Polio Vaccine Security Framework

1 Executive Summary

Long-term polio vaccine security – *the timely, sustained, and uninterrupted supply of suitable types of affordable, quality-assured polio vaccines* – is essential in the global effort to achieve and maintain a polio free world. However, fragmented approaches and short-term planning pose considerable challenges to securing long-term polio vaccine security.

This framework is designed to enhance the efforts of existing structures and workstreams within the Global Polio Eradication Initiative (GPEI) and other stakeholders by improving communication and coordination on vaccine security. Ensuring vaccine security is crucial for maintaining a timely, sustained, and uninterrupted supply of affordable, quality-assured polio vaccines in the global fight to achieve and sustain a polio-free world. However, challenges such as fragmented approaches, short-term planning, a dynamic policy environment, and a diverse product pipeline present significant risks to long-term vaccine security. This framework emphasizes the need for alignment and coordination across key polio operational domains, including Poliovirus Containment, Research and Development, and Vaccine Manufacturing and Supply. It also underscores the critical role of normative frameworks and policies in shaping long-term vaccine strategies that guide these operational areas. Additionally, it highlights the importance of cross-cutting elements such as financing and access to resources, along with the integration of communication, coordination, and advocacy efforts, as essential enablers for achieving vaccine security. To secure long-term vaccine supply, it is imperative to enhance alignment and strengthen coordinated efforts across workstreams and with stakeholders, including vaccine manufacturers.

Recognizing that vaccine security is an ongoing endeavor, requiring continuous monitoring and adaptation, this framework will undergo regular updates and revisions. Initially, the management of the framework will be carried out by the GPEI Vaccine Supply Group (VSG).

2 Introduction

Ensuring polio vaccine security – *the timely, sustained, and uninterrupted supply of suitable types of affordable, quality assured polio vaccines* – during the course of the Global Polio Eradication Strategy 2022-2029[1] and beyond, is vital for effectively protecting against poliomyelitis. Polio vaccine security plays a pivotal role in the success of eradication efforts, maintaining the gains achieved thus far, and preventing the re-emergence or re-introduction of the virus. However, the evolving nature of poliovirus epidemiology, poliovirus genetics and consequently GPEI timelines, a dynamic policy environment, and diverse product pipeline present unique challenges for securing long-term polio vaccine security. Fragmented approaches and/or parallel objectives between workstreams and short-term planning and

[1] GPEI-Strategy-extension-20241113.pdf

funding horizons also pose risks to ensuring sufficient quantities of vaccines for the polio programme.

Several recent examples illustrate vulnerability in polio vaccine supply, especially during periods of transition, and its consequences on programmatic objectives. For example, a shortage of Inactivated Polio Vaccine (IPV) following the 2013 SAGE recommendation that all countries should have at least one dose of IPV in their routine programmes in advance of the trivalent Oral Polio Vaccine (tOPV) (containing serotypes 1, 2 and 3) to bivalent Oral Polio Vaccine (bOPV) (containing serotypes 1 and 3) switch in 2016 was due to an underestimation of the complexity of scaling up the production of biological products within the required timeframe. It resulted in programmatic reprioritization of allocation of available vaccine, leading to interruption of vaccine supply to countries that had already introduced but were considered less at risk for reintroducing polio, reprioritized / delayed introductions, low initial coverage, and missed children, with an estimated 43 million children subsequently requiring catch-up IPV vaccination.[2]

Following the global phase-out of the type 2 component from the trivalent oral polio vaccine (tOPV), shortages in the type 2 vaccine-containing stockpile intended for managing outbreaks of circulating vaccine-derived poliovirus serotype 2 (cVDPV2) initially arose from inadequate forecasting, e.g. initially forecasting based on historical consumption in a situation where demand doubled between years, leading to supply shortages. More recently, the situation has been exacerbated by production and testing issues linked to reliance on a single supplier. This led to a significant shortfall, with an estimated 193 million doses of nOPV2 missing from the 2022–2023 supply targets. Furthermore, the implementation of SAGE recommendations—which urged immediate outbreak responses using available vaccines rather than waiting for nOPV2—was largely unsuccessful. Many member states, encouraged by the advantages of nOPV2, hesitated to extensively use mOPV2, resulting in delayed responses to cVDPV2 outbreaks. Such delays risk further propagation of the virus.

(More detailed information on these supply shortages is available in Annex A).

Lessons learned from the 2016 switch from tOPV to bOPV have informed the rationale for this polio vaccine security framework, particularly as the program prepares for the critical milestone of bOPV cessation. These lessons underscore the importance of providing the polio program with clear visibility on strategies, including real-time engagement with manufacturers on policy decisions. Long-term demand visibility is crucial for communicating timelines with sufficient lead time, enabling manufacturers to make informed decisions on vaccine development and production, while also considering containment requirements where applicable. Proactive communication regarding changes in containment requirements is essential, allowing timely upgrades of facilities or the establishment of new sites to secure supply (such as in cases where waivers for nOPVs and S19 are withdrawn) Effective communication, coordinated planning, economic incentives and risk mitigation strategies are essential to prevent premature and/or unanticipated withdrawal of manufacturers from the polio vaccine market. These same strategies are also critical to avoid excess production of vaccines which are not needed by the program, which can result in financial losses if

[2] Sutter RW, Cochi SL. Inactivated Poliovirus Vaccine Supply Shortage: Is There Light at the End of the Tunnel? J Infect Dis. 2019 Oct 8;220(10):1545-1546. doi: 10.1093/infdis/jiy739. PMID: 30958545; PMCID: PMC10547123.

manufacturers have produced in advance of purchase agreements and demand does not materialize ("at-risk production"). Such events could have a negative impact on the achievement of programmatic objectives.

RECOMMENDATIONS FROM THE CHAIRS OF THE ADVISORY GROUPS
Polio research and commodities

7. CAG recommends the development of an inclusive strategy for new polio vaccines including research-safe and cost-effective production technologies- and containment. Whenever possible, CAG recommends the development of new vaccines that would require less stringent containment requirements to provide incentives to newer developments. This should involve WHO Containment (CNT) programme, WHO Polio Research (PRD) programme and the GPEI Vaccine Supply Group (VSG).

8. CAG recommends the development of an inclusive blueprint for polio research, if not already available with approaches for accelerating research in new polio products (polio vaccine, diagnostics and treatment) and other initiatives, expedited regulatory pathways such as using the WHO Emergency Use Assessment and Listing Procedure (EUAL), containment consideration, where applicable and other approaches modelled after the WHO R&D Blueprint for Action to Prevent Epidemics for research on epidemic-prone emerging pathogens.

Advisory groups to the GPEI have stressed the necessity for explicit attention to long-term planning and alignment concerning polio vaccine supply and demand. The Chairs of the Advisory Groups on Global Certification Commission and Containment Advisory Group (CAG) offered explicit recommendations in January 2023 for an inclusive approach to introduction and transition of polio vaccines. These recommendations emphasize the need for collaboration among the GPEI working groups managing polio vaccine supply, poliovirus containment, and polio research and product development. They emphasized the need for a polio vaccine specific blueprint to plan research into new polio products, including regulatory pathways, containment considerations, and other approaches. [3]

Furthermore, the Independent Monitoring Board (IMB) for Polio Eradication and the Polio Transition Independent Monitoring Board (TIMB), emphasized the importance of alignment and coordination in regard to vaccine supply. These groups recommended shifting towards longer-term planning; awareness of eradication conditionality of timelines and key milestones (elimination, OPV cessation, stockpile, outbreak response, global eradication of cVDPV), ensuring collaboration for a coordinated post-certification vaccine strategy through the established goals (e.g., containment goal end-2026); and the importance of global collaboration on goals, methods, and timelines among countries, international organizations, and vaccine manufacturers to ensure sustainable vaccine supply.[4]

Finally, stakeholder feedback has been taken into consideration in the development of this framework and priority areas recommended for action. Notably, discussions took place with participants during the 22nd Annual Consultation between the GPEI and Poliovirus Vaccine Manufacturers, National Authorities for Containment (NACs), and National Regulatory Authorities (NRAs), during which the participants provided feedback and ideas for consideration in the development of this framework. Priorities highlighted by this group of stakeholders focused on forecasting, normative landscape, funding and containment (*see summary in Annex B*).

[3] Report of the Sixth Meeting of the Poliovirus Containment Advisory Group (CAG6), 23-25 January 2023 (https://polioeradication.org/wp-content/uploads/2023/02/CAG6-Preliminary-Report-EN.pdf)
[4] IMB, 22nd Report, Sept 2023 (https://polioeradication.org/wp-content/uploads/2023/09/22nd-Report-of-The-Independent-Monitoring-Board-IMB.pdf); TIMB, 6th report, July 2023 (https://polioeradication.org/wp-content/uploads/2023/08/6th-TIMB-report-Ambiguities-and-certainties-20230731.pdf)

3 Goal and Objectives of a Polio Vaccine Security Framework

Goal of the Polio Vaccine Security Framework
To ensure the *timely, sustained, and uninterrupted supply of suitable types of affordable, quality assured polio vaccines* as a cornerstone in the global effort to achieve and maintain a polio-free world.

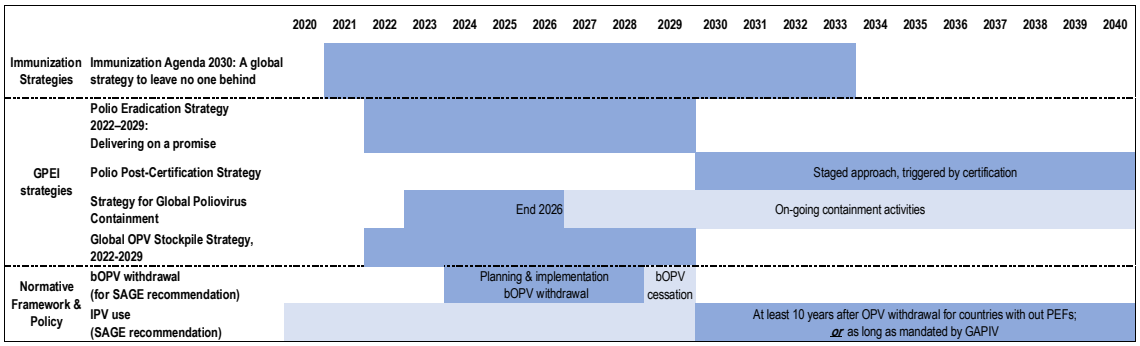
Objectives:

1. **Strengthened Communication, Coordination, and Advocacy:**
    - Foster enhanced communication, coordination, and advocacy efforts to ensure comprehensive awareness of workstreams and coherent action and support for polio vaccine security among global health stakeholders.
2. **Development of a Coherent Normative and Policy Framework:**
    - Establish a comprehensive and aligned normative and policy framework including vaccine supply, containment, and research and development that underpins the long-term use of polio vaccines, ensuring global standards and guidelines are met.
3. **Improved Financing and Access to Resources:**
    - Prevent / mitigate financial risk and identify when and where financing may be required to do so, and improve access to resources across vaccine supply, containment, research, and product development functions to support uninterrupted polio vaccine security.

4 Elements of a Polio Vaccine Security Framework

Cross-coordinated effort and strong communication, including information sharing, across stakeholders is required for achieving the goal of long-term polio vaccine security. This framework builds on and recognizes, but also highlights the need to strengthen, existing resources and accountabilities of different GPEI and partner workstreams and stakeholders. Gaps and inconsistencies exist that present a risk to long-term polio vaccine security. By mapping what already exists (*see summary in Annex C*), on-going efforts, and identifying gaps, this framework proposes a series of concrete actions for strengthening this coordinated effort across stakeholders.

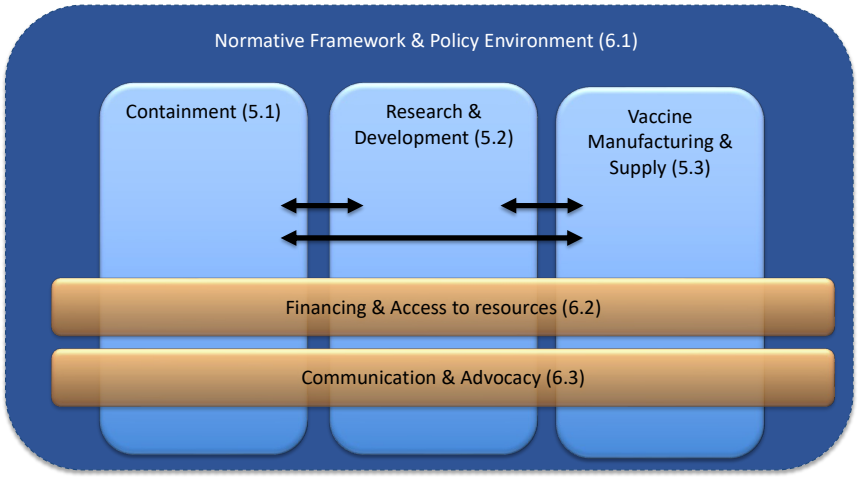
Figure 1: Mapping of strategies and policies related to Polio Vaccine Security (note: timelines presented as applicable at time of drafting this framework, some timelines are under revision and will be noted in future versions) (Links to documents referenced are provided in Annex C).



This framework identifies six main, interrelated elements for achieving polio vaccine security:

- Three independent but interconnected operational workstreams — namely poliovirus **containment** (*section 5.1*), **research and development** (*section 5.2*), and **vaccine manufacturing and supply** (*section 5.3*) —directly impact polio vaccine security.
- **The normative framework and policy environment** (*section 6.1*) play a crucial role in guiding the strategic direction across the entire framework, informing and interacting with the three operational workstreams, while simultaneously adapting to their advancements to inform vaccine policy decisions effectively.
- Two additional key cross-cutting enablers – **financing and access to resources** (*section 6.2*) **as well as communication, coordination, and advocacy** (*section 6.3*) – are integral to supporting these workstreams. These enablers facilitate the seamless integration and implementation of strategies across containment, research and development, and vaccine supply efforts, ensuring that policy directions are aligned with practical needs and developments.

Figure 2: Elements of the Polio Vaccine Security Framework (with corresponding sections in this framework)



Polio vaccine security will not be achieved when focus is too narrow on individual areas of work. These three operational workstreams are at the same time independent and

interconnected; individually and together they are essential for achieving polio vaccine security. As such, the goal of this framework will only materialize when coordinated efforts between these crucially important areas are strongly rooted in operational, strategic and policy domains.

Finally, it is acknowledged that achieving polio vaccine security is not a one-off event given the dynamic reality of the polio programme; it requires continuous engagement, adjustment, planning for different scenarios and monitoring as the epidemiology and product technologies evolve over time. Therefore, it is expected that this framework will need to be regularly reviewed and updated over time.

5 Operational workstreams contributing to Polio Vaccine Security

As noted above, this framework focuses on three independent but interconnected operational workstreams that, together, are critical to achieving polio vaccine security. This section provides an overview of each workstream and proposes actions for each workstream to contribute to strengthening of polio vaccine security now and in the future.

5.1 Poliovirus Containment

Containment refers to biorisk management policies and standards and their implementation towards achieving safe and secure poliovirus containment. The requirements govern laboratories and their staff that handle poliovirus, vaccine production sites, Quality Control sites and other facilities that handle or store polioviruses for polio vaccine production, research, and quality control against the overarching goal of minimizing a facility-associated risk of release of poliovirus directly or indirectly into communities post-eradication[5]. Containment was prioritized through a resolution at the 71st World Health Assembly (2018)[6] and is defined at the strategic and policy level through the GPEI Strategy for Global Poliovirus Containment (2022) and the Global Poliovirus Containment Action Plan, 2022-2024, while at the operational level through the biorisk management standards described in the WHO Global Action Plan for Containment, GAPIV (2022) and others. Stakeholders who decide to retain polioviruses, together with their government and relevant authorities, understand the responsibilities inherent in achieving and sustaining the required facility, immunization coverage, and environmental safeguards and in achieving safe and secure poliovirus containment. The timelines to achieve the containment requirements[7] for the certification of WPV eradication by end-2026 will remain in place independent of the status of eradication[8]. As of the GCC recommendations of November 2023, all viruses are required to move into containment as soon as possible. Facilities retaining WPVs and VDPVs must apply for an ICC

[5] Strategy for Global Poliovirus Containment, pg. 1.
[6] Resolution WHA71.16. Poliomyelitis – containment of polioviruses. In: Seventy-first World Health Assembly, Geneva, 26 May 2018. Geneva: World Health Organization; 2018 (https://apps.who.int/gb/ebwha/pdf_files/WHA71/A71_R16-en.pdf).
[7] Safe and secure containment of WPV retained in facilities, such as laboratories and vaccine manufacturing facilities - all facilities retaining WPVs should have a Containment Certificate, or an Interim Containment Certificate, with a clear end-point for obtaining a CC agreed with the GCC. (Source: Report of the 17th meeting of the Global Commission for the Certification of the Eradication of Poliomyelitis, 26-27 February 2018, Geneva, Switzerland. Available at: https://polioeradication.org/wp-content/uploads/2018/04/polio-eradication-certification-17th-meeting-global-commission-for-certification-of-poliomyelitis-eradication-20180412.pdf)
[8] ** Report of the 24th meeting of the Global Commission for the Certification of the Eradication of Poliomyelitis, 22-23 November 2023, Geneva, Switzerland. Available at: https://polioeradication.org/tools-and-library/policy-reports/certification-reports/global-certification-commission/)

immediately. There are other polioviruses that may be moved into GAPIV containment in the future. These include Sabin 1 and 3 and novel poliovirus strains e.g., nOPV1, nOPV2, nOPV3, S19 as these are also live polioviruses, but currently exempted from containment requirements.

WHO, in coordination with the NACs[9], is supporting implementation of containment at the country level and actively monitoring progress. As of 16 July 2024, 23 countries have reported progress towards poliovirus containment, as illustrated in the table below.[10] This table includes countries that have indicated their intent to retain polioviruses.

Country progress towards poliovirus containment certification

Data as of 16 July 2024

WHO Region	Country	No of facilities designated*	No of facilities with CP†	No of facilities with plans to pursue ICC†	No of facilities with ICC†
WHO Region of the Americas	Canada	2			2
	Cuba	1	1	1	
	USA	24	21	9	3
	Regional Total	27	22	10	5
WHO Eastern Mediterranean Region	Islamic Republic of Iran	1	1	1	
	Pakistan	1	1	0	N/A
	Regional Total	2	2	1	0
WHO European Region	Belarus	1	1	1	
	Belgium	2			2
	Denmark	1	1	1	
	France	11	8	6	3
	Hungary	1			1
	Netherlands	4	3	3	1
	Romania‡,§	1		Not known¶	
	Russian Federation	7	7	7	
	Serbia	1	1	1	
	Sweden	1	1	0	N/A
	United Kingdom of Great Britain and Northern Ireland	2	1	1	
	Regional Total	32	23	20	7
WHO South East Asia Region	Indonesia	1	1	1	
	India	3	3	1	
	Regional Total	4	4	2	0
WHO Western Pacific Region	Australia	1	1	1	
	China	8	1	8	
	Japan	3			3
	Republic of Korea	1			1
	Regional Total	13	2	9	4
	Global	78	53	42	16

Abbreviations: CP: Certificate of Participation; ICC: Interim Certificate of Containment.

*Facilities are designated by ministries of health or another national authorities as serving critical functions requiring the retention of polioviruses. Numbers represent facilities currently designated and does not include those that have withdrawn from the Containment Certification Scheme (CCS) due to cessation of work with poliovirus or otherwise.

†The Containment Certification Scheme includes three stages of containment certification: (1) Certificate of Participation (CP); (2) Interim Certificate of Containment (ICC); and (3) Certificate of Containment (CC). Facilities may only hold one certificate type at point in time.

‡ Country has yet to establish a National Authority for Containment.

§Country has yet to register their facilities in the CCS.

¶Information not yet available at WHO

All facilities retaining polioviruses, for whatever reason, including to maintain polio vaccine security, are expected to enter the Containment Certification Scheme (CCS) process and move through an incremental process that allow facilities to increase compliance with requirements and to finally obtain a Certificate of Containment (CC).

[9] The NAC is responsible for independently auditing and verifying compliance against GAPIV requirements, not in providing direct support with implementation of those requirements at the facility.

[10] WHO publishes updates on country progress towards containment on a quarterly basis, available at https://polioeradication.org/polio-today/preparing-for-a-polio-free-world/containment/

A policy framework and guidance for containment exists and containment certification is progressing. Research and development facilities as well as manufacturers have moved forward in the containment process. Of the 16 Interim Certificates of Containment (ICCs) that have been endorsed by the Containment Working Group (CWG), 43% have been issued to vaccine manufacturers, 36% to research and development laboratories, and 21% to storage only facilities.

Through stakeholder consultation, comments related to containment include:

- Challenges obtaining financial resources to implement containment requirements
- Lack of understanding of the mechanisms for implementing containment certification scheme
- Concerns about duration of existing WHO temporary waivers for containment for nOPVs and S19
- Uncertainties regarding containment requirements for the continued production (or research use) of these products under waivers, as well as the status of future products, given that they are considered live polioviruses, rendering their use incompatible with eradication efforts
- Lack of coordination among global laboratories for testing related to vaccine production (in order to avoid the need for countries to establish their own facilities).
- Concern that lessening containment requirements for some manufacturers while others have moved forward with containment creates an imbalance and unfair marketplace
- Recommendation to include containment prerequisites for WHO prequalification (new and existing ones) and for UNICEF tenders
- Request that any containment policy change needs to be anticipated with enough notice to enable the suppliers to implement in time in compliance with the NAC. Stakeholders in the consultation have also appreciated in the past being involved in public consultation upfront for any update or new documents

In summary, while progress has been made by some manufacturers, research facilities and laboratories in achieving GAPIV containment requirements, there is an opportunity to improve awareness and implementation of existing containment policy and guidance among some manufacturers and research and development partners.

5.1.1 Actions: Poliovirus Containment

The following actions will be undertaken by the GPEI to strengthen implementation of containment to contribute to long-term polio vaccine security:

⇒ Improve alignment and communication across GPEI workstreams in order to ensure a common understanding of containment policy, requirements and guidelines, and roles and responsibilities of containment partners (PEFs, NACs, CWG, GCC, CAG). This may include targeted guidance on specific technical topics related to containment, such as those issues already mentioned above.

⇒ Support NACs to ensure they have appropriate resources to fulfill their containment obligations

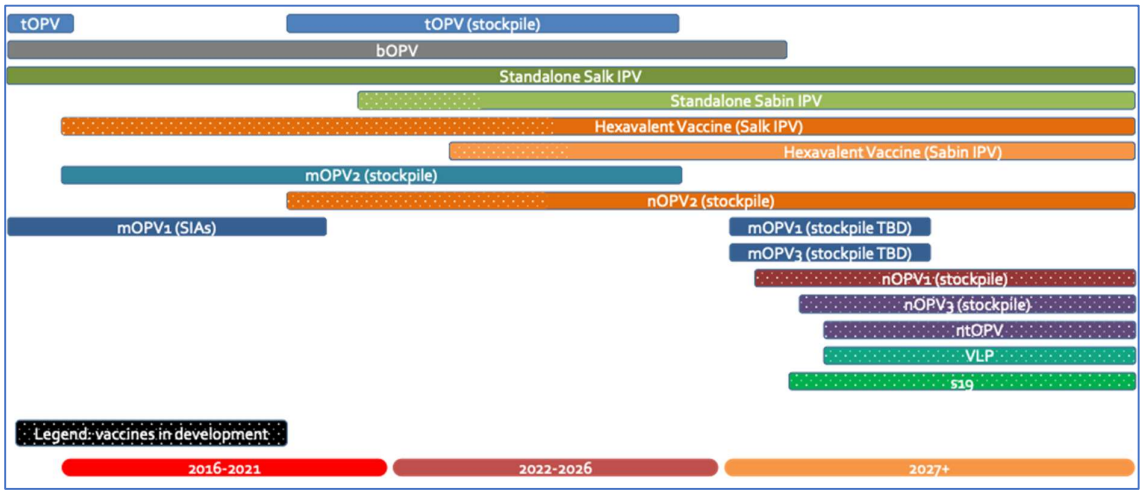
⇒ Starting in 2024, provide an overview of containment at the annual polio research meetings to provide researchers with an update on containment progress and requirements

⇒ Track implementation of containment requirements and facilitate dialogue with containment partners and other operational workstreams that will inform future evolution of the containment framework and longer-term visibility on future changes to requirements.

5.2 Research and development

There is a diverse product pipeline for polio vaccines, as illustrated below.

Figure 2: Mapping of current and future polio vaccines (as of 21 June 2024)



Additionally, a number of research and development activities are on-going under the auspices of the GPEI Polio Research and Analytics Group (PRAG) as well as with other GPEI stakeholders and manufacturers. The mandate of PRAG is to support and coordinate research activities (including clinical, operational research; and development of new products) in order to generate scientific data and tools to accelerate and sustain poliovirus eradication; and review data and analyses on poliovirus epidemiology to provide evidence-based recommendations such as projections on future vaccine needs and choices. In conducting this work, PRAG coordinates with various stakeholders including manufacturers. Research products currently under development are summarized below.

- **nOPV types 1 & 3**: Under development for outbreak response with enhanced genetic stability as compared with Sabin counterparts; expected to have lower reversion risk versus Sabin. Earliest availability forecasted as ~2028 for nOPV1 and approximately one year later for nOPV3, provided acceptable for Emergency Use Listing (EUL) procedure.
- **Trivalent nOPV**: In early clinical development for outbreak response to multi-serotype outbreaks. Earliest availability forecasted as ~2029 assuming EUL procedure, but uncertainties remain.

- **sIPV**: Sabin-based IPV (sIPV) Current research focuses on the optimization of sIPV schedules. In a post-eradication future, sIPV could be preferred over Salk IPV given lower biosecurity risks.
- **S19**: S19 viruses have been designed to be hyper-attenuated and unable to replicate at human body temperature. These viruses have Salk or Sabin capsids that confer an immunogenic response, and are able to replicate in cell culture, but have much lower risk of causing outbreaks due to accidental manufacturing release given their replication limitations. S19 is in early clinical development for stand-alone and hexavalent formulations. S19 viruses have also been used as alternatives to Sabin viruses for microneutralization testing. This use-case could become increasingly important as containment proceeds, though additional research may be needed to extend the current temporary waiver for S19.
- **VLPs**: Vaccines based on virus-like particles (VLPs) are in early clinical development (most advanced candidate). VLPs would be a preferred post-eradication option due to the fact that they are manufactured without use of live poliovirus. These vaccines are envisioned as a potential future replacement to IPV for routine immunization as a standalone vaccine or a hexavalent component, depending on technical and regulatory success. Potential to be used in outbreak response would be based on vaccine properties. Earliest availability would be ~2029/2030. VLPs could also be considered as an option to potentially replace live virus for certain laboratory assays, pending additional future evaluation.
- **Hexavalent vaccines:** Lower-cost hexavalent vaccines incorporating whole-cell pertussis antigen instead of acellular pertussis (for use in LMICs) could potentially increase polio immunity levels by simplifying delivery of IPV (reduction in number of products and vaccinations needed to immunize a child). Several additional hexavalent vaccines are in development, including early exploration of incorporation of VLP-based polio antigens.
- **Therapeutic options for iVDPV**: Treatment of immunodeficiency-related vaccine-derived polio virus (iVDPV) shedders will be important to attaining and especially maintaining eradication. Several potential options are under development for this indication, including small-molecule antivirals (e.g., pocapavir, available under compassionate use in select geographies) as well as antibody-based therapies (monoclonal antibodies as well as single variable domain heavy chain-only antibodies).

Several challenges have been identified within the research and development sphere, notably the intricate relationship between policy decisions and the research agenda. For instance, critical questions arise around the role of novel Oral Polio Vaccines types 1 and 3 (nOPV1 & nOPV3) in the cessation of the bOPV, including whether their availability is a precondition for withdrawing bOPV. This leads to subsequent questions about the regulatory prerequisites for nOPVs and the timelines involved. Yet, there remains uncertainty regarding how nOPV1 and nOPV3 will perform in real-world settings and the extent to which they are necessary for the successful discontinuation of bOPV, specifically in preventing the continued spread of circulating vaccine-derived polioviruses (cVDPV1s/3s) after cessation. This underscores the need for both clearer and longer-term vaccine policies.

Additionally, as already noted, the Chairs of the different WHO Advisory Groups supporting polio eradication and containment highlighted the need for a cohesive strategy for new

product development to support prioritization and alignment of technical and financial resources and messaging to manufacturers, and to enable long-term planning and forecasting for new products and product transitions. Alignment on product transitions, in terms of timing, product use and quantification, is important to minimize disruptions to vaccine supply. There is also need for increased understanding about how containment requirements affect research and development – now and in the future – (as already noted above) as well as some uncertainty of regulatory and marketing pathways for new products.

All of these different aspects have direct implications for long-term polio vaccine security, especially in the context of long-term planning, priority setting and communication with manufacturers. There are also direct implications on research and development decisions, including investments, technology transfers and development initiatives with manufacturers that impact current manufacturing and supply.

5.2.1 Actions: Research and Development

The following actions will be undertaken by the GPEI to provide clarity on the research and development strategy as well as enable closer collaboration and communication across GPEI workstreams, partners and vaccine manufacturers in the context of long-term polio vaccine security:

- ⇒ In alignment with vaccine policy (under the responsibility of the SAGE), formulate a unified strategy for polio vaccines that includes a research and development roadmap. This roadmap should plan research into new polio products, define paths for product development and regulation, define target product profiles, specify intended programmatic usages, outline critical decision points, and establish decision-making mechanisms. The strategy should be developed collaboratively with vaccine supply and containment teams to foster ownership and leverage available expertise. The timing and mechanism for this strategy will be led by the PRAG.
- ⇒ As the lead on research and development, the PRAG will coordinate with the VSG and containment on implementation of research and development priorities, plans and decision points.
- ⇒ Integrate containment requirements into selection of research and development partners (e.g., when operating with poliovirus types under containment, research partners must be a part of the Containment Certification Scheme and pursuing a Certificate of Containment (CC) by end-2026).
- ⇒ Facilitate product development partnerships and technology transfer for new polio vaccines by providing support throughout product development, identifying potential commercial partners, coordinating collaboration agreements.

5.3 Vaccine manufacturing and supply

In the context of this framework, vaccine manufacturing and supply incorporates areas of work related to both polio vaccine manufacturing directly as well as activities to facilitate the availability of polio vaccines to countries and/or the GPEI programme (e.g., forecasting, procurement and stockpiling). As noted above, vaccine security is highly interdependent, requiring coordination across multiple workstreams; however, the onus of finally securing vaccine supply remains the primary responsibility of those responsible for vaccine manufacturing and supply.

Figure 3: Countries with polio vaccine production

Polio vaccine type	UNICEF sources of supply	National sources of supply
bOPV	Belgium, China, India, Indonesia	Brazil, China, India, Iran, Mexico, Russian Federation, Vietnam
IPV-containing vaccines	*IPV standalone procured from manufacturers based in the following countries:* France, Netherlands, Denmark, Republic of Korea, India	*Manufacturers with licensed IPV-containing vaccines are based in the following countries:* Belgium, Brazil, China, Denmark, France, India, Indonesia, Japan, Russian Federation, Republic of Korea
nOPV2	Indonesia, India	
Sabin OPV stockpile	France, Belgium, Indonesia	

As indicated in Figure 3[11], polio vaccines are currently produced in a number of countries, some for export (as indicated as "UNICEF sources of supply") and some for national programmes (as indicated as "national sources of supply").

As of March 2024, there are 47 unique (by vaccine and presentation) polio vaccines pre-qualified (PQ) by WHO.[12] Continued coordination and prioritization with the WHO PQ team is imperative for timely access to quality-assured polio vaccines,[13] as WHO PQ is a comprehensive assessment process aimed at ensuring that vaccines intended for distribution through United Nations agencies and other large-scale immunization programs meet global standards for quality, safety, and efficacy.. However, it is also noted that additional products are available globally, which are used for national programmes and/or other markets that do not rely on WHO PQ (as noted in Figure 3 above).

While there are a variety of polio vaccines from multiple different manufacturers, not all of these vaccines are currently in production and there are limited sources of bulk; therefore, the polio vaccine market remains vulnerable with some vaccines currently considered at high risk for supply disruptions. For example, constraints in bulk supply manufactured by a limited number of sources can pose a risk to overall global supply of finished products. Some products are only produced to order (mOPV1 and mOPV3); and some manufacturers are winding down their activities and although they have prequalified products, they are no longer producing. Furthermore, specific vaccines are designated for particular scenarios; for example, nOPV2 is only available through a stockpile and for outbreak response.

Management of polio vaccine supply and demand requires a concerted effort by multiple stakeholders to ensure continued, on-time availability. The total estimated global supply and

[11] Data source: WHO MI4A 2023 Global Market Dataset; UNICEF Supply Division
[12] https://extranet.who.int/prequal/vaccines/prequalified-vaccines
[13] Prioritization of vaccines eligible for WHO Prequalification is established by WHO in consultation with UNICEF and the PAHO Revolving Fund and with established criteria. The Vaccines Prequalification Priority List 2024-2026 is available online at https://extranet.who.int/prequal/vaccines/vaccines-eligible-who-prequalification

demand of bOPV is approximately 1.3 billion doses annually, manufactured by 12 producers (including national producers). The supply of nOPV2 stands at about 500 million doses, with current production from a single manufacturer, and an additional producer expected to join by mid-2024. IPV-containing vaccine is available from 17 manufacturers (including national producers), with an annual supply of around 150-200 million doses.[14]

UNICEF, the single largest (but not only) buyer of polio vaccines, procures 600–800 million doses of bOPV annually. These doses support preventive Supplementary Immunization Activities (SIAs), outbreak response, and routine immunization in around 80 countries. Demand fluctuation and cancellation of activities, particularly for preventive campaigns, necessitates dynamic collaboration with manufacturers for supply adjustments, flexibility with countries for the acceptance of vaccines with shorter shelf lives, and joint forecasting efforts with programme partners and countries.

In 2023, UNICEF's procurement of IPV reached approximately 98 million doses, and is expected to surpass 100 million annually by 2024. The transition towards the whole-cell pertussis (wP) hexavalent vaccine, which includes IPV, may impact the demand for standalone IPV doses as well as supply due to competition for access to drug substance. This evolving landscape underscores the need for vigilant planning and market monitoring, due to both uncertainty of hexavalent demand materialization and expected increase of IPV demand with implementation of a three or four dose schedule of hexavalent, as outlined in the Gavi Combined Supply and Procurement Roadmap[15].

Beyond UNICEF's procurement for GPEI and various countries, large countries, such as India and China, along with high-income countries, engage in direct or bilateral procurement of polio or polio containing vaccines. Additional pooled procurement mechanisms, such as the PAHO Revolving Fund, facilitate procurement for their member states, indicating a diversified approach to securing polio vaccines that extends beyond the volumes mentioned above, with nuances in product choices, such as the acellular pertussis (aP) versus wP hexavalent vaccines.

Live, oral vaccines containing type 2 are now only used for global stockpiles, and there are no commercial markets. Vaccines are produced to order with the demand risks, contrary to other products, fully sitting with the GPEI. Supplies available in stockpiles include tOPV, Sabin mOPV2 and nOPV2, but since early 2023 there is demand only for the nOPV2 vaccine following recommendations from SAGE that this should be the preferred product due to inherent risks related to use of Sabin OPVs. Stocks of Sabin OPV2 is still available as of 2024; work is underway to phase these out. The first nOPV2 vaccine was prequalified by WHO in December 2023; a second product is currently under WHO PQ and it is expected the doses can be available immediately upon WHO PQ.

Securing the manufacturing and supply of vaccines faces various challenges and risks, including those inherent to vaccine production, but also those related to signals to manufacturers, such as adequately forecasting and communicating demand with sufficient lead-time, especially for products with limited sources of bulk and limited sources of finished

[14] Data source: WHO MI4A 2023 Global Market Dataset
[15] Penta-IPV-Hexa-Roadmap-Public-Summary-2020.pdf (gavi.org)

product. However, it is crucial to understand that these challenges often depend on the specific market or product and the timing within the polio programme. For instance, the switch from the tOPV taught us that changing from one product to another can introduce unique risks that need specific solutions. Through careful planning of the switch, sufficient supply of tOPV was secured to meet the programme requirements until withdrawal in April 2016, and sufficient bOPV was secured based on forecasting to allow roll out in 155 countries and territories. However, these risks and the ways to handle them may not be the same at other times or for other vaccine types. While also planned as part of the same exercise, IPV was not secured in sufficient volumes to allow 126 countries to introduce in advance of the switch due to challenges in scaling up production.

Throughout the development of this framework, specific challenges related to a vulnerable supply base on forecasting were highlighted.

5.3.1 Vulnerable supply base

A vulnerable supplier base presents an enormous risk to polio vaccine security – in all phases of the programme, but especially at times of product transition and leading up to cessation. Rapid market changes and the early or unplanned exit of key manufacturers can exacerbate supply vulnerabilities, demanding strategies for stable, diverse sourcing, and contingency plans for sudden disruptions.

The current polio vaccine supplier base faces three key vulnerabilities:

- first, OPV (bulk) **manufacturers may exit the polio market too early** due to lack of long-term sustainability and profitability (as was experienced after the tOPV-bOPV switch, when two bulk manufacturers exited the polio market);
- second, there is **high reliance on single sources of bulk** of critical products needed for the eradication programme (e.g., Sabin bulks type 1 and 3, nOPVs) and for long-term supply (e.g., IPV for a fully implemented 4-dose hexavalent schedule). Reliance on a single source of bulk poses a risk to sustainable supply for any vaccine, due to risks related to production of biologicals, testing and release and manufacturer and government priorities; and

Reliance on single sources of bulk is a risk for vaccine supply

Novel OPV2 to respond to cVDPV2 outbreaks are currently relying on a single source of bulk vaccine and finished product. Due to testing problems in second half of 2022 and filling problems in late 2023/early 2024, the speed and scale of outbreak responses required reductions and reprioritisation of activities.

Additionally, for hexavalent vaccine there will initially be a strong dependency on a single source of IPV bulk vaccine, which may set the stage for supply interruptions, if other suppliers with IPV bulk production are further delayed and demand ramps up substantially.

- third, as noted above, there is a concern that lack of commitment or perceived ability from manufacturers to move forward on meeting increasing **containment requirements pose a potential challenge to vaccine supply,** including for research and development activities, on-going manufacturing and new entrants.

Vulnerable Supply Base: bOPV example

The global annual market for bOPV is estimated at around 1.3 billion doses. Given the strong dependency on one primary supplier of drug substance to the global markets, there is a high risk of supply interruption, as was seen in 2023 when a large self-procuring country had to cancel activities due to a technical production problem; and the prospects of the upcoming bOPV cessation does not incentivize manufacturers to enter bulk production, or make considerable investments to upgrade facilities for GMP, containment or other requirements given the anticipated limited time of use before sunsetting.

5.3.2 Forecasting

The ability to anticipate future vaccine requirements and make accurate projections is critical in achieving sustainable vaccine supply. Existing inconsistencies and short-term forecasting have emphasized the necessity of a framework that can provide a more holistic view and approach to future supply and demand dynamics.

While there are examples of extensive efforts to develop product-specific demand forecasts, there is a need for more comprehensive and longer-term forecasting across polio vaccines and markets. The forecasts that exist tend to be product-specific, for specific short-medium term durations (e.g., linked to a specific programmatic strategy or tender period) and/or procurement-agency or country specific; additionally, polio programme forecasts are often too optimistic and do not sufficiently account for delays in timelines, changes in approaches or issues such as country-readiness (which may be relevant in the context of bOPV withdrawal). There is currently a lack of a more comprehensive forecast for polio vaccines, illustrating product transitions and covering longer planning horizons. The Gavi Roadmap provides an example of a longer-term forecast that considers the interdependencies between products (Penta-IPV-Hexa) and could be a model for a future comprehensive polio vaccine forecast moving forward.

Feedback from the GPEI consultation with vaccine manufacturers, NACs, and NRAs also highlighted the need to provide visibility on not only quantities but also funded demand as well as assumptions and drivers behind demand forecasts so that manufacturers can plan ahead and make informed decisions.

Finally, it is noted that demand forecasts are highly dependent on clarity on the normative landscape (such as policy and planning for bOPV cessation) and new product use cases, timelines, and transitions; therefore, clarity on the long-term polio vaccine policy, including new product strategies, which incorporate risk adjustments and potential back-up plans, is a foundation for developing a long-term demand forecast (*see section 6.1).*

5.3.3 Actions: Vaccine Manufacturing and Supply

Following actions will be undertaken by the GPEI to address the challenges noted above:

⇒ Explore opportunities for strengthening the polio vaccine business case for manufacturers, especially during periods of uncertainty, such as:
- Risk-sharing mechanisms, especially leading up to critical periods of transition (e.g. bOPV withdrawal) in order to maintain manufacturing capacity and compliance; and financial support for early at-risk product development.
- Procurement and contracting approaches depending on market profile and supplier base - these may consider product-specific risk sharing mechanisms.
- Long-term benefits of manufacturing new polio vaccines/products (e.g., research and development, technology transfer).

⇒ Building on existing forecasts and methodologies, and consulting with countries, regions, modelers, and forecasting experts, establish principles and methodologies for integrated, long-term forecasts for various polio products. These forecasts should provide 5-10-20 year visibility for global volumes across different vaccine types, procurement mechanisms, and market segments, considering policy implications. Develop and disseminate these forecasts among stakeholders to inform their planning.

Potential Forecasting Methodology

In addition to leveraging existing forecasting processes, a combination of additional methods may be considered in developing a long-term, integrated forecast of polio vaccines, for example:

- Consumption-Based Forecasting
- Cohort Component Method
- Time-Series Analysis (ARIMA)
- Epidemiological Modeling

⇒ Improve engagement, communication and information sharing with polio vaccine manufacturers, including with vaccine industry associations (DCVMN, IFPMA), for example through demand and supply scenario mapping to inform longer-term forecasting and incorporating views from IFPMA and DCVMN to ensure suppliers' perspectives and capabilities are factored into strategic decisions and vaccine policy.

⇒ Advocate for compliance to containment requirements with vaccine manufacturers, for example through consultations and through UNICEF tenders (e.g., all suppliers must be a part of the Containment Certification Scheme and pursuing a CC by end-2026).

6 Critical cross-cutting areas

6.1 Normative Landscape and Policy Environment

The normative and policy landscape is multifaceted, influenced by poliovirus spread and epidemiology. It is intricately linked to the GPEI timelines, certification and containment milestones, research and development, future regulatory and market pathways for vaccines, as well as product use and transitions. This necessitates a dynamic, adaptable framework that can swiftly respond to evolving vaccination policies, strategic shifts in vaccine types, and new clinical evidence, in order to effectively address epidemiological changes and achieve polio eradication.

However, this dynamic landscape makes it difficult to provide certainty on programmatic timelines and future vaccine needs and requirements. Consequently, it is challenging for manufacturers to plan production capacity, upgrades to meet increasing GMP, containment and environmental requirements and make medium- to long-term investment decisions in order to ensure sufficient quantities of the right vaccines at the right time.

Additionally, there is a risk that manufacturers will exit the market in an unplanned manner due to messaging that certain vaccines will no longer be required (as experienced during the 2013-2018 strategic period and leading up to the tOPV to bOPV switch). As a result, there may not be sufficient quantities of the right type of vaccines for countries when they are needed, in particular if critical milestones are being delayed (*see 5.3.1 above*).

While not exhaustive, some specific examples of current uncertainty of the normative landscape and policy environment that pose a significant risk to vaccine security include:

- **Long-term polio vaccination policy framework**: there is need for clarity on a long-term vaccine policy, providing a framework for understanding which vaccines are needed when, including product characteristics, timelines, transitions/milestones and conditions for vaccination. Clarity on what is needed to maintain polio eradication in the long-term is also needed, as this will influence supplier decisions around life cycle management (e.g., transition to polio vaccine technologies not requiring live virus for production). This is needed to be able to inform the research and development agenda, advise vaccine manufacturers and prevent supply disruptions, particularly during periods of high vulnerability. Some specific examples highlighted include:
    - bOPV cessation planning including pre-cessation requirements (including immunity boosting vaccination requirements), triggers, timelines and overall policy
    - Regulatory pathway for nOPV1 and 3, if these will be accepted under EUL based on phase 2 clinical data or if full WHO PQ will be required before any usage. This will affect the timelines for availability of future OPV products, implicating future use and demand forecasting.
    - Which types of vaccines to be used at which stages of the programme, including in order to meet containment requirements
    - Guidance on what vaccines will be needed 5-10 years from now or even 20+ years into the future and duration of product use
    - Long-term IPV strategy, including for IPV-combinations – how long will IPV be recommended for use post-eradication? What will be the extent of uptake of wP hexavalent vaccines? How might this differ in different markets (e.g., in countries continuing to have PEFs)?
    - Product withdrawal and new product development priorities and conditions, such as in relation to poliovirus containment requirements
- **Policy dialogue around the containment requirements and standards** to ensure shared understanding of current requirements and standards and potential refinements that impact vaccine manufacturing and research and development activities and priorities.

6.1.1 Recommended Actions: Normative Landscape and Policy Environment

Under coordination of the PRAG and in collaboration with containment and the VSG:

⇒ Provide clarity on a long-term polio vaccine policy, including recommendations for use, vaccine characteristics, transitions and timelines and critical decision points, as it has direct implications for achieving long-term polio vaccine security.

⇒ Subsequently, mainstream policy guidance in the operational workstreams through implementation plans

Additionally, the following actions related to the normative landscape and policy environment were included under the specific operational areas above:

⇒ Track implementation of containment requirements and facilitate dialogue with containment partners and other operational workstreams that will inform future evolution of the containment framework and longer-term visibility on future changes to requirements. (*see 5.1.1 above*)

⇒ In coordination with vaccine policy (under the responsibility of the SAGE Polio Working group), formulate a unified strategy for the development of new polio vaccines, incorporating a research and development roadmap to plan research into new polio products, which encompass well-defined paths for product development and regulation, profiles of targeted products, intended programmatic usages, critical decision points, and mechanisms for making decisions. Overall, the strategy should be crafted through a collaborative process to foster a sense of ownership and to leverage the wealth of expertise and experience available. The timing and mechanism for developing this strategy will be led by the PRAG. (*see 5.2.1 above*)

6.2 Financing and Access to Resources

Access to resources in the context of polio vaccine security incorporate possible financial resources needed to mitigate risks and enable continued supply during critical periods as well as access to training, information and technology. Two main themes were identified during development of this framework:

- Polio vaccine manufacturing business case
    - Risk sharing mechanisms as a way to mitigate supplier risks, especially during critical periods of product transition. Some manufacturers have expressed interest in some financing mechanism for producing vaccines at-risk and to secure polio vaccine supply over the long-term
    - Financial support for early at-risk research and product development
    - Technology transfer as a long-term benefit of manufacturing new polio vaccines / products
- Access to resources related to containment
    - Coordinated access to reference laboratories
    - Training of auditors, audit teams and facilities retaining polioviruses on GAP

While it is expected that the financial and resources needs will evolve over time, actions focus on coordination and providing a forum to address resource needs.

6.2.1 Recommended Actions: Financing and Access to Resources

⇒ As part of the annual strategy and work-planning session (*see 6.3.1 below*), hold a dedicated session to explore gaps and possible requirements on financing and access to resources to have a comprehensive overview of needs, who is supporting what and any priority areas for support.

6.3 Communication, Coordination and Advocacy

There are multiple stakeholders engaged in polio that impact vaccine security of supply; however, there can be different priorities and approaches between stakeholders for contributing to vaccine security, which unintentionally impacts supply availability. Some of these gaps have already been highlighted above, such as the lack of a new product development strategy, which can lead to inconsistent messaging to manufacturers or inefficient use of resources, or product-specific forecasts instead of providing integrated, longer-term visibility.

Alignment on communication and messaging on vaccine manufacturing and supply among the above three workstreams and towards vaccine manufacturers was highlighted as a gap. Lack of alignment between various GPEI workstreams / stakeholders can lead to inconsistent communication with manufacturers regarding priorities and future needs. Manufacturers also flagged that a lack of coordination and visibility on upstream activities (such as research and development support and investments in capacity expansion) can result in oversupply.

Additionally, there is a need to improve overall communication with and between vaccine manufacturers, NACs, and NRAs. The importance of providing visibility on strategies, policy decisions, long-term visibility on demand, and timelines with sufficient lead time for manufacturers to make informed decisions on polio vaccine production is an important lesson learned from the tOPV withdrawal.

The annual GPEI consultation with vaccine manufacturers, NACs, and NRAs is an important event bringing together key partners in polio vaccine security of supply. It draws participation from over 250 representatives spanning 28 countries. This assembly is instrumental for fostering collaboration, sharing strategic insights, and discussing progress in polio eradication efforts. The involvement of key partners such as UNICEF, the Bill & Melinda Gates Foundation (BMGF), Gavi, the Vaccine Alliance, and various WHO departments underscores the consultation's approach to addressing the challenges of polio vaccine supply in a collaborative manner.

While established mechanisms such as the annual consultation and mid-year update exist as well as bilateral meetings in the course of normal operations, there is a need to improve quality of materials, including on programmatic information, policy decisions and polio product forecasting, among others, to support industry decision making.

Addressing these fragmented approaches is one of the fundamental reasons for developing this long-term polio vaccine security framework.

6.3.1 Recommended Actions: Communication, Coordination and Advocacy

- ⇒ The VSG, as the Secretariat for managing this framework, should convene an annual strategy and work-planning session with the workstreams for vaccine supply and manufacturing, containment, research and development, ideally including WHO PQ in its capacity as steward of continued compliance with global standards for quality, safety and efficacy of vaccine supply through UN with the objective of strengthening coordination and prioritization, especially related to interactions and messaging with manufacturers and access to financing and / or resources. The first strategy and work-planning session in the context of this framework should be held in Q3 2024, following completion of this framework.
- ⇒ Enhance and expand upon established platforms, under the auspices of the VSG, such as the GPEI consultations with Polio Vaccine Manufacturers, NACs, and NRAs (including the annual consultation with expanded stakeholders, mid-year and monthly updates)
- ⇒ Build on the UNICEF Vaccine Industry Consultation (VIC) and other fora to strengthen communication among diverse stakeholders engaged in polio vaccine security

6.4 Management of a Polio Vaccine Security Framework

Recognizing that vaccine security is an ongoing endeavor requiring continuous monitoring and adaptation, the framework will undergo regular updates and revisions. Initially the management of the framework will be carried out by the GPEI VSG.

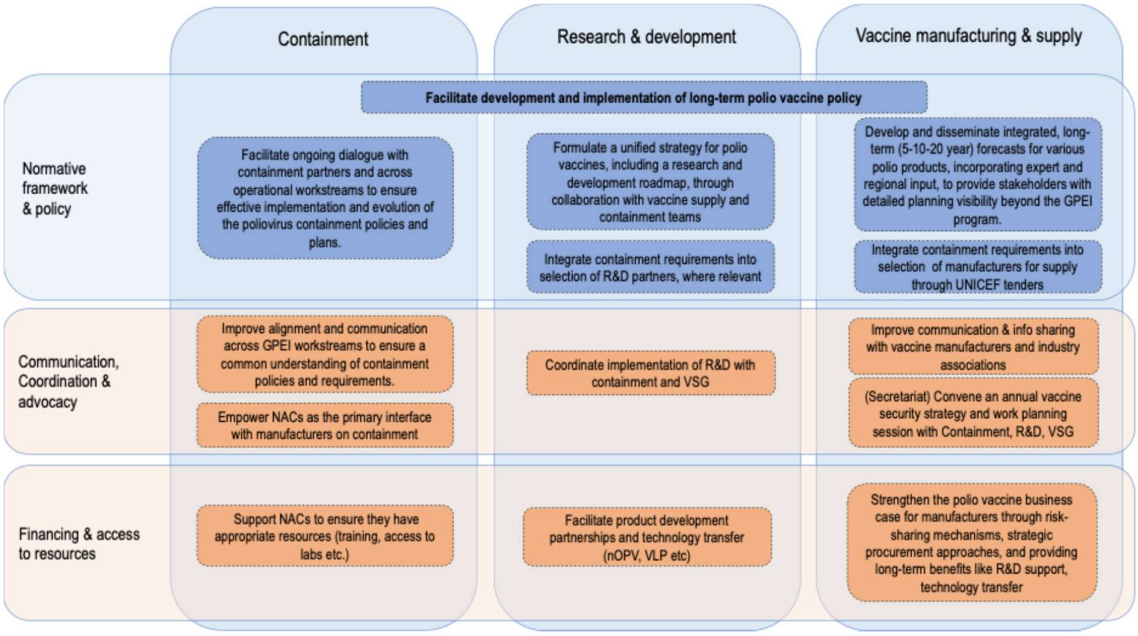
The actions identified in this framework will be monitored on a regular basis by the VSG, in collaboration with PRAG and containment, and reported annually to the GPEI Strategy Committee, following the annual strategy and work-planning session with GPEI stakeholders. Monitoring will include progress, risks, course corrections, and any additional actions, as needed. Progress and updates will also be communicated to vaccine manufacturers, NACs and NRAs during the annual GPEI consultation.

(More information on management and implementation of this framework is available in Annex D).

7 Summary of Recommended Actions

The following provides a summary of the recommended activities to address the current gaps and risks for achieving polio vaccine security of supply in the near, medium and long-term. Many of these actions are interdependent and influence others for contributing to polio vaccine security of supply, as illustrated below.

Figure 4: Summary of recommended actions



This graphic illustrates the interconnectedness of the operational workstreams, cross-cutting elements and corresponding activities identified in this framework. The boxes correspond to the recommended actions and are positioned based on ownership / accountability for the action.

It is expected that the scope of activities needed will evolve over time depending on GPEI priorities, the post-GPEI landscape and polio vaccine market developments. Therefore, monitoring and updating the actions identified in this framework will be critical for achieving long-term polio vaccine security.

Annex A:

Management and Oversight of the Polio Vaccine Security Framework

1. Introduction

The effective implementation of the Polio Vaccine Security Framework is essential for ensuring the timely, sustained, and uninterrupted supply of suitable types of affordable, quality-assured polio vaccines. This chapter outlines the management, implementation, budgeting, and monitoring and evaluation (M&E) strategies necessary to achieve these goals.

2. Management and Oversight Structure

2.1. Vaccine Supply Group to Strategy Committee

The management of the Polio Vaccine Security Framework will be overseen by the GPEI Vaccine Supply Group (VSG), which was responsible for the development of the framework. The VSG will provide direction, coordinate activities across workstreams, and ensure accountability to the partnership through the Strategy Committee.

2.2. Accountability

An improved technical coordination across the workstreams will be ensured through appointment of focal points from the VSG, the PRAG and the CMG. The focal points will be accountable to the partnership through the Vaccine Supply Group, ensuring transparency and alignment with the broader objectives and structure of the GPEI.

3. Implementation Strategy

3.1. Roles and Responsibilities

- VSG**:** Oversees the overall implementation of the framework, ensuring coordination and alignment across workstreams.
- **Focal points convening:** The focal points convening will support the development of monitoring framework, convening of annual meeting, focus on coordination activities, monitoring progress and report on outcomes; anticipated to be supplemented by a project coordination contract/consultant support especially during kick off, and during annual meetings.
- **Operational Workstreams:** The Vaccine Supply, Containment, and Research and Development Workstreams will carry out the specific activities outlined in the framework. These workstreams already have the necessary resources allocated within their budgets to support the framework's implementation.

3.2. Secretariat Support

The secretariat functions necessary for managing, implementing, and overseeing the framework will be integrated into the existing structures of the Vaccine Supply, Containment, and Research and Development Workstreams. This integration ensures efficient use of resources and leverages existing capabilities.

3.3. Annual Work Plans

An important mechanism for implementing the framework will be the development of annual work plans. These plans will be developed jointly by the Containment Management Group (CMG), the Polio Research and Advisory Group (PRAG), and the Vaccine Supply Group (VSG) in Q1 of 2025. The annual work plans will outline specific activities, timelines, and responsibilities, serving as a foundation for monitoring progress and evaluating performance.

4. Budgeting

The financial resources required to implement and oversee the Polio Vaccine Security Framework are primarily covered within the existing budgets of the Vaccine Supply, Containment, and Research and Development Workstreams. There will be a need for project coordination contract/consultant support in the kick off phase with a limited budget requirement.

4.1. Budget Breakdown

- **Project coordination contract/consultant:** TBD as part of the upcoming annual work plan exercise
- **Existing Resources:** Budgets for the necessary activities and positions within the Vaccine Supply, Containment, and Research and Development Workstreams.

5. Monitoring and Evaluation

A robust M&E framework is essential to track progress, identify challenges, and ensure the successful implementation of the Polio Vaccine Security Framework. The M&E framework will be finalized with specific indicators in collaboration between the CMG, PRAG, and VSG during Q1 2025.

5.1. Key Performance Indicators (KPIs)

- **Impact Indicator:** Availability of the right mix of polio vaccines, ensuring no delays or cancellations due to supply issues.
- **Outcome Indicators:**

- Compliance with poliovirus containment standards.
- Smooth and uninterrupted vaccine withdrawals and introductions.
- Equipping manufacturers with necessary planning information, such as vaccine demand forecasts and strategies.

5.2. Annual Reviews

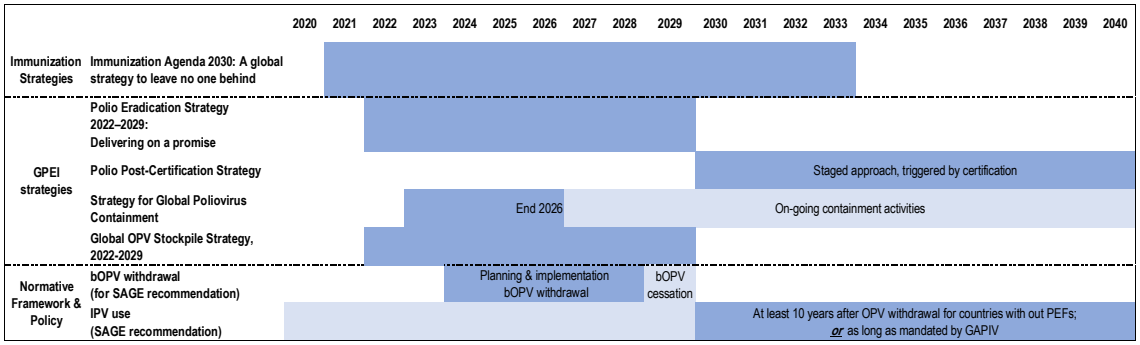
Annual reviews will be conducted to assess the effectiveness of the framework's implementation, identify areas for improvement, and make necessary adjustments.

5.3. Reporting

- **Quarterly Reports:** Summarize progress, achievements, and challenges.
- **Annual Reports:** Provide a comprehensive evaluation of activities, outcomes, and stakeholder feedback.

Annex B: Existing strategies and resources

Many strategies and resources that contribute to vaccine supply, planning, regulation and policy already exist, but they can be fragmented and have different time horizons, providing different levels of visibility that affect vaccine supply.



- **Polio Eradication Strategy, 2022-2026: Delivering on a Promise**[16] – presents a comprehensive set of actions that will position the GPEI to deliver on a promise that brought the world together in a collective commitment to eradicate polio. through five mutually reinforcing objectives that lay the foundation to achieve two elemental goals: *Goal One* to permanently interrupt all poliovirus transmission in the final WPV-endemic countries of Afghanistan and Pakistan, and *Goal Two* to stop circulating vaccine-derived poliovirus (cVDPV) transmission and prevent outbreaks in non-endemic countries.
- **Polio Post-Certification Strategy** - a comprehensive strategy that was developed to define the global technical standards or core set of activities that will be needed in order to sustain a polio-free world after global certification of wild poliovirus eradication. The Post-Certification Strategy specifies at a global level the technical standards for functions (e.g. containment, vaccination, and surveillance) that are essential to maintain a polio-free world in the decade following certification.
- **Strategy for Global Poliovirus Containment** - defines the goals and objectives to safely contain polioviruses through efforts coordinated across the GPEI partnership, Ministries of Health (MoHs), vaccine manufacturers, laboratories, and other facilities retaining infectious and potentially infectious materials (IM and PIM) that include live vaccines and samples collected through surveillance for cases of acute flaccid paralysis (AFP) and environmental surveillance (ES).
  - Country progress towards poliovirus containment certification is publicly available and updated on a quarterly basis
  - WHO Global Action Plan for Polio Virus Containment, GAPIV - After certification of eradication and OPV cessation, facilities that store and/or work with poliovirus represent the most significant threat to maintaining global eradication. This standard describes the safe handling requirements and community safeguards for facilities that intend to retain WPV/VDPV and Sabin/OPV infectious materials (IM) as well as WPV potentially infectious materials (PIM).

[16] GPEI-Strategy-extension-20241113.pdf

- **Global OPV Stockpile Strategy, 2022-2026**[17] extended to 2029 - lays out the strategy for developing and managing the Global OPV Stockpile for the period 2022-2029, in support of and in alignment with the GPEI 2022-2029 strategy. Additionally, as the OPV stockpile forms an integral part of the longer-term preparedness for response to polio outbreaks, this strategy incorporates activities that will prepare the Global OPV Stockpile for the post-OPV cessation period

The **SAGE Working Group on Polio** is a policy and normative body that provides recommendations to the Strategic Advisory Group of Experts (SAGE) on Immunization. This working group on polio was established in August 2008 to review the available scientific evidence and provide SAGE and the Global Polio Eradication Initiative (GPEI) with technical guidance on the Polio Eradication and Endgame Strategy. The scope of work includes policy guidance on polio vaccine current and future use, such as coordinated OPV cessation, mOPV stockpiles and response mechanisms, novel OPV formulations, assessing current and future OPV and IPV products, and long-term IPV policies.

Within the GPEI there are several Global Programme Support (GPS) groups that have responsibilities directly related to polio vaccine supply:

- **Vaccine Supply Group (VSG)** – The VSG is leading the GPEI efforts to ensure uninterrupted supply of required types of vaccines and other supplies necessary to conduct quality immunization campaigns against the polioviruses as well as establishing and updating procedures and normative guidance to ensure timely and predictable vaccine delivery and their management in the field.
- **Polio Research and Analytics Group (PRAG)** – The PRAG exists to: 1) support and coordinate research activities (including clinical, operational research; and development of new products) in order to generate scientific data and tools to accelerate and sustain poliovirus eradication; and 2) review data and analyses on poliovirus epidemiology including modelling outputs; and provide evidence-based recommendations to the Strategy Committee on programme actions, and projections on future vaccine needs and choices.
- **nOPV2 Group** – The nOPV Group is a time-limited group (sun-setted end 2023) that will manage and coordinate GPEI's activities to enable a rapid and effective roll out of nOPV2 as the tool of choice for responding to cVDPV2 outbreaks. As the development of nOPV candidates for other serotypes of polio advances, the nOPV group will facilitate programmatic alignment and decision-making related to their future deployment on behalf of GPEI.
- **Containment Management Group (CMG)** – The CMG exists to manage and coordinate poliovirus containment activities of GPEI partner agencies and stakeholders, as aligned with the global polio eradication strategy.

The **GPEI holds an annual consultation with Poliovirus Vaccine Manufacturers, NACs and NRAs** to provide updates on progress towards eradication, strategies and vaccine requirements to provide visibility on programme strategies and plans, including to support decisions on polio vaccine production over the span of the current eradication strategy. The GPEI also provides mid-year and monthly updates.

[17] GPEI-Strategy-extension-20241113.pdf

Gavi Combined Supply and Procurement Roadmap [Penta-IPV-Hexa-Booster2ndY] - integrates analyses and market shaping considerations on four interrelated markets where Gavi Partners are involved in market shaping: Pentavalent, IPV, Hexavalent, and DTwP-containing boosters during the second year of life (Booster2ndY). The intention is to ensure that market-to-market issues are integrated into a portfolio view that is relevant both to Gavi Partners and to vaccine manufacturers with the following benefits:

- Reach a better understanding of potential future dynamics between markets,
- Consider implications related to market or portfolio opportunities and risks,
- Seek the best outcome short-, mid-, and long-term for the interrelated portfolio of vaccines,
- Deliver clear and consistent market signals that help manufacturers decide and prioritise investments, with the aim to contribute to better future market health.

UNICEF provides market updates on different polio vaccine markets through published market notes and the Vaccine Industry Consultation. These updates provide information on supply and demand, pricing through UNICEF, and medium-term market prospects and outlook:

- Bivalent Oral Polio Vaccines Supply and Demand Update (last update: April 2024)
- Diphtheria Tetanus and Pertussis Containing Vaccines: Market and Supply Update (last update: June 2023) – includes hexavalent vaccines
- IPV: supply update[18] (last update: August 2019)
- Vaccine Industry Consultation (VIC) 2023 (September 2023) – Session 22: Programme and vaccine market update - Polio
    - VIC Pentavalent and Hexavalent Vaccines market and supply update (September 2023)
    - VIC IPV market and supply update (September 2023)
    - VIC bOPV market and supply update (September 2023)

[18] inactivated-polio-vaccine-IPV-market-update-2019.pdf

Annex C: Examples of polio vaccine supply disruptions

Several recent examples illustrate vulnerability in polio vaccine supply, especially during periods of transition, and its consequences on programmatic priorities.

IPV

There was an IPV shortage following the 2013 SAGE recommendation that all countries should have at least 1 dose of IPV into their routine immunization programmes in advance of the tOPV to bOPV switch. This recommendation required 126 countries to introduce IPV at an unprecedented pace for a new vaccine introduction. Although the recommendation took guidance from an industry survey that confirmed that this increase in demand could be met, in reality experienced manufacturers underestimated the complexity of scaling up the production of biological products in the required timeframe. This required programmatic reprioritization for the available vaccine to be used in highest risk areas and resulted in interruption of supplies to countries which had already introduced IPV in their programmes, postponement of introductions in lower risk countries, and low initial coverage (for several years after the switch) and missed children, with an estimated 43 million children subsequently requiring catch-up IPV vaccination.[19] The supply of IPV increased gradually and only in 2018 (3 years after the switch) was supply sufficient to fully meet demand.[20] As of 2023, the IPV market stand-alone is considered healthy, now allowing all countries to introduce a minimum of two doses of IPV and complete catch-up campaigns.[21] The impact of the potential transition to an IPV-containing hexavalent vaccine on the supply market for IPV stand-alone vaccines will depend on the uptake of the hexavalent vaccine and the pace at which manufacturers with in-house IPV bulk production will have their products prequalified by WHO and/or are able to scale up their IPV bulk production.

Type 2 containing stockpiles

Following the global phase-out of the type 2 component from the trivalent oral polio vaccine (tOPV), shortages in the type 2 vaccine-containing stockpile intended for managing outbreaks of circulating vaccine-derived poliovirus serotype 2 (cVDPV2) initially arose from inadequate forecasting, e.g. initially forecasting based on historical consumption in a situation where demand doubled between years, leading to supply shortages. More recently, the situation has been exacerbated by production and testing issues linked to reliance on a single supplier. This led to a significant shortfall, with an estimated 193 million doses of nOPV2 missing from the 2022–2023 supply targets. Furthermore, the implementation of SAGE recommendations—which urged immediate outbreak responses using available vaccines rather than waiting for nOPV2—was largely unsuccessful. Many member states, encouraged by the advantages of nOPV2, hesitated to extensively use mOPV2, resulting in delayed responses to cVDPV2 outbreaks. Such delays risked further propagation of the virus.

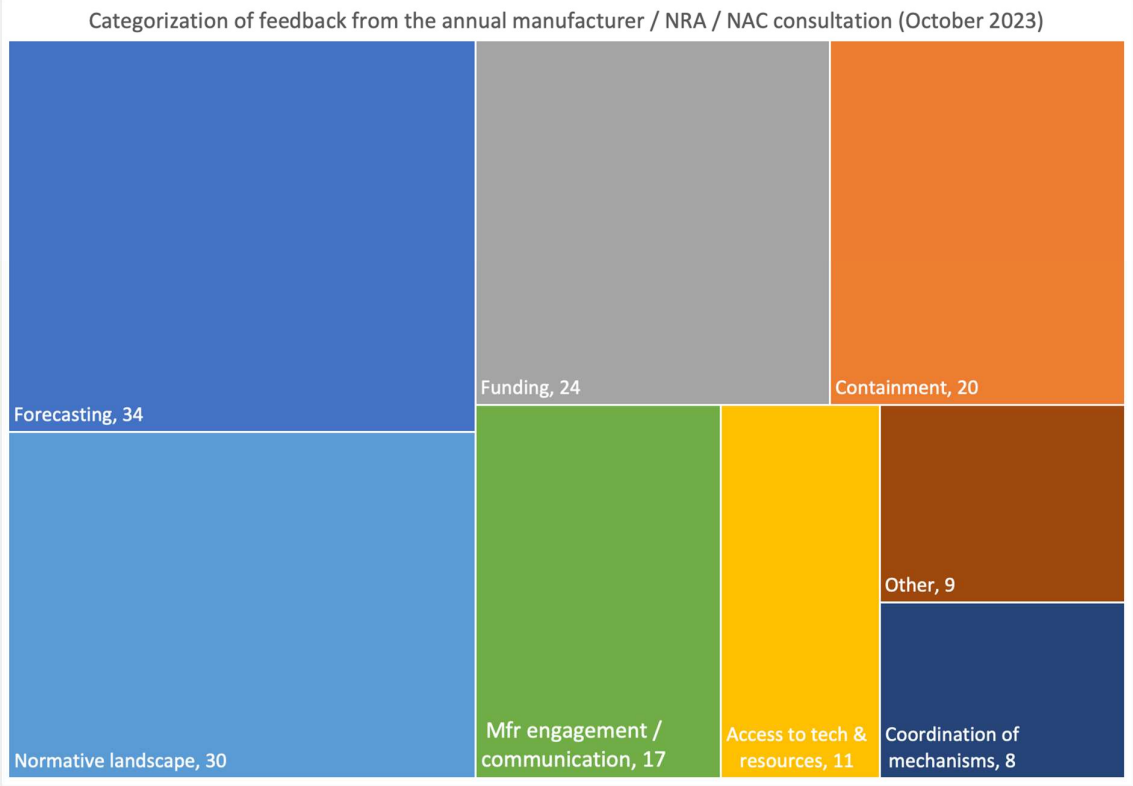
[19] Sutter RW, Cochi SL. Inactivated Poliovirus Vaccine Supply Shortage: Is There Light at the End of the Tunnel? J Infect Dis. 2019 Oct 8;220(10):1545-1546. doi: 10.1093/infdis/jiy739. PMID: 30958545; PMCID: PMC10547123.
[20] UNICEF Supply Division, Inactivated Polio Vaccine: Supply Update. August 2019.
[21] UNICEF Vaccine Industry Consultation 2023, Session 22: Programme and vaccine market update – Polio. September 2023 (https://www.unicef.org/supply/media/19101/file/UNICEF-VIC2023-Session22-Polioupdate-UNICEF_rev-2023.pdf=)

In both instances, constraints have been due to quality and production issues at the sole manufacturing facility, coupled with the complexity of manufacturing this new vaccine – with the consequence that the programme had to change scope and scale of activities and prioritize certain geographies over others based on risk assessment, potentially leading to further spread of the virus. To mitigate risks, a second supplier has been identified and a technology transfer taken place, with at-risk production currently ongoing in anticipation of WHO prequalification of this product around mid 2024.

Annex D: Feedback from GPEI consultations with manufacturers, NACs and NRAs

The 22nd Annual Consultation between the GPEI and Poliovirus Vaccine Manufacturers, National Authorities (NACs), and Regulatory Authorities (NRAs) took place in October 2023. meeting participants provided feedback and ideas for this framework. During the Consultation, there was a specific session on developing a long-term polio vaccine security framework, including breakout groups with participants to provide input. Feedback from the breakout groups and a subsequent post-meeting survey was grouped into seven common themes, plus one "other" category. The priority areas highlighted by this group of stakeholders focused on forecasting, normative landscape, funding and containment.

Figure 5: Summary of feedback from Manufacturer / NRA / NAC consultation



Examples of comments provided by theme are indicated below:

- **Forecasting**: long-term approach to planning and providing visibility on demand, including quantities, categories of products (and how they influence each other, where relevant), funding, duration, and assumptions/drivers.
- **Normative landscape**: long-term policy and strategy; policies and policy drivers/assumptions, regulatory aspects for new products, duration of product use and types of vaccines to be used by the programme.
- **Funding**: visibility on available funding and funded demand, sustainability of funding, sustainable profitability / commercial viability for manufacturers, incentives to secure

commitment from manufacturers and mitigate uncertainties; financial support to establish PEFs, research activities

- **Containment**: clarity and timely updates on containment requirements and implications on supply including specific products, testing, research and development of new products, alignment with eradication and cessation timelines
- **Access to technology and resources**: Requests from NACs and manufacturers to enable access to resources and networks, e.g., global lab networks, access to S19, VLPs; access to raw materials; training GAP auditors and staff; testing and scientific support, support for R&D and introduction of new products, improve GMP management system through training and communication
- **Manufacturer engagement and communication**: information exchange, transparency, coordination, engagement with manufacturer associations and regional agencies
- **Coordination of mechanisms**: multi-party collaboration to ensure the supply of qualified vaccines, coordination of market shaping efforts and upstream activities, engaging other actors (e.g., NGOs, education sector), coordination with relevant teams in WHO supporting the implementation of this framework

Annex E: Stakeholder consultations

This framework has been developed by a Steering team with representatives from the GPEI Containment Management Group (CMG), Polio Research and Analytics Group (PRAG) and the Vaccine Supply Group (VSG). The framework has been reviewed and signed off by the GPEI Strategy Committee, which includes representatives from partner organizations and the donor community.

In addition, the following groups / organizations have been consulted during the development of this framework:

GPEI Advisory Groups on Containment:

- Global Certification Commission Containment Working Group (GCC-CWG) (Chair)

GPEI Global Programme Support Groups:

- Containment Management Group (CMG)
- Financing Management Group (FMG)
- Global Communications Group (CGC)
- nOPV Group
- Outbreak Response & Preparedness Group (ORPG)
- Political Advocacy Group (PAG)
- Polio Research and Analytics Group (PRAG)
- Resource Mobilization Group (RMG)
- Gender Mainstreaming Group (GMG)

Partner organizations:

- Bill and Melinda Gates Foundation
- Gavi, the Vaccine Alliance
- World Health Organization, Containment Management Team (CMT)
- World Health Organization Immunization, Vaccines and Biologicals (IVB)
- World Health Organization Prequalification Team (PQT)

Manufacturer Associations

- Developing Countries Vaccine Manufacturers Network (DCVMN)
- International Federation of Pharmaceutical Manufacturers and Associations (IFPMA)

Manufacturers, NACs and NRAs via the Annual GPEI Consultation and circulation of the draft framework for comments.

Manufacturers

ADM Consulting, on behalf of Beijing Institute of Biological Products	Central Institute for Experimental Animals	Poonawalla Science Park
AIM Vaccine Group	China National Biotec Group Company Limited	PT Bio Farma
AJ Vaccines	Chumakov FSC R&D IBP RAS	Razi Vaccine and Serum Research Institute of Iran

BATAVIA biosciences	Clean Cells	Reliance
Beijing Bio-Institute of Biological Products Co., Ltd. (BIBP)	GlaxoSmithKline Vaccines	Sanofi Pasteur SA
Beijing Minhai Biotechnology Company	Haffkine Bio Pharmaceutical Corporation Ltd	Serum Institute of India
Bharat Biotech International Limited	Institute of Medical Biology, Chinese Academy of Medical Sciences	Sinovac Biotech Co Ltd
BIKEN	Intravacc	Taconic Biosciences
Bilthoven Biologicals B.V.	Janssen Vaccines	Temptime Corporation
BioGeneric Pharma	KM Biologics Co. Ltd	VABIOTECH
Biological E	LG Chem Ltd	Valneva Sweden AB
Biomanguinhos	Naobios	Viroclinics
Bio-Net Asia	Panacea Biotec Ltd.	Zydus Cadila
CanSinoBio	Pasteur Institute of Iran	
Center for research and production of vaccine and biological (POLYVAC)	Pharmajet, Inc.	

National Regulatory Authorities (NRAs)

NRA China	NRA India	NRA Russian Federation
NRA France	NRA Indonesia	

National Authorities on Containment (NACs)

NAC Belgium	NAC Indonesia	NAC Russian Federation
NAC Canada	NAC Iran	NAC South Africa
NAC Denmark	NAC Japan	NAC United Kingdom
NAC France	NAC Republic of Korea	NAC United States
NAC Hungary	NAC The Netherlands	
NAC India	NAC Romania	