicals B.V.	The Netherlands
Biological E	India
Biomanguinhos	Brazil
Center for research and production of vaccine and biological (POLYVAC)	Viet Nam
Centers for Disease Control and Prevention	USA
Central Institute for Experimental Animals	Japan
China National Biotec Group Company Limited	China
China NRA	China
Chumakov FSC R&D IBP RAS	Russian Federation
Denmark NAC	Denmark
Food and Drug Administration	USA
France NAC	France
France NRA	France
GAVI Alliance	Switzerland
GCC-CWG	Canada / USA
GlaxoSmithKline Vaccines	Belgium
Gryphon Scientific	USA
Health Canada	Canada
Hungary NAC	Hungary
India NAC	India
Indonesia NAC	Indonesia
Indonesia NRA	Indonesia
Institute of Medical Biology, Chinese Academy of Medical Sciences	China
Intravacc	The Netherlands
Islamic Republic of Iran NAC/NRA	Islamic Republic of Iran
Janssen Vaccines	The Netherlands
Japan NAC	Japan
KM Biologics Co. Ltd.	Japan

LG Chem Ltd.	Republic of Korea
NIBSC	UK
Panacea Biotec Ltd.	India
PATH	USA
Pharmajet, Inc.	USA
Polio Program – Pakistan	Pakistan
PT Bio Farma	Indonesia
Reliance	India
Riskren	Singapore
ROK NAC	Republic of Korea
ROTARY INTERNATIONAL	Germany
Russian Federation NAC	Russian Federation
Russian Federation NRA	Russian Federation
Sanofi Healthcare India Private Limited	India
Sanofi Pasteur SA	France
Serum Institute of India	India
Sinovac Biotech Co. Ltd.	China
South Africa NAC	South Africa
Taconic Biosciences	USA
Temptime Corporation	USA
The Netherlands NAC	The Netherlands
UK NAC	UK
UNICEF	Denmark / Switzerland
University College London	UK
University of Leeds	UK
USA NAC	USA
VABIOTECH	Viet Nam
Viroclinics	The Netherlands
WHO AFRO	Congo
WHO EMRO	Pakistan / Jordan
WHO EURO	Denmark
WHO HQ	Switzerland
WHO PAHO	USA
WHO SEARO	India / Indonesia
WHO WPRO	Philippines

Global Polio Eradication Initiative
World Health Organization
20 Avenue Appia
1211 Geneva 27, Switzerland

www.polioeradication.org

POLIO GLOBAL ERADICATION INITIATIVE