



Global OPV Stockpile Strategy 2022-2026

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POLIO | GLOBAL
ERADICATION
INITIATIVE

Contents

Acronyms and Abbreviations.....	2
Executive Summary.....	3
Risks and proposed mitigation strategies.....	5
Conclusion	5
Background.....	6
History	6
Governance and Management	6
2022-2026 Strategic Objectives	8
I. 2022-2026 Supply Plan	9
II. Global OPV Stockpile plan and budget	11
III. OPV production landscape.....	12
IV. Poliovirus Containment and Implications for OPV Supply	14
V. Enabling Activities (Normative Work and Capacity Building).....	16
Risks and Mitigation	16
Lack of supplier diversification and limited supply capacity:	16
Uncertainties associated with polio epidemiology and outbreak response quality.....	17
Inability to diversify donor base for the Global OPV Stockpile and adequately finance it.....	17
Low Sabin OPV uptake.....	Error! Bookmark not defined.
Long lead-times for OPV production.....	17
Looking Ahead: Key Decisions and Milestones.....	17
Appendix 1: Global OPV Stockpile planning horizon and objectives	19
Appendix 2: Detail on OPV2 Demand Estimate Scenarios	21

Acronyms and Abbreviations

CMO	Contracting Manufacturing Organization
DG	WHO Director General
EUL	Emergency Use Listing
GAP III	Global Action Plan to Minimize Post-Eradication Poliovirus Facility-Associated Risk, Third Edition
GAP IV	Global Action Plan to Minimize Post-Eradication Poliovirus Facility-Associated Risk, Fourth Edition
GMP	Good Manufacturing Practices
GoI	Government of India
GPEI	Global Polio Eradication Initiative
IHR	International Health Regulations
IPV	Inactivated Polio Vaccine
fIPV	Fractional Inactivated Polio Vaccine
sIPV	Sabin Inactivated Polio Vaccine
IVB	WHO Department of Immunization, Vaccines and Biologics
NAC	National Authority for Containment
NRA	National Regulatory Authority
OPV	Oral Polio Vaccine
bOPV	Bivalent Oral Polio Vaccine
mOPV1	Sabin Monovalent Oral Polio Vaccine Type 1
mOPV2	Sabin Monovalent Oral Polio Vaccine Type 2
mOPV3	Sabin Monovalent Oral Polio Vaccine Type 3
nOPV1	Novel Monovalent Oral Polio Vaccine Type 1
nOPV2	Novel Monovalent Oral Polio Vaccine Type 2
nOPV3	Novel Monovalent Oral Polio Vaccine Type 3
tOPV	Sabin Trivalent Oral Polio Vaccine
ntOPV	Novel Trivalent Oral Polio Vaccine
PV1	Poliovirus Type 1
PV2	Poliovirus Type 2
PV3	Poliovirus Type 3
PAHO	Pan American Health Organization
PSWG	Polio Stockpile Working Group
SC	Strategy Committee
SIA	Supplementary Immunization Activity
UNICEF SD	United Nations Children's Fund Supply Division
VAPP	Vaccine-Associated Paralytic Poliomyelitis
aVDPV	Ambiguous Vaccine-Derived Poliovirus
cVDPV	Circulating Vaccine-Derived Poliovirus
iVDPV	Immunodeficiency-Associated Vaccine-Derived Poliovirus
VSG	Vaccine Supply Group
WHA	World Health Assembly
WHE	WHO Health Emergencies Programme
WHO	World Health Organization
WPV	Wild Poliovirus

Executive Summary

The Global Polio Eradication Initiative (GPEI) has made steady progress toward eradication over the last decade. The WHO South-East Asia Region was declared wild poliovirus-free in 2014, and the WHO African Region was certified free of wild poliovirus (WPV) in August 2020. The final steps toward eradication, however, have proven to be the most difficult.

The Polio Eradication Strategy 2022-2026 provides a comprehensive set of actions that will position the GPEI to fulfil a promise that united the world in a collective commitment to eradicate polio. Many of these actions will strengthen and empower the GPEI to meet challenges head on and achieve and sustain a polio-free world.

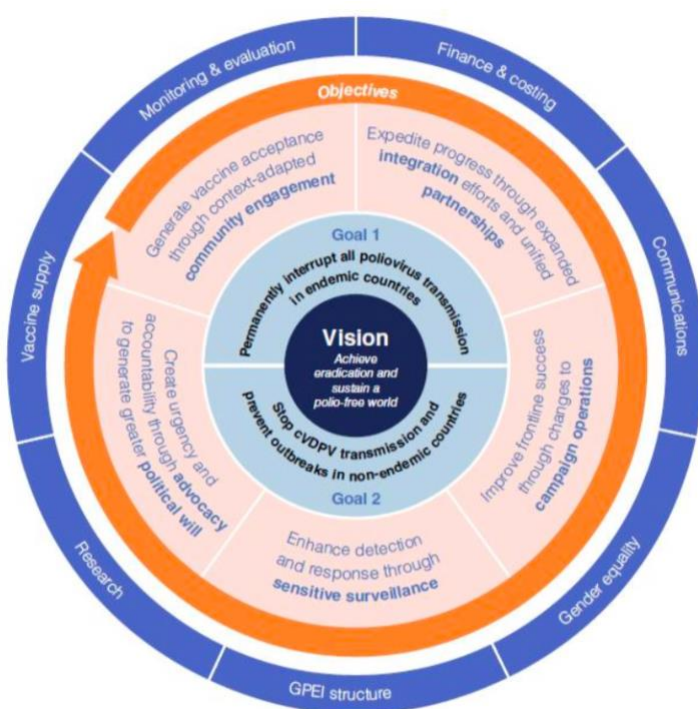


FIGURE 1: POLIO ERADICATION STRATEGY 2022-2026 STRATEGIC FRAMEWORK

The uninterrupted polio vaccine supply is one of the key enabling factors of the GPEI strategy, in which the Global OPV Stockpile plays an essential role (Fig 1).

The global OPV stockpile was established in accordance with the resolutions of the 68th World Health Assembly to ensure GPEI's readiness to respond to poliovirus outbreaks following the withdrawal of OPVs from routine immunization. The stockpile for Type 2 OPV was operationalized in 2015, ahead of the transition from tOPV to bOPV. Since then, more than 1.2B doses of OPV2 have been released from the stockpile to respond to cVDPV2 outbreaks in 30 countries¹. Stockpiles of Types 1 and 3 poliovirus vaccines will be established following the eradication of type 1 and 3 wild polioviruses (WPV) and prior to the global synchronized withdrawal of Type 1 and 3 components of OPV in order to maintain robust preparedness for potential polio outbreaks in the post bOPV cessation era.

¹ As of September 2022

The purpose of this document is to lay out the strategy for developing and managing the Global OPV Stockpile for the period 2022-2026, in support of and in alignment with the GPEI 2022-2026 strategy. Additionally, as the OPV stockpile forms an integral part of the longer-term preparedness for response to polio outbreaks (see Annex 1), this strategy incorporates activities that will prepare the Global OPV Stockpile for the post-OPV cessation period.

Thus, the Global OPV Strategy 2022-2026 consists of three objectives:

1. Establish a Stockpile of Type 1 OPV, Type 3 OPV and new products to prepare for bOPV cessation.
2. Ensure uninterrupted supply of OPV2 to combat ongoing cVDPV2 outbreaks and establish OPV2 stockpile for the period following global certification of wild poliovirus eradication
3. Prepare for potential catastrophic contingencies

Global OPV Stockpile 2022-2026 plan and budget

To progress towards achieving the Global OPV Stockpile objectives, the VSG created a **four-component plan and budget** that sets out the scope of work and resources needed to implement it in the 2022-2026 timeframe:

1. *Component 1: Establishing a stockpile of Type 1 OPV and Type 3 OPV in preparation for bOPV cessation (\$162M).*
2. *Component 2: Supply of OPV2 doses required to stop cVDPV2 transmission and establish a stockpile for the period following global certification of wild poliovirus eradication (\$482M).*
3. *Component 3: Preparedness for potential contingencies (\$61M).*
4. *Component 4: Normative work (100K).*

In total, the VSG currently estimates that the financial resources required to implement the 2022-2026 Global OPV Stockpile strategy will be \$706M.

This is a high-level estimate that may understate future costs associated with potential changes in vaccine and vaccine management costs, larger than expected outbreaks, as well as polio eradication program standards. It may also underestimate the cost required to build early preparedness for bOPV withdrawal from routine immunization with Sabin OPV prior to the availability of Novel OPV 1&3.

Global OPV Stockpile 2022-2026 strategy milestones

Along with the procurement plan and budget, the strategy also maps a number of **critical milestones** that are going to determine the development of the Global OPV Stockpile over the next five years through to the end of 2026. The milestone plan includes targets for supplier diversification, development of novel OPVs, management of Sabin OPVs and the Global OPV strategy reviews (Figure 2).

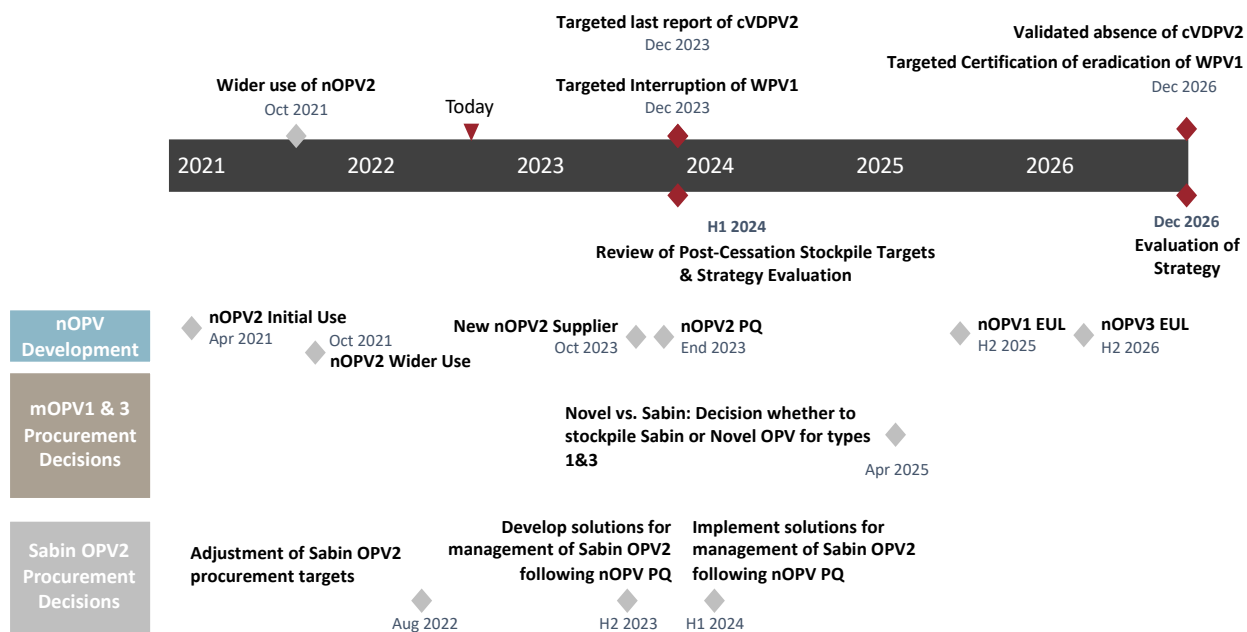


FIGURE 2: GLOBAL OPV STOCKPILE 2022-2026 STRATEGY DECISIONS AND MILESTONES

Risks and proposed mitigation strategies

Several potential risks listed below have been identified by the VSG that could hinder the achievement of the stockpile's strategic objectives.

1. Lack of OPV supplier diversification and limited production capacities.
2. Uncertainties associated with polio epidemiology and outbreak response quality.
3. Inability to diversify donor base for the Global OPV Stockpile and adequately finance it.
4. Large quantities of Sabin OPV2 may expire and be destroyed due to low uptake of this vaccine.
5. Long lead-times for vaccine production.

This VSG has developed and is currently operationalizing strategies for prevention, mitigation, and management of these risks across the lifespan of this strategy.

Conclusion

This document outlines the strategy for 2022-2026 to ensure that the Global OPV Stockpile supports the achievement of GPEI 2022-2026 goals. VSG will continue to monitor whether new programmatic decisions or epidemiology change any of the strategy's core underlying assumptions. If key assumptions change, the VSG will seek guidance and confirmation from the GPEI's Strategy Committee on how the approach to stockpiling should adjust.

Background²

History

The Global OPV Stockpile was established in advance of the global switch from use of tOPV to bOPV in routine immunization. Given the risk that Sabin mOPV2 poses to seeding a VDPV2 emergence in low mucosal immunity settings, SAGE recommended that stockpiles of Sabin mOPV2 be established and maintained at the global level. Planning activities began in 2005 and procurement activities for the global stockpile were initiated in 2009. The 2015 WHA formally endorsed the SAGE recommendation to establish a stockpile and charged WHO to establish a mechanism for timely release of vaccine to respond to outbreaks (see Governance and Management section below for more details). In April 2016, the globally synchronized switch was implemented. Between 2016 and 2021, over 1.2B doses of vaccine have been released from the global stockpile to respond to cVDPV2 outbreaks in 30 countries (see figure below).

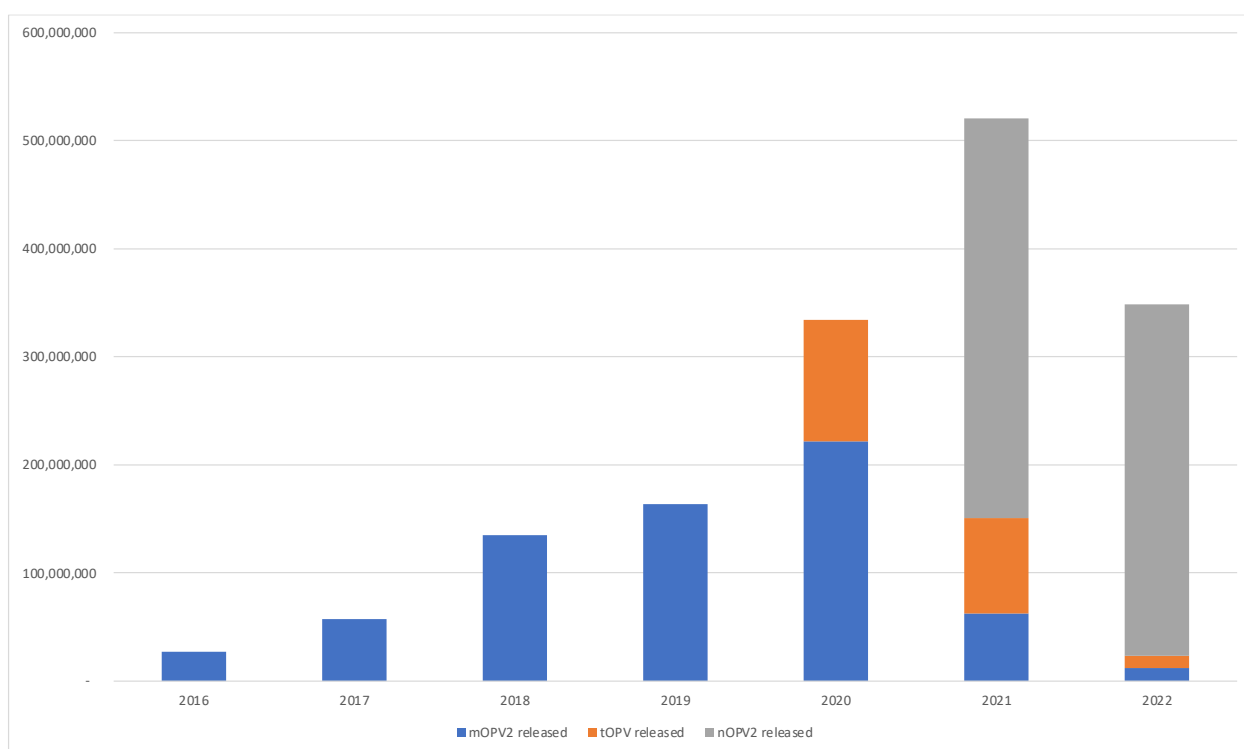


FIGURE 3: RELEASES FROM THE GLOBAL OPV STOCKPILE (APR 2016 – SEP 2022)

Governance and Management

[Resolution A68/21](#) of the World Health Assembly places the management of global OPV stockpiles under the purview of the WHO Director-General (DG). Within the Polio Eradication Department at WHO Headquarters, a team is responsible for managing the stockpile, including oversight, planning, and monitoring. The stockpile is managed jointly by the WHO Polio Eradication Department and the UNICEF Supply Division under bilateral

² For further information on the background of the GPEI Global OPV stockpile, see Harutyunyan V, Quddus A, Pallansch M, Zipursky S, Woods D, Ottosen A, Vertefeuille J, Lewis I. Global oral poliovirus vaccine stockpile management as an essential preparedness and response mechanism for type 2 poliovirus outbreaks following global oral poliovirus vaccine type 2 withdrawal. *Vaccine*. 2022 Mar 10;S0264-410X(22)00204-3. doi: 10.1016/j.vaccine.2022.02.058. Epub ahead of print. PMID: 35282924.

agreement that describe their respective roles and responsibilities. It enables UNICEF Supply Division to engage with the vaccine manufacturers to negotiate supply agreements on behalf of WHO, secure replenishment of the stockpile, and manage vaccine shipments to affected countries.

The VSG is the global program support group that leads planning and management of OPV stockpiles within the GPEI. The VSG reports to the GPEI Strategy Committee (SC) through the Executive Management Unit (EMU), which was formed to coordinate inputs from global and regional program support groups. Its responsibilities include quarterly reviews of stockpile status, forecasting and planning of OPV supply, and identification and mitigation of risks associated with polio outbreaks, with input from and consultation with other relevant GPEI Working Groups.

WHA Resolution A68/21 and WHO Executive Board decision EB146/21 Add.1 urged the WHO DG to ensure adequate supplies of OPV2 for PV2 outbreak responses and ensure processes are in place to allocate vaccines distributed from the Global OPV Stockpile equitably and based on evidence.

There are currently two separate processes in place that facilitate the DG's decision to release OPV2 from the Global OPV Stockpile. The first is guided by the Advisory Group on Sabin mOPV2 Vaccine provision (OPV2 AG) and examines country requests for Sabin OPV2-containing vaccines (mOPV2 and tOPV). The OPV2 AG consists of members of the GPEI agencies and independent experts.

The second mechanism includes two stages: verification of country readiness, managed by the nOPV WG, and then advice to the WHO DG on releasing nOPV2 from the Global OPV Stockpile, managed by the ORPG.

- The nOPV WG is a time-limited group responsible for managing and coordinating GPEI's activities to ensure a rapid and effective roll out of nOPV2 for response to cVDPV2 outbreaks. It coordinates the nOPV2 Readiness Verification Team (RVT), which is in charge of reviewing the elements of a country's readiness to deploy nOPV2 in accordance with the EUL requirements and approving the readiness required to begin the process of releasing nOPV2 from the Global OPV Stockpile.
- The ORPG's primary goals are to improve global and regional capacity to respond quickly and effectively to polio outbreaks; to coordinate the deployment of global GPEI resources during an outbreak response; to provide necessary support to country teams in outbreak response management; to provide technical support and guidance to improve SIA quality in priority countries during outbreak response; and to support outbreak preparedness in high-risk countries. The ORPG, in collaboration with the WHO and UNICEF regional offices, reviews and approves the risk assessments including scope of cVDPV2 outbreak responses, and advise the WHO DG on the quantities of nOPV2 required to implement these responses.

Several additional groups play a role in vaccine governance. The PRAG supports the VSG to estimate future demand for OPV2 and the size of the stockpile needed to ensure uninterrupted supply of this vaccine for polio outbreak responses. The SAGE Working group on Polio, while not playing a direct role in stockpile governance and management, provides important guidance that inform the size and composition of the Global OPV Stockpile, OPV2 deployment and replenishment. The VSG also collaborates with the GPEI Finance Management Group (FMG) on Global OPV Stockpile budgeting and financing, as well as the Containment Management Group (CMG) on poliovirus containment within the scope of vaccine production.

2022-2026 Strategic Objectives

The GPEI Global OPV Strategy is intended to guide OPV stockpile development and management in support of and alignment with the GPEI Polio Eradication Strategy 2022-2026: Delivering on a Promise.

The two goals of the GPEI 2022-2026 Eradication Strategy are:

- I. Permanently interrupt all poliovirus transmission in endemic countries
- II. Stop cVDPV2 transmission to prevent outbreaks in non-endemic countries

GPEI's ability to ensure an uninterrupted supply of polio vaccines to support immunization activities is critical to achieving polio eradication program goals. The Global OPV Stockpile is an important mechanism that enables the supply of vaccines to respond to poliovirus outbreaks after the use of OPV in routine immunization has been discontinued.

The key objectives of the Global OPV Strategy during the 2022-2026 period are:

1. Establish a Stockpile of Type 1 OPV, Type 3 OPV and new products to prepare for bOPV cessation.
2. Ensure uninterrupted supply of OPV2 to combat ongoing cVDPV2 outbreaks and establish OPV2 stockpile for the period following global certification of wild poliovirus eradication
3. Prepare for potential catastrophic contingencies (e.g. nOPV2 failure to achieve licensure, rapidly expanding outbreaks exceeding GPEI response capacity).

The below table maps the GPEI 2022-2026 goals against the objectives of the Global OPV Stockpile Strategy

GPEI 2022-2026 Polio Eradication Goal	Global Stockpile Supporting Objective
i. Permanently Interrupt All Poliovirus Transmission in endemic countries	(1) Establish a Stockpile of Type 1 OPV, Type 3 OPV and new products to prepare for cessation (the establishment of OPV1 and OPV3 stockpiles serves as a mechanism to safeguard GPEI progress on wild poliovirus eradication during the post bOPV cessation period)
ii. Stop cVDPV2 transmission to prevent outbreaks in non-endemic countries	(2) Ensure uninterrupted supply of OPV2 to combat ongoing cVDPV2 outbreaks (3) Establish preparedness to potential catastrophic contingencies

TABLE 1: GPEI GOALS AND GLOBAL OPV STOCKPILE OBJECTIVES

This strategy builds on guidance and decisions provided in 2017 following the *Polio Stockpile Program Review* as well as GPEI SC-endorsed OPV2 demand forecasts from 2021 and early 2022 to ensure that the Global OPV Stockpile program appropriately addresses changes in epidemiology (e.g. concurrent circulation of WPV1 and cVDPV2), vaccine innovations (e.g. WHO Emergency Use Listing (EUL) approval of nOPV2) and stockpile funding capacity.

It also builds on the milestones set out in the polio eradication program, including the interruption of WPV1 and cVDPV2 transmission by the end of 2023, followed by global certification of interruption by the end of 2026. A withdrawal of bOPV will follow approximately one year after global certification.

There is an understanding that the above milestones and planning parameters may need to be revised in the future. The timelines for stopping WPV1 and cVDPV transmission may shift and the bOPV cessation timelines and parameters are still to be ascertained by bOPV Cessation Working Group and the post-certification strategy development process. To ensure that this strategy remains responsive to the needs of the Global Polio Eradication Program, the VSG will review the strategy's implementation and the broader polio eradication context at midterm in 2024, with the goal of adapting it to best contribute to the polio eradication goals. In addition, the VSG will annually review and modify the OPV replenishment plan considering changing demand forecasts.

The remainder of this document outlines the key activities required to achieve the strategic objectives of the Global OPV Stockpile strategy:

- I. Develop a **supply plan for 2022-2026** based on the most recent epidemiology to secure the required number of OPV2 doses to respond to cVDPV2 outbreaks, and to establish stockpile of OPV 1,2, and 3 for post bOPV cessation period.
- II. **Estimate the financial resources** required to implement the supply2022-2026 supply plan.
- III. **Assess the current OPV production landscape** and assure that the supplier capacity and diversification required to meet the OPV requirements of the GPEI program are in place.
- IV. Ensure that production of vaccines for the Global OPV Stockpile meets **poliovirus containment standards**.
- V. **Determine the risks** associated with the implementation of the Global OPV Stockpile Strategy and **establish risk mitigation and management plans** to ensure a sufficient, uninterrupted supply of OPVs for the program.
- VI. Outline **critical stockpile milestones and decision points** for the stockpile strategy period

I. 2022-2026 Supply Plan

Detailed below are the components of the OPV supply plan that will be implemented as part of the Global OPV Stockpile Strategy 2022-2026:

Stockpile objective 1: Establish a Stockpile of Type 1 OPV, Type 3 OPV and new products to prepare for cessation

To prepare for the discontinuation of bOPV in routine immunization following polio eradication, OPV 1 & 3 stockpiles must be established ahead of time to respond to polio outbreaks. The VSG relied on the Polio Stockpile Working Group's (PSWG) 2017 review and the May 2021 planning exercise to estimate the volumes of OPV1 and OPV3 to be included in the stockpile. According to the PSWG work, 1 billion bulk doses and 100 million converted doses of OPV1, as well as 500 million bulk doses and 50 million converted doses of OPV3, should be repositioned in the Global OPV stockpile for the post-bOPV cessation period.

Novel OPVs types 1 and 3 are currently being developed. The precise timing of the products' availability remains unknown due to 1) the general uncertainty associated with product development timelines; and 2) the question of whether nOPV 1 and 3 could be made available for use under the WHO EUL, or if alternatively a full clinical development would be required. Specific risks include potential clinical study implementation challenges and delays including in production or testing of clinical trial material, ethical and other approvals of studies, laboratory capacity for completion of assays, and regulatory (EUL) eligibility of the vaccines based on phase II data, or the requirement to provide a full data set for licensure and prequalification based on phase III data should EUL no longer be applicable. With these caveats in mind, current projections are that

should EUL be granted to these vaccines based on phase II study data, nOPV1 may become available by mid-2026 (dossier submission planned for Q4/2025), followed by nOPV3 availability in early 2027 (dossier submission planned for Q1/2026). If these vaccines are not considered eligible for EUL and if full clinical development is required before use, WHO Prequalification is tentatively expected in 2028 / early 2029 for both nOPV1 and nOPV3. In addition, a combination novel vaccine is being developed, with WHO PQ approval anticipated by mid-2029.³ These timelines will be reviewed and updated in mid-2024. Depending on the timing of nOPV1 and 3 availability and timing of bOPV withdrawal, Sabin OPV1 and 3 may need to be provisionally stockpiled first to secure supply capacity and meet expected bOPV withdrawal readiness criteria, with nOPV1 and 3 stockpiling occurring later. (For more information, see the budget section.)

Stockpile Objective 2: Ensure uninterrupted supply of OPV2 to combat ongoing cVDPV2 outbreaks

Continued cVDPV2 transmission jeopardizes achievement of the GPEI 2022-2026 strategy goals. Having a sufficient supply of OPV2 to respond to cVDPV2 outbreaks is a critical enabler of achieving goal two of the global polio strategy. To ensure effective planning of OPV2 supply, the VSG, with assistance from LSHTM, developed a model-based demand forecast of the vaccine for the period 2022-2026. The model, at a high level, reflects a low risk tolerance for nOPV2 shortages. While accounting for increased nOPV2 stability, it also considers the possibility of significant geographical spread of cVDPV2 and failure to stop cVDPV2 outbreaks by 2023. While this forecast is intended to cover a wide range of scenarios, some events, such as outbreaks requiring continent-wide or multi-region synchronized campaigns, are not covered. If the program decides to respond to such events, the model must be revised. (For more information on the forecast model and its methodology, see Appendix 2). On January 26th, 2022, GPEI SC approved this forecast as a basis for planning of the Global OPV Stockpile replenishments.

Stockpile Objective 3: Prepare for potential catastrophic contingencies

Given that nOPV2 is not yet fully licensed and prequalified and is supplied via the WHO EUL mechanism, the SC approved a strategy in early 2022 under which the program would continue stockpiling Sabin OPV2 as a backup in the event of nOPV2 WHO prequalification delay or failure, as well as in the event of acute nOPV2 shortages. The VSG estimates that supply of Sabin OPV2 would be required in 2022-2023, followed by a phase out of this vaccine from the stockpile in the event of successful nOPV2 prequalification.

Table 2 depicts the Global OPV Stockpile supply plan for the duration of this strategy. Planning for an additional year 2027 was included to ensure a smooth transition of the Global OPV Stockpile to the Post Certification period. Actual annual supply plans will be based on this multi-year plan but will be adjusted as needed to reflect changes in OPV demand forecasts, as well as polio outbreak response policies and standards.

M doses	Presentation	Product	2022	2023	2024	2025	2026	2027	TOTAL
1. Type 1 and 3 OPV Stockpile	Bulk	OPV1	-	-	-	500	500		1,000
		OPV3	-	-	-	250	250	-	500
	Filled	OPV 1 & 3	-	-	-	-	150	-	150
2. nOPV2	Filled	nOPV	750	433	623	481	502	494	3,283
	Bulk				250	250	250	250	1,000
3. Catastrophic contingencies	Filled	mOPV2 / tOPV	355	490	-	-	-		845

³ Timeline estimates are based on information available May 2023.

TABLE 2: SC APPROVED 2022-2026(27) OPV SUPPLY PLAN

II. Global OPV Stockpile plan and budget

The costing of the activities planned within the scope of this strategy resulted in a four-component budget that outlines the size and distribution of financing required over the course of the strategy's five years:

1. **Establishing a stockpile of Type 1 OPV and Type 3 OPV in preparation for bOPV cessation (\$162M).** The VSG relied upon the 2017 PSWG review and the 2021 SC-endorsed OPV demand scenario to estimate the required number of doses to establish a stockpile for Type 1 and 3 OPV vaccines. As a result, 1B doses of OPV1 and 0.5B doses of OPV3 bulk will need to be prepositioned to meet the need during the post-bOPV cessation period. Of these 100 million doses of mOPV1 and 50 million doses of mOPV3 will be filled and completed by the end of 2026, allowing vaccines to be ready for deployment in the event of an outbreak. The VSG plans to refine these estimates in 2024, once the program is closer to cessation. The figures may be revised sooner as the timelines and parameters for bOPV cessation become clearer.
2. **Supply of OPV2 doses required to stop cVDPV2 transmission (\$482M).** The VSG worked in partnership with LSHTM and ORPG to estimate the required amount of OPV2 needed to respond to VDPV2 outbreaks and permanently interrupt its transmission. (See *Appendix 2* for more details). This exercise estimated that 3,283mds of OPV2 will be needed from 2022-2026, that factors in additional supply to respond to potential contingencies (see *Appendix 2*), at an estimated cost of \$414M. The strategy further assumes the program will build a bulk nOPV2 stockpile of 1B doses, with 750mds being procured in the strategy period at an estimated cost of \$68M.
3. **Preparedness for potential contingencies (\$61M).** Since nOPV2 is used under a WHO EUL under the Public Health Emergency of International Concerns and pending full clinical development, there remains a small risk that nOPV2 could fail to secure full licensure, or that it may be delayed. While the likelihood of this occurring is considered low, given the considerable risk to the program, additional mitigation measures have been included in this strategy. Initially, it was estimated that 845 million doses of Sabin OPV2-containing vaccine would be needed as a backup in case the development of nOPV2 encountered difficulties. This figure was later reduced to 600mds after the risks associated with the nOPV2 were reassessed as lower.
 - (1) **Normative / Capacity Building** – Normative and capacity-building activities are critical enablers for ensuring a sufficient and high-quality distribution of vaccines at country level. A budget of \$100,000 has been planned in this strategy to carry out the necessary activities in this field.

The high-level 5-year costs have been outlined for the four primary dimensions of the global OPV stockpile budget, and the below table highlights the estimated year over year cost.⁴ The 2022 and 2023 budgets reflect annual operational budgets approved by the Polio Oversight Board, while 2024-2026 reflect estimates that will continue to be adjusted based on demand forecasts and production constraints.

⁴ There may be minor differences in the final operational budgets for 2022-2023 based on small adjustments in procurement amounts and calculation of program support costs.

Item	2022	2023	2024	2025	2026	TOTAL
1. Type 1 and 3 OPV Stockpile	\$	\$	\$	\$68	\$94	\$162
2. nOPV2	\$90	\$116	\$100	\$103	\$72	\$482
3. Catastrophic contingencies (Sabin OPV)	\$17	\$20	\$8	\$8	\$8	\$61
4. Normative / Capacity Building	\$.02	\$.02	\$.02	\$.02	\$.02	\$.10
Total Stockpile Costs - Current 2022-2026 Budget	\$107	\$137	\$108	\$180	\$174	\$706
<i>Catastrophic contingencies (Sabin OPV) (included in original MYB but deprioritized in Sept. 2022)</i>	\$	\$88	\$	\$	\$	\$88
Total Stockpile Costs - MYB Prior to Sept 2022 Adj.	\$107	\$224	\$108	\$180	\$174	\$793

TABLE 3: 2022-2026 STOCKPILE BUDGET

It should be noted this estimate for the 5-year multi-year cost to implement the stockpile strategy does not account for:

- Potential overlapping procurement of Sabin OPV1 and OPV3 and novel OPV1 and OPV3 to build type 1 and 3 stockpiles. The need to initially stockpile Sabin bulk and finished product and later replace by novels may increase in likelihood if the cessation timeline is shortened by 1 year.
- Potential costs associated with pursuing a 20-dose presentation of nOPV2 should it become available
- Potential inflation of supply prices

III. OPV production landscape

A diversified supplier base is one of the key enablers for the achievement of the objectives of the 2022–2026 stockpile strategy. Another critical enabler is total production capacity.

Because the vaccines distributed through the Global OPV Stockpile are strictly controlled, there is no free market for them. Given this, as well as the high cost of manufacturing these vaccines due to containment requirements, the supplier base for the stockpile is extremely limited. A deliberate strategy of supplier diversification is being pursued to address these challenges and reduce risks to vaccine supply. This may come at the cost of increasing the price of the vaccine since vaccine orders will need to be split across multiple manufacturers, thereby reducing the ability to benefit from production at scale. Furthermore, the GPEI has to be prepared to cover the costs of technology transfer as well as investments to improve the production capacities of potential suppliers to bring them onboard. Finally, longer-term demand visibility must be established and communicated to suppliers in order for them to better plan their production and prioritize against other products.

Novel OPV2

nOPV2 is the first vaccine in history that was deployed under the WHO EUL in 2020. In 2022, only one supplier produces nOPV2. There is a significant risk that nOPV2 supply will be disrupted due to reliance on a single supplier producing vaccine in a single location and a single national regulatory authority. To reduce this risk, the GPEI is funding technology transfer so that a second manufacturer can start producing nOPV2 in 2024. Furthermore, GPEI is supporting the current supplier to increase nOPV2 production capacity and exploring other risk mitigation measures such as establishing a buffer stock of nOPV2.

Figure 3 depicts the projection of nOPV2 production capacity vs. the supply as of November 2022.⁵ Exact figures on both the supply and demand sides are dynamic, with adjustments made on a regular basis. Beginning in 2024, total production capacity will significantly exceed GPEI demand estimates due to efforts to diversify the nOPV supply base.

⁵ Actual 2022 production fell below the projected level indicated in the chart, with some dose releases shifting to 2023.

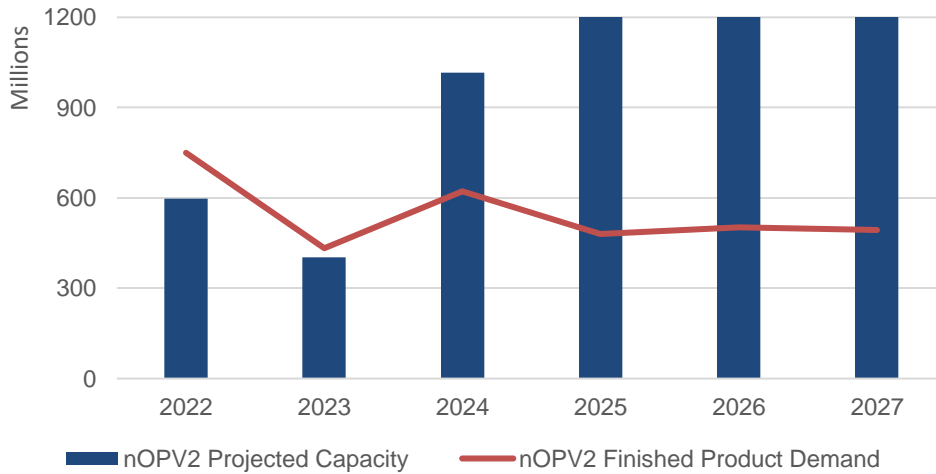


Figure 3: nOPV2 Production capacity (50 dose) vs. 2022-2026 SC approved demand forecast

It will be important to ensure that there are sufficient financial incentives for the second manufacturer to enter and remain in the market. This can be done either through reducing the costs of entering the market; or by ensuring that prices and market shares appropriately allow for an acceptable return on investment, including opportunity costs of resources engaged in the nOPV2 development and commercialization. As the product is solely intended for the Global OPV Stockpile, decisions regarding fulfilment of the procurement plan starting 2023 and beyond, need to factor in this dimension of ensuring supplier diversification in the nOPV2 market.

Sabin OPV2

Two manufacturers were awarded contracts to supply the global program following the first OPV bulk supply tender in 2009. To meet rising demand for mOPV2, the program's supplier pool was expanded to three in 2019. At the moment, all Sabin mOPV2 bulk in the stockpile has been converted, and no manufacturers are producing OPV2 bulk for the Global OPV Stockpile. In 2020, UNICEF and WHO identified a potential supplier of Sabin OPV2 bulk. The decision to award it a supply contract has since been suspended while GPEI assesses whether the current stock of Sabin OPV2 is sufficient to meet the needs of the eradication program.

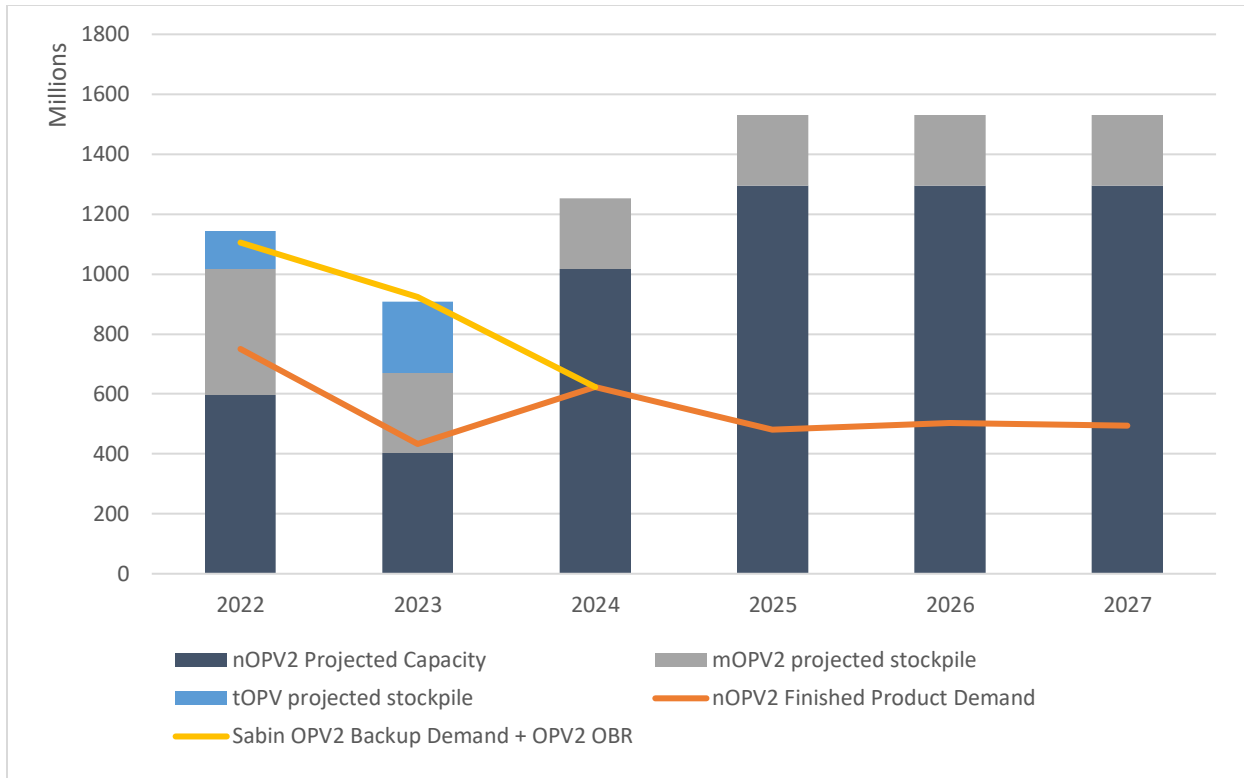


FIGURE 4: NOPV2 PRODUCTION CAPACITY + MOPV2 AND TOPV STOCKPILES VS. 2022-2026 SUPPLY PLAN

OPV1 and OPV3

Based on the current timeline for bOPV withdrawal, the work to engage suppliers of OPV1 and OPV3 is scheduled to begin in 2025, after a decision is made on whether to start stockpiling Sabin or Novel OPV (see Figure 2: Summary of Key Supply Decisions).

Manufacturers engaged in nOPV2 production are expected to be able to supply the Global OPV Stockpile with nOPV1 and nOPV3 once clinically developed and approved by WHO. The activities associated with manufacturing at scale are not yet included and will be determined through a separate assessment to be completed in 2024. This assessment will be informed by factors including manufacturer capacity as demonstrated through nOPV2 production, and emerging information on yields of nOPV1 and nOPV3 based on pilot scale yields and assumptions on capacity at larger scale production.

IV. Poliovirus Containment and Implications for OPV Supply

One of the GPEI's objectives is to ensure proper containment of all live polioviruses to reduce the risk of reintroduction of eradicated wild or vaccine-derived polioviruses from the facilities where they are handled. GPEI 2022-2026 GPEI strategy emphasizes the following measures to achieve this objective:

1. Reducing the number of facilities retaining poliovirus materials
2. Handling of retained polio materials according to international standards
3. Post-certification containment needs and transitioning PV containment

Because the majority of WPV containment breaches documented in recent years have occurred at vaccine manufacturing sites, ensuring full certification for polio vaccine producers as soon as possible is a critical

component of the containment strategy. The WHO Global Action Plan for Poliovirus Containment (GAP IV) provides the most recent guidance on containment requirements at polio vaccine manufacturing sites

The following specific areas related to containment could potentially have considerable impact on supply and will require close monitoring and management by VSG moving forward

1. Current Status of Containment Requirements and Implications for Suppliers

Type 2 Containing Oral Poliovirus Vaccines

As of today, GAP III/GAPIV containment standards apply only to type-2 containing vaccine manufacturing. For the global stockpile, this primarily has implications for type-2 Sabin mOPV2 and tOPV. Based on available safety data, nOPV2 has not been placed under additional requirements under GAP III though it is handled pursuant to GMP BSL-II requirements. With the removal of type 2 OPV from routine immunization in April 2016, manufacturers of Sabin OPV2 have been required to work with their relevant national authority of containment (NAC) to achieve a certification of containment.

To date, most manufacturers that actively produce vaccines under contract to GPEI have entered into the GAP III certification process in compliance with global guidelines. The remaining manufacturers have indicated their plans to exit production of poliovirus vaccines. Given this state of compliance, no changes are actively planned for manufacturers that supply to GPEI. The compliance of suppliers with GAP III will continue to be monitored in coordination with the CWG.

Type 1 and Type 3 Containing Oral Poliovirus Vaccines

WPV3 was declared eradicated in 2019 but with global decisions so far to maintain use of bOPV in routine immunization, type 3 containing vaccines are not currently subject to the same containment requirements as type 2 containing vaccines. Type 3 containing materials such as lab materials are subject to containment requirements. The current 2022-2026 GPEI strategy targets interruption of WPV1 transmission by the end of 2023. If this is achieved, bOPV use is currently planned to continue until 2027. Only once cessation of bOPV is fully implemented producers of type 1 and type 3 containing vaccines need to meet enhanced containment requirements in their facilities. Since this is expected to occur in 2027, it falls outside the scope of this current iteration of the stockpile strategy. If cessation of bOPV2 occurs prior to 2027, the VSG will closely coordinate with the CWG to understand implications for manufacturers to minimize polio vaccine supply disruptions while also maximizing compliance to containment.

2. Areas for coordination during the 2022-2026 period between the VSG and CMG

There are two primary areas of focus for coordination between the VSG and CMG during the 2022-2026 period: i) establishing a smooth process for evaluating whether current or potential suppliers to GPEI are in compliance with or in process of becoming compliant with containment requirements; and ii) ensuring coordinated monitoring of type 2 containing vaccine stocks in the field. This coordination will be achieved through communications and ad hoc teleconferences as required to establish these processes.

3. Potential risks to uninterrupted supply and proposed mitigation strategies

- Risk: Access to and efforts to expand and diversify supply may be hampered if nOPV2 becomes subject to GAP IV requirements.
 - Mitigation: Proactive communication and planning between VSG and CWG, involving nOPV2 manufacturers as and when necessary.

V. Enabling Activities (Normative Work and Capacity Building)

The work on developing norms and standards for the Global OPV Stockpile is an essential part of this strategy, which allows for the timely supply of high-quality vaccines in response to poliovirus outbreaks.

Furthermore, VSG will support capacity building activities to ensure that the aforementioned norms and standards are learned and followed throughout the OPV supply chain, from vaccine production and storage to vaccine withdrawal and utilization.

The following is a non-exhaustive list of the key normative documents, developed by the VSG, currently posted on polioeradication.org:

- Vaccine Request Forms (for each vaccine – mOPV2, tOPV and nOPV2 – in a range of languages).
- Cold chain logistics and vaccine management during SIAs.
- Technical guidance on vaccine management, monitoring, removal and disposal for type-2 containing vaccines.
- GPEI position statement: use of the novel oral polio vaccine type 2 in light of shelf-life of 12 months or less.

These documents are updated to align with any changes, e.g. new wastage requirements or new outbreak response SOPs.

Key capacity-building activities include:

- Remote and face-to-face trainings for Cold Chain Logistics and Vaccine Management (CCL/VM) professionals (including guidance on operation in the context of the Covid-19 pandemic).
- Introductory webinars for each country team on the use of type-2 containing vaccines in advance of developing their outbreak response plans.
- Preparing standardized training materials and job aids for the in-country pre-campaign capacity building for supervisors and vaccinators.
- Documenting and sharing lessons learned.
- Establishing a CCL/VM community of practice by introducing technical web forums and webinars.

Risks and Mitigation

Risk mapping and mitigation is a key activity undertaken as part of this strategy, which aims to improve the predictability and reliability of OPV supply in response to poliovirus outbreaks in the post-OPV cessation period. The following are the risks that GPEI will manage between 2022 and 2026.

Lack of supplier diversification and limited supply capacity:

The number of manufacturers producing bulk Sabin OPV for the GPEI has decreased in recent years. By the end of 2022, all three Sabin OPV2 suppliers will have depleted their Sabin OPV2 bulk stocks. Two of the three Sabin OPV2 stockpile manufacturers intend to phase out mOPV2 stock management by 2023 and 2025, respectively. For nOPV2 the GPEI is currently dependent on a sole supplier, and therefore one country of production and one national regulatory authority. This limited supplier base poses a significant risk to nOPV2 supply. (Refer to the “**OPV production landscape**” section for description of measures undertaken to manage this risk.

Uncertainties associated with polio epidemiology and outbreak response quality.

The dynamics of cVDPV2 outbreaks and the GPEI's ability to effectively respond to them have a significant impact on OPV2 demand estimates. The Global OPV Stockpile supply plan for the period 2022-2026 includes additional vaccine supply to mitigate negative impact in the event of an unexpected increase in OPV2 demand due to large-scale outbreaks or changes in GPEI policies necessitating the implementation of large-scale campaigns targeting a broader age group population.

VSG will collaborate closely with PRAG, ORPG, and other groups to review Global OPV Stockpile planning parameters on an annual basis and adjust the replenishment plan accordingly. Extraordinary reviews will be conducted in response to any unexpected change in context that affects demand for vaccines supplied through the Global OPV Stockpile.

Inability to expand donor base for the Global OPV Stockpile and to adequately finance it

In general, GPEI is still mobilizing funding for the five-year budget, which has a projected shortfall in 2023 and beyond. Predictable funding will be especially important for implementing this strategy because the program will need to make binding commitments far in advance to secure OPV production capacity and timely vaccine supply.

The VSG will continue assisting FMG in identifying and enabling alternative sources of financing for the Global OPV Stockpile in order to address stockpile financing challenges. This will be accomplished by sharing data and assisting in the development of proposals and other materials to support the FMG's fundraising efforts.

Large quantities of Sabin OPV2 may expire and be destroyed due to low uptake of this vaccine.

The Sabin OPV2 remains one of the important tools in the GPEI inventory. However, uptake of the vaccine has been low since 2021 with the introduction of nOPV2, despite that it remains recommended for the use in outbreak responses by the Strategic Advisory Group of Experts on Immunization (SAGE) and notwithstanding shortages of the nOPV2 throughout 2022. This elevates risks in terms of delaying responses to polio outbreaks, overstocking of Sabin OPV2 vaccines, and loss of this vaccine due to expiry.

To mitigate these risks VSG is working with the GPEI SC and global support groups to adjust demand estimates and supply of Sabin OPV2. In addition, the group will continue its advocacy and technical support to maximize uptake of Sabin OPV2 where appropriate. Advance preparations are being made for long-term storage and utilization of this vaccine.

Long lead-times for OPV production

Production of vaccines have been disrupted in recent years. The factors responsible for these disruptions are expected to continue in the future. In order to accommodate these challenges, the VSG extended supply lead times in its planning from 6 to 12 months to account for potential continued increased production leadtimes.

Looking Ahead: Key Decisions and Milestones

There are a number of key decisions during the 2022-2026 stockpile period. The VSG will present recommendations on these decisions close to each decision deadline to allow for the most comprehensive information to be presented to the SC (e.g. latest epidemiology and corresponding demand estimates). The anticipated key decisions during this period are described below and summarized in Figure 2.

- 1. Novel vs Sabin: Decision whether to stockpile Sabin or Novel for types 1&3** – depending upon preferences of the program and timelines for eradication and cessation, a decision will need to be taken on whether to stockpile novel or Sabin products. The preferred approach will be evaluated

further by the VSG and brought to the SC closer to the time of post-cessation stockpiling. Based on development timelines for novel stand alone products and cessation, there may be a need to initially store Sabin and then transition to novel.

2. **Decision to store or move and destroy Sabin OPV2 post-2023** – as is detailed in the market dynamics section, suppliers discontinued production of Sabin mOPV2 before the switch due to declining demand and increasing requirements to meet containment standards. One manufacturer has indicated that continued storage beyond 2023 is no longer possible. Accordingly, the WHO has launched an RFP to evaluate the potential costs of moving and storing the Sabin mOPV2 at another location. Based upon the findings of the RFP, the VSG will work with the WHO to present a proposal for how to approach handling the Sabin mOPV2.
3. **Store or destroy Sabin mOPV2 post-2025** – similar to decision #2, a current manufacturer has expressed their intent to no longer store Sabin mOPV2 post-2025. A decision will need to be taken in 2024 whether to seek to move the Sabin mOPV2 or request the manufacturer to destroy the supply.

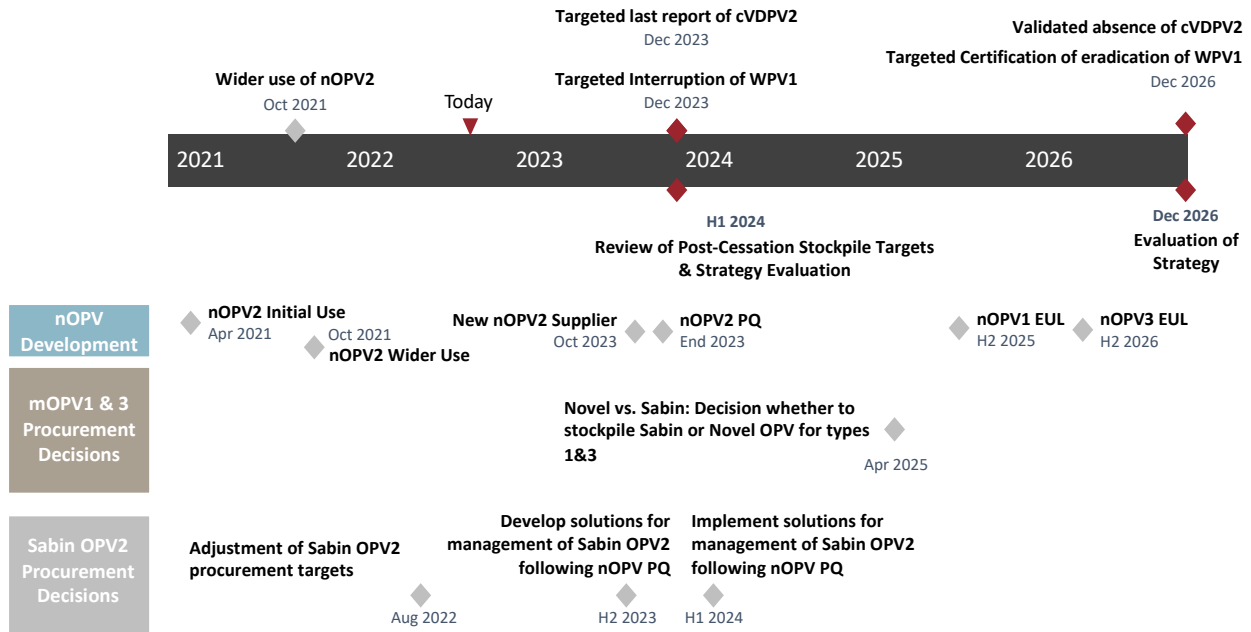


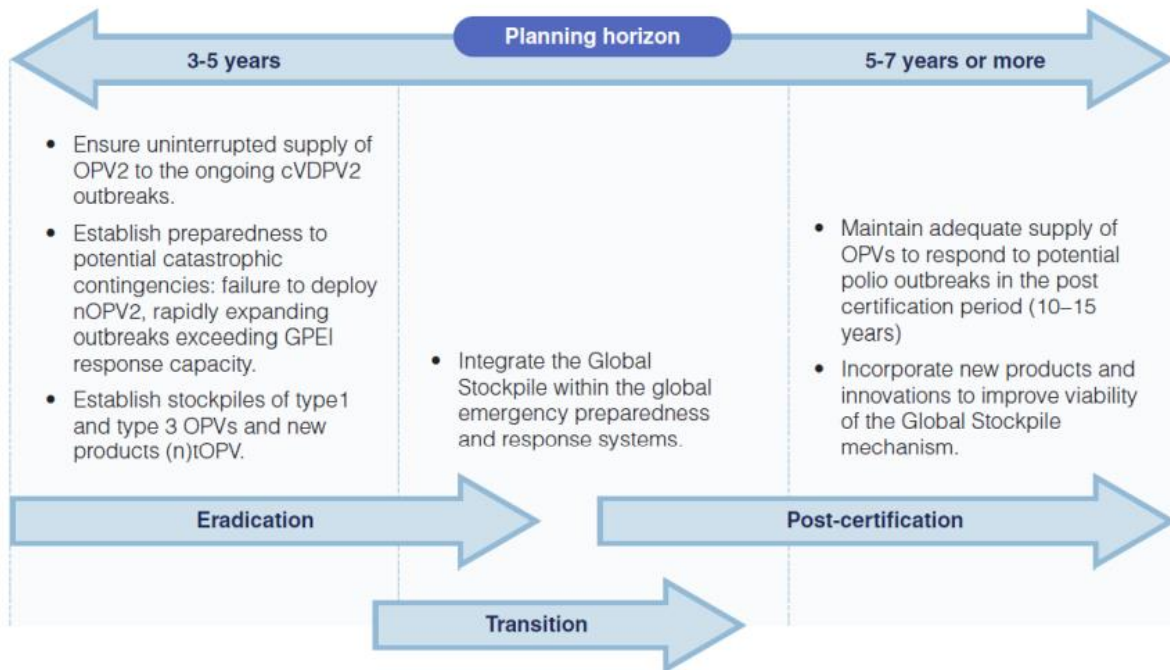
FIGURE 5: GLOBAL OPV STOCKPILE 2022-2026 STRATEGY DECISIONS AND MILESTONES

GENDER:

In terms of gender balance, OPV chain management is one of the better positioned sectors. According to recent Gartner surveys, women make up approximately 40% of the global supply chain workforce, but only approximately 30% of management positions. When responding to outbreaks, GPEI's cold chain logistics and vaccine management team collaborates with MoHs and other local partners. GPEI is providing equal opportunities to male and female candidates when filling vaccine management positions as part of this collaboration.

GPEI does not discriminate against any gender in terms of training opportunities, and it makes concerted efforts to attract female-owned businesses in both online and face-to-face training programs.

Appendix 1: Global OPV Stockpile planning horizon and objectives



Appendix 2: Detail on OPV2 Demand Estimate Scenarios

Model Framework

The model consists of a simulated cohort in space-time where population immunity, VDPV2 emergences and outbreak responses are tracked for each month. All districts within the AFRO and EMRO WHO region are modelled. Starting with the first year of the model (2022) we assume that there are 21 cVDPV2 outbreaks that will require an outbreak response. In 2022 a majority of outbreak responses are with nOPV2, but we assume up to 130million doses of mOPV2/tOPV are used. For the outbreak responses detailed in **Scenario 1** we model the scope, SIA number and success under the following criteria;

- Scope: small (1.3 million doses) or large (3 million doses), with some variability
- SIA number; between 2-4 SIAs per outbreak are assumed, with some variability
- Success: No further detections are observed the following year in 80% or 60% of outbreaks. For those where detections are observed, responses continue into the next year.

In addition to the targeted outbreak responses, we include the possibility large-scale outbreak responses (included in **Scenario 2**) that consist of SIAs reaching 100million children per year in 3 SIA rounds, totaling 300million doses. While it is hoped that large responses would reduce transmission, the model conservatively assumes the same breakthrough and spread as from the targeted SIAs.

An upper limit of vaccine stockpile of 500million doses was set for 2022-2023. If the number of doses exceeds this limit the large-scale outbreak responses are smaller in size (determined by the available doses).

Each of the outbreak responses result in OPV2 use within specific districts. We assume that the SIAs increase population immunity, and have the potential to seed new VDPV2 emergences. The number of nOPV2 and mOPV2 doses used per district are tracked as inputs to estimate future emergence risk. The SIAs for each year are calculated from the emergent events forecast for that year, based on activities from previous time periods. The SIA activities are modelled up to 2027. During this time it is expected that the age groups targeted in SIAs will need to increase to 0-9 years where there are cohorts above five years of age that have not received OPV2 vaccines, and that population size will increase as projected by UN population division. If SIAs are selected in a district that has not been vaccinated since 2016, we assume an expanded age.

Several iterations (n=100) of the model are run to account for the variability in SIA activities and resultant emergent events. We report the 90th percentile of iterations in the document as conservative estimates, but full measures of uncertainty are available.

There are some limitations to this modelling approach. We consider only cVDPV2 outbreaks within the AFRO and EMRO regions. This decision was taken because the majority of cVDPV2 outbreaks have occurred in these WHO regions, and the epidemiology of emergence and spread is better understood. Outbreaks may occur outside of these regions 2023-2027 but are more challenging to predict; however, the response required will likely be equivalent to the SOPs, and the recommendation to select Procurement Scenario 2 should mean that sufficient nOPV2 doses will be available for response. Specific details of geographic range of infections are not modelled, and the timeliness of responses are not explicitly modelled; the main outcome modelled is the proportion of outbreaks that continue beyond 365 days. Should a majority of outbreaks continue beyond 365 days the model will likely underestimate the nOPV2 doses required. The impact of short-term 'stockouts' are not modelled, but with increasing nOPV2 availability and improved planning it is hoped this this will become less of a limiting factor.

Parameter Estimation from Data

The prediction of VDPV2 emergencies are reliant on knowing the seeding risk of vaccines and the effect of population susceptibility. District level data on population immunity, SIA activities and VDPV2 emergencies from Jan 2013 to Sep 2021 were used to estimate the seeding risk, scaled by population immunity. From this analysis we estimate that VDPV2 detections were observed approximately 4.6 (95% CI 3.7-7.3) months after SIA activities, consistent with previously derived estimates. Population immunity plays a large role in emergence risk, as illustrated by an increase in emergencies since 2019 despite a reduced number of mOPV2 activities. The emergence risk estimates for mOPV2 are used for mOPV2 SIAs. To account for the remote possibility of VDPV2 emergencies associated with nOPV2 use a scaling factor of 0.01 was applied the mOPV2 emergence estimates.

Updated demand forecasts for outbreak response

The model is an update of one used to inform the OPV2 replenishment plan that the GPEI Strategy Committee approved in May 2021. It updates several important assumptions from the previous demand model, including:

1. The target population for the demand estimates was raised to <10 years old (where SIAs are implemented in districts with no Type 2 SIAs since 2016) to account for the growing number of children who have not received OPV2.
2. The model recalibrated risk of mOPV2 reversion based on recent experience, and allows for nOPV2 reversion (1% relative risk compared to mOPV2).
3. Wide-scale cVDPV2 outbreak response campaigns are included in the estimates as a specific Demand Scenario (DS2).
4. The model is based on more realistic assumptions regarding the timeliness and quality of outbreak responses (20-40% of new outbreaks continue beyond a year).
5. Demand forecasts (pre-addition of wastage (x1.33) and safeguard) include the impact of limited nOPV2 production capacity between 2021 and 2023.
6. Demand is conservatively estimated by using the upper 90% of simulations.
7. Scenarios include a 150mds 'safeguard' in annual demand estimates to account for unexpected events.

Further modelling details are provided in the Appendix.

Three OPV2 demand scenarios were developed as outlined below.

Demand Scenario 1 (DS1) (mds): Regulatory Success of nOPV2 + Limited Scale Campaigns

Outbreak response when VDPV2 is detected, following current SOP. Assumes no wide-scale outbreak response campaigns.

<i>M Doses</i>	2022	2023	2024	2025	2026	2027
Model (90 th percentile)	167	70	94	57	44	41
Wastage	55	23	31	19	15	14
Safeguard (incl. wastage)	150	150	150	150	150	150

Total	372	243	275	226	209	205
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Demand Scenario 2 (DS2) (mds): Regulatory Success of nOPV2 + Wide Scale Campaigns

Outbreak response when VDPV2 detected, following current SOP. Includes adequate supply for wide-scale outbreak response campaigns. These could include detections beyond outbreak response zones, or the need for repeated responses in the same areas due to low coverage and/or low efficacy.

<i>M Doses</i>	2022	2023	2024	2025	2026	2027
Model (90 th percentile)	451	213	356	249	265	259
Wastage	149	70	117	82	87	85
Safeguard (incl. wastage)	150	150	150	150	150	150
Total	750	433	623	481	502	494

Demand Scenario 3 (DS3) (mds): Regulatory Failure of nOPV2 + Its Withdrawal from Programme

Regulatory failure of nOPV2 and return to mOPV2 use. This scenario is taken from the previous CRTT stockpile modeling effort in 2021, approved by the SC in May 2021, and involves responses according to existing practice. Estimates include wastage and safeguard equivalents for Sabin OPV. Listed doses are for outbreak response only, and additional supply would be needed for reintroduction into routine immunization or any required catch-up campaigns. Estimates include a 1.15 wastage factor.

	2022	2023	2024	2025	2026	2027
Total	355	490	660+	660+	660+	660+

Demand Scenario 3 (DS3) (mds): Regulatory Failure of nOPV2 + Its Withdrawal from Programme

Regulatory failure of nOPV2 and return to mOPV2 use. This scenario is taken from the previous CRTT stockpile modeling effort in 2021, approved by the SC in May 2021, and involves responses according to existing practice. Estimates include wastage and safeguard equivalents for Sabin OPV. Listed doses are for outbreak response only, and additional supply would be needed for reintroduction into routine immunization or any required catch-up campaigns.

	2022	2023	2024	2025	2026	2027
Total	355	490	660+	660+	660+	660+