Post-Certification Strategic Plan

Contents

Acronyms and Abbreviations

To be added with the final draft

Executive Summary

To be developed with the third draft

I. Statement of Intent

A. Purpose of the Plan

The Post-Certification Strategic Plan (PCS) provides recommendations for mainstreaming the essential functions for maintaining a polio-free world after global wild poliovirus eradication has been certified.

With certification of wild poliovirus (WPV) eradication, the global health community will mark an enormous achievement. Polio will be the second human vaccine-preventable disease (after smallpox) to be eradicated, and the first in the 21st century. Three decades ago, the World Health Assembly agreed to eradicate polio, and the Global Polio Eradication Initiative (GPEI) was founded in 1988. Since then, the GPEI has reduced the global incidence of polio by more than 99.9%, preventing paralysis and possibly death for more than 16 million people. In financial terms, polio eradication has saved more than US$ 27 billion since 1988—and looking forward past eradication, an additional US$ 20-25 billion is projected to be saved by 2035 through prevented treatment costs and gains in productivity.[1]

But a polio-free world is not just a world without polio; it's also a world made better by the effort needed to achieve eradication. This effort has taken the concentrated and coordinated work of all 194 WHO member states, private and public sector partners, over 140 laboratories within the GPEI Global Polio Laboratory Network (GPLN) that conduct disease surveillance for polio and beyond, 150,000 polio-funded frontline workers,[2] a network of more than 18,000 dedicated polio staff,[3] and millions of volunteers—including vaccinators, all of whom are critical for outbreak response, vaccination campaigns, routine immunization, and the delivery of a number of other primary healthcare services. Through this large-scale collaboration, the GPEI developed a strategy for reaching the world's most vulnerable in operationally challenging areas. But the GPEI has become more than a case study for targeting and eliminating disease; it has also broadly contributed to strengthening health systems by training public health staff, developing outreach strategies, and creating a comprehensive laboratory network linked to epidemiologic investigations of diseases that extend far beyond poliomyelitis.

[1] GPEI. Investment Case: Executive Summary. March 2017. http://polioeradication.org/wp-content/uploads/2017/03/InvestmentCase.pdf. See also Duintjer Tebbens RJ, Pallansch MA, Cochi SL, Wassilak SGF, Linkins J, Sutter RW, Aylward RB, Thompson KM. Economic analysis of the Global Polio Eradication Initiative. *Vaccine* 2011;29(2):334-343.
[2] GPEI. Investment Case: Executive Summary. March 2017.
[3] GPEI, the Bill and Melinda Gates Foundation and McKinsey & Company. Economic Case for Eradicating Polio. 2014. http://polioeradication.org/wp-content/uploads/2016/07/EconomicCase.pdf

While the achievement of global eradication merits recognition for the scale and scope of work it has required, the activities and functions that were critical for "getting the job done" must now be reimagined for the post-certification era in order to secure the gains of the GPEI and protect a polio-free world. As such, the Strategy Committee of the GPEI called for the development of a comprehensive plan to define the global strategies needed to sustain polio eradication after certification. The PCS fulfills this mandate by providing the technical standards for polio-essential functions that must remain in place post-certification (some for the short term, others indefinitely), as well as an organizational framework that outlines the governance and financing needed to sustain WPV eradication.

To solidify and protect the hard-won gains made through polio eradication, the PCS identifies the potential future risks jeopardizing polio eradication and defines the mitigating steps that must be taken to minimize and eliminate these risks, to the extent possible. These risk-mitigating measures are organized according to the three strategic goals:

- **Contain poliovirus sources:** Ensure potential polioviruses are properly controlled or removed
- **Protect populations:** Withdraw the oral live attenuated polio vaccine (OPV) from use and immunize populations with inactivated polio vaccine (IPV) against possible re-emergence of any poliovirus
- **Detect and respond:** Promptly detect any poliovirus reintroduction and rapidly respond to prevent transmission

Additionally, the PCS will provide a **set of enabling and cross-cutting recommendations** to ensure ongoing polio functions are either embedded in existing structures or in newly developed mechanisms to sustain the above goals. Other activities, functions, and knowledge which have been critical to achieving polio eradication may transition to support broader health programs.

B. Plan Engagement, Audience, and Duration

The PCS is being developed through an iterative consultative process and extensive engagement with experts within and beyond the GPEI (*See **Annex A** for PCS Engagement List.*). Such outreach is intended to provide stakeholders at the global, regional, and national level with opportunities to understand and provide input on the approach and elements of the strategy before its finalization. The PCS also draws upon programme-generated plans and guidelines to ensure that the strategy is data-driven and based on realistic needs, assumptions, and achievements, both past and future.[4]

The PCS is intended for use by core private- and public-sector partners, technical advisory groups of the GPEI and, more broadly, the future managers of global health—which will include new implementing agencies and donors outside of the GPEI. In the full course of its development, the PCS also provides broad strategic recommendations to the WHO Health Emergencies Programme (WHE), Expanded Programmes on Immunization (EPIs), and more generally for Ministries of Health (MoH).

[4] Such reports include: The Stockpile Requirements Plan by the Vaccine Supply Task Team (VSTT); bOPV Cessation Guidelines by the Immunization Systems Management Group (IMG); the Global Surveillance Plan by the Surveillance Task Team (STT), Environmental Surveillance Working Group (ESWG), and the Global Polio Laboratory Network (GPLN); and Outbreak Response Standard Operating Procedures by the Eradication and Outbreak Management Group (EOMG). (*Note: This will become an annex in future drafts.)*

The high-level technical standards and recommendations for mainstreaming polio-essential functions that are included in the PCS are offered as the last strategic phase of the eradication effort. To provide visibility into the strategy for polio-essential functions after global certification and to allow for the planning required, the PCS will be developed by the end of 2017. However, implementation of the high-level guidance contained in the PCS will not begin until after global certification of eradication, with the exception of specific activities that are required to start earlier in preparation of certification and bOPV withdrawal. *(See **Annex B** for a summary of the prerequisites and assumptions that inform the PCS, and specifically its relation to existing workplans of the eradication effort.)*

The PCS covers the period starting from an expected date of certification (2021) and extending for 10 years (2030). Depending on the epidemiology of poliovirus transmission after 2017, the GPEI, donors, and country governments will identify the need for adjustments in the end date of eradication and anticipated date of certification. Similarly, the PCS will require updates as risks to organizational, environmental, and programmatic factors change over time. While the PCS anticipates periods of revision—likely to include a year prior to certification, after bOPV cessation, and at the midterm of the PCS's ten-year duration—it is the future owners of the PCS who will re-evaluate the plan, as and when appropriate.

II. Background

The GPEI was launched in 1988 following a global commitment to polio eradication formalized in the Resolution from the World Health Assembly. Its founding partners—Rotary International, the World Health Organization (WHO), United Nations International Children's Emergency Fund (UNICEF), and the Centers for Disease Control and Prevention (CDC), later joined by the Bill and Melinda Gates Foundation (BMGF)—provide the overall technical guidance, direction, and support to the implementation efforts led by countries around the world.

The current strategies for the GPEI were developed in 2012 to guide the final stages of polio eradication. The **Polio Eradication and Endgame Strategic Plan 2013-2018** (PEEPS), also referred to as the endgame strategy, defined four objectives: 1) to detect and interrupt poliovirus transmission, 2) to strengthen immunization systems and coordinate OPV withdrawal, 3) to implement poliovirus containment and certify global polio eradication; and 4) to begin transition planning for the post-eradication era. [5] In 2015, an in-depth **Midterm Review** validated the core strategies as appropriate to eradicate polio even as it extended the timeline by a year due to challenges posed by access and security risks in the last remaining endemic countries.[6]

The PCS provides a strategic vision for a key provision of transition planning, the fourth objective of the endgame strategy, particularly as it is situated in relation to broader global health strategies.

[5] GPEI, WHO. Polio Eradication & Endgame Strategy 2013-2018. February 2013. http://polioeradication.org/wp-content/uploads/2016/07/PEESP_EN_A4.pdf
[6] GPEI, WHO. Polio Eradication & Endgame Midterm Review. July 2015. http://polioeradication.org/wp-content/uploads/2016/07/GPEI-MTR_July2015.pdf

1. The Role of the PCS within Global Health Strategies

With the historic milestone of WPV eradication and the significance it holds for global health, it is important to situate the PCS within broader global public health regulations, specifically the International Health Regulations (IHR). The IHR provides a foundational premise that a "health threat anywhere is a health threat everywhere." With globalization and the risk for the international spread of dangerous pathogens, the IHR puts forward global regulations that direct countries to detect, assess, report, and respond to public health events without interfering or interrupting international travel and trade.[7]

In addition to a focus on the core objectives of protection, detection, and response, the IHR calls for the multilateral, multi-sectoral coordination to strengthen country, region, and global capacity for international health concerns and health security risks. Such multi-sectoral, multilateral coordination is also central to the PCS as it provides recommendations for polio-essential functions that must be mainstreamed by agencies and countries, and ultimately resides under the umbrella of the IHR to ensure global health security.

In a post-certification world, polio will be both a pathogen that presents risks to global security and an ongoing part of routine immunization programmes. As such, the recommendations of the PCS share in the principles of the Global Vaccine Action Plan (GVAP), a framework for global equity through universal access to immunization.[8] The GVAP framework provided a focus on equity for the development of the PCS, particularly in relation to the risks of different countries and regions. GVAP was designed to strengthen routine immunization to meet vaccination coverage targets; accelerate control of vaccine-preventable diseases with polio eradication as its first milestone; and introduce new and improved vaccines and spur research and development for the next generation. As polio eradication fulfills one of the goals put forward by GVAP, and as the Decade of Vaccines comes to a close with a possibility of extension into the next decade, GPEI partners will engage with other GVAP stakeholders on how to best keep polio-essential functions within the future framework that succeeds the 2011–2020 plan.

2. The Role of the PCS within Transition Planning

The work of the PCS is also part of a larger coordinated transition planning effort that addresses the eventual changes with global certification of eradication and the closure of the GPEI. [9]

Transition planning has three goals:

- Goal One**:** Maintain and mainstream polio-essential functions after eradication has been certified, to protect a polio-free world
- Goal Two: Where feasible, desirable and appropriate, transition the capacities, processes, and assets that the GPEI has created to support other health priorities
- Goal Three: Capture and disseminate the lessons of polio eradication

[7] WHO. International Health Regulations, third edition. 2016. http://www.who.int/ihr/publications/9789241580496/en/
[8] WHO. Global Vaccine Action Plan 2011-2020. May 2012. http://www.who.int/immunization/global_vaccine_action_plan/
[9] See GPEI. Transitioning Planning Framework. March 2017.

The PCS fulfills *Goal One* by providing global standards and guidelines to maintain polio-essential functions post-certification, specifically by identifying the financial requirements and technical assistance infrastructure needed after global certification of WPV eradication.

IV. Certification and the Path Forward

1. Global Certification

Regions can consider certification of WPV eradication only when all countries in the area demonstrate the absence of wild poliovirus transmission for at least three consecutive years in the presence of certification-standard surveillance. The Region of the Americas was first to receive certification in 1994, followed by the Western Pacific Region (2000) and the European Region (2002). The last region to be certified was the South-East Asian Region, with the last case detected on 13 January 2011 in India and regional certification granted on 27 March 2014. Regions that have yet to receive certification due to endemic transmission in Afghanistan, Pakistan, and Nigeria are the Eastern Mediterranean Region and the African Region.

Comprised of public health and scientific experts, Regional Certification Commissions (RCCs) independently verify polio eradication for all countries in the region. They are supported by National Certification Commissions (NCCs) that collect, review, and decide on national documentation through consultations. After regional certification, the Global Certification Committee (GCC) oversees the global certification process, receives and reviews regional commission reports and – if and when appropriate – will issue a report to the WHO Director-General to certify that the circulation of wild polioviruses has been interrupted globally.

Placeholder: This is a general discussion in need of requirements for global certification and the process to global certification, and messaging on how VDPV certification will be handled after WPV certification.

2. Post-Certification Timeline

Transition planning has already been initiated except for the endemic countries. As the last WPV cases are identified, GPEI will accelerate efforts to transition responsibilities to other groups as it prepares for the closure of its partnership. The programme has facilitated a large number of functions that have been essential to reach this stage of global eradication. As the programme moves forward, it will phase out its support for previously essential functions which are no longer needed, based on consensus among the partnering agencies around polio activities, the achievement of key indicators or outcomes, and the assessment of any related risks and mitigation strategies needed to support the work of maintaining a polio-free world. *(See **Figure 1**: Polio essential functions mapped across post-certification intervals).*

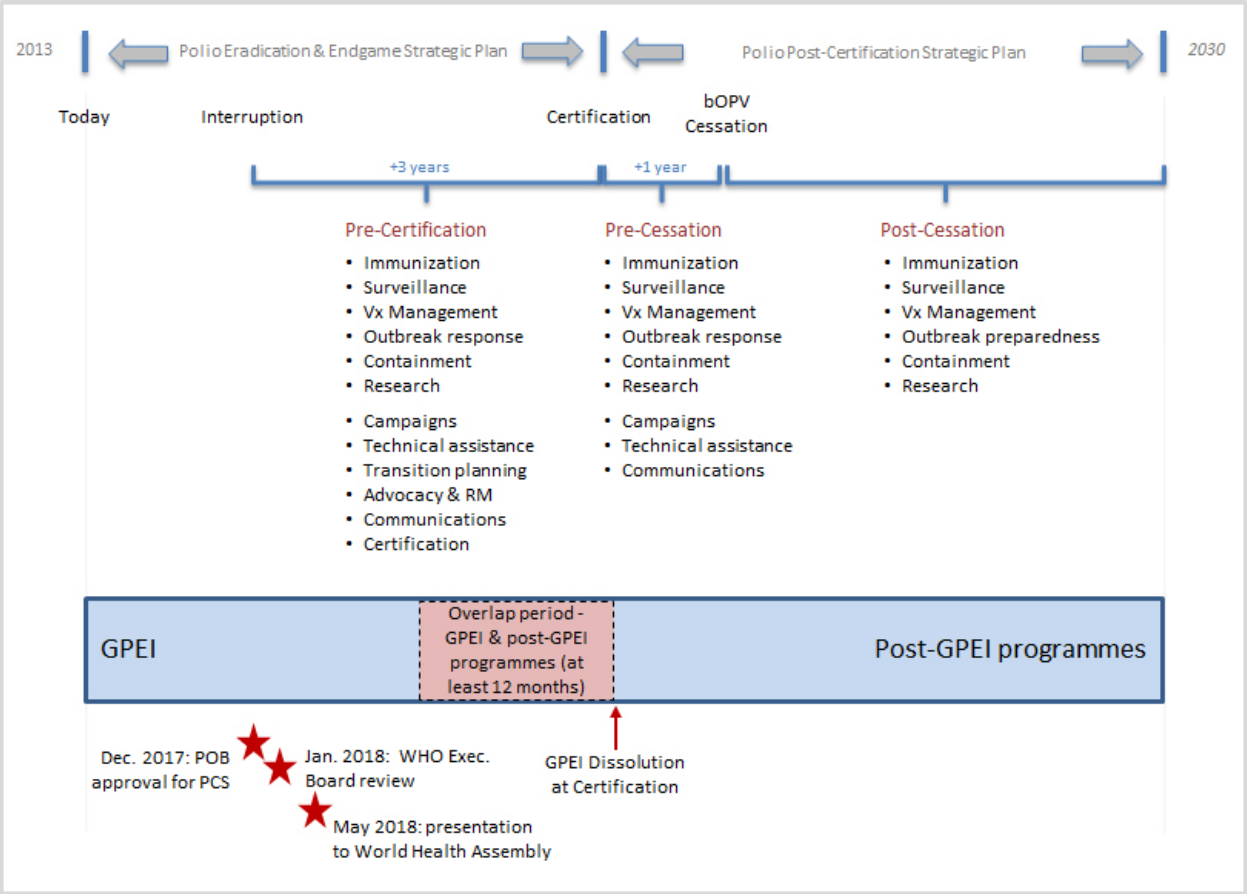


Figure 1: Polio-essential functions mapped across post-certification intervals

The PCS will identify elements of a governance structure that will be needed to support functions during each post-certification interval. The GPEI as an organizational entity will dissolve at certification, but many of the same agencies will still be engaged with implementing the strategies required at the global level. As part of transition planning, each partner agency has its own transition planning group. Additionally, national governments are responsible for their own country-level transition planning by developing implementation plans that include the mobilization of resources to mainstream polio-essential functions and achieve the standards laid out in the PCS.

IV. Plan Overview & Rationale

A. Risks

The PCS provides a blueprint for sustaining a polio-free world that is the inheritance of the GPEI. Securing the world from the re-emergence of poliovirus is dependent on recognizing and addressing the risks which threaten this achievement. While no strategy can fully eliminate all potential risks, identifying the known risks is a critical step to informing health policy and programme interventions to reduce their possibility and limit their consequences, if they do occur. Other global or systemic risks may be beyond immediate intervention but should be acknowledged.

From this perspective, three types of risk can be identified:

1. Sources of poliovirus re-emergence which could result in further cases of paralytic poliomyelitis after certification
2. External global factors outside of the health system which may impact poliovirus re-emergence or the proposed mitigation measures
3. Factors internal to health systems which directly affect implementation of all the plan's strategies

The blueprint proposed in the PCS is based on current knowledge and will necessarily evolve with an unfolding understanding of these risks over time, as well as more effective approaches and interventions for meeting them *(See **Research** in Enabling and Cross-Cutting Areas)*.

1. Risks of Poliovirus Re-emergence

The major risks for re-emergence in the post-certification period can arise from three categories of poliovirus:

1. **Live attenuated poliovirus strains, or Sabin strains**
   In addition to OPV production and vaccination of children until bOPV cessation, Sabin strains are as reference standards in vaccine quality assurance and as controls for diagnostic testing. An individual OPV recipient will usually shed Sabin vaccine viruses into the environment for only a time-limited period, usually a few days to a week. Due to secondary spread, vaccine viruses can remain detectable in the environment for approximately three to four months after the last use of OPV.
2. **Vaccine-derived polioviruses**
   Very sporadically, OPV can cause vaccine-associated paralytic poliomyelitis (VAPP). Mutations can also occur in attenuation of the transmissibility and neurovirulence of the vaccine virus leading to vaccine-derived polioviruses (VDPVs). Particularly in populations with low immunization coverage, these mutated viruses can begin circulating in the community, known as circulating vaccine-derived polioviruses (cVDPVs). Additionally, primary immunodeficient (PID) individuals exposed to OPV can excrete the virus for prolonged periods, resulting in immunodeficient VDPVs (iVDPVs). Isolated mutated vaccine viruses detected in humans or the environment, referred to as ambiguous or aVDPVs, may spontaneously die out or can become cVDPVs.

3. **Wild Polioviruses**
   WPVs should no longer be circulating post-certification but may continue to be used to seed viruses for IPV production and potentially for other therapeutic purposes.

Poliovirus may be reintroduced and re-establish transmission in the post-certification era from several sources. Inadvertent unsafe handling of poliovirus during testing, vaccine manufacture or research, may result in a release into the environment or infection of workers that could further spread in the community. Prolonged intestinal infection in an immunodeficient individual or prolonged circulation in a population with low vaccine coverage may result in the emergences of VDPVs. The global risk of any of these emergences and the likelihood and severity of an outbreak depend on a multitude of factors, including: virus type (WPV and VDPVs have higher transmissibility and neurovirulence than Sabin strains contained in OPV), population characteristics (e.g., immunity, density, and mobility), and force of infection (e.g., sanitation and environment). In general, a specific country's risk profile and most likely source of poliovirus re-emergence will be determined by its prior history of OPV use, as well income level and hygiene standards.

The primary risk and source of re-emergence is expected to vary over time after bOPV cessation *(see **Figure 2**).* While the figure shows the intensity or likelihood of specific risks, some risks may be consistent over time even as their importance relative to other risks can vary, as is the case with a containment breach. It bears mention that the consequences for each risk might vary considerably depending on when and where the re-introduction occurs. A discussion of the projected magnitude and frequency of each risk is presented in each section on the PCS Goals.

- Pre-cessation to Immediate post-cessation period: Although still projected to be relatively rare occurrences, the most likely risk of a poliovirus re-emergence in the pre-cessation (i.e., 0-1 year post-certification) and immediate post-cessation periods (i.e., 2-5 years post-certification) will come from VDPVs. While the precise risk of an a VDPV (either aVDPV or cVDPV) being detected and resulting in further community transmission will depend on multiple local circumstances, the risk of a cVDPVs emergence is highest in the period 12-18 months after bOPV withdrawal. This risk will steadily decline with time; yet the consequences and risk of wider transmission will steadily accelerate due to waning mucosal immunity in the population.[10]

- Intermediate post-cessation period: As the risk of cVDPV wanes, the primary risk for poliovirus re-emergence in the intermediate post-cessation period (i.e., 6-9 years post-certification) will come from the excretion of an iVDPV spreading within a community. Examples of such community spread of an iVDPV have not been confirmed to date; nevertheless, this is a possibility that needs to be considered. While the rare occurrences of PID infection and excretion can take place at any time, the risk for transmission into the community will rise if population immunity declines post bOPV cessation. The highest risk for this scenario is among under-immunized populations in a few middle-income countries with a history of OPV use and a relatively high prevalence of PID patients.

[10] See Grassly NC. The final stages of the global eradication of poliomyelitis. Phil Trans R Soc. B 2013 368, 20120140. Duintjer Tebbens RJ, et al. An economic analysis of poliovirus risk management polio options for 2013-2052. MBM Infect Dis 2015; 15:389, doi: 10.1186/s12879-015-1112-8.

- Post-cessation period: A containment breach of any category of poliovirus (WPV, VDPV, or Sabin) is unlikely, but examples have occurred.[11] This risk, along with an even less likely possibility of a bioterrorist release, is inherent at all times. The relative importance of this risk, however, will arise primarily in the 10 years after certification. The risk for a containment breach will remain as long as facilities are still storing and handling polioviruses.

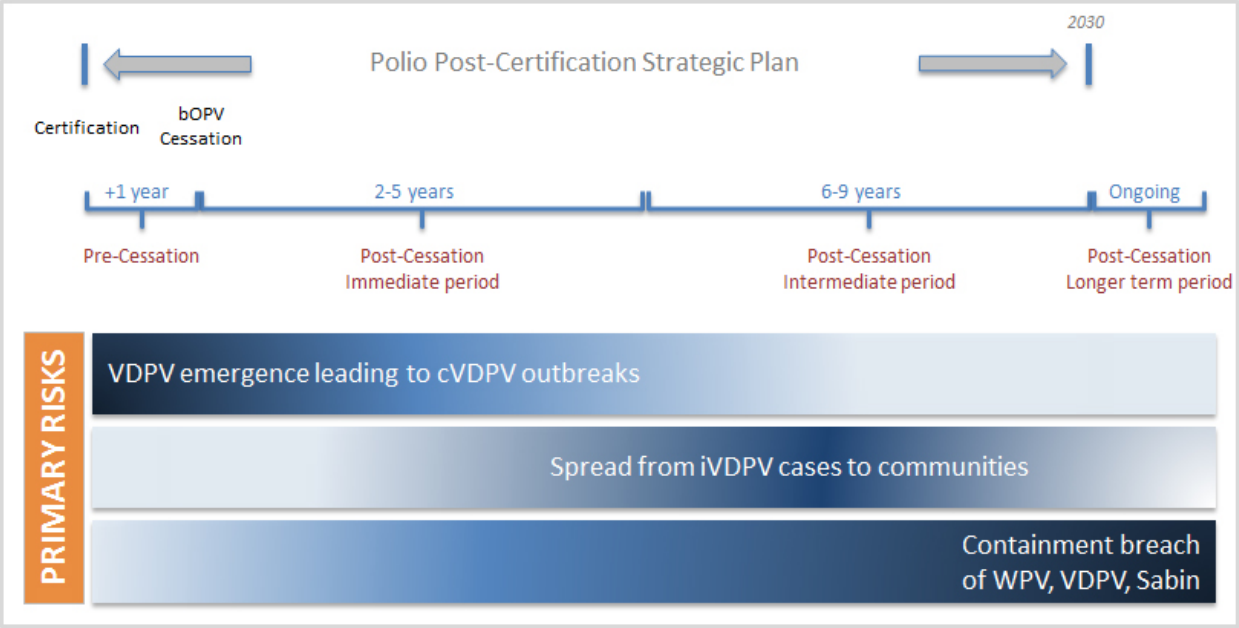


Figure 2: Primary risk of poliovirus re-emergence of circulation over time

2. Global Risks Affecting Re-emergence

The global arena is undergoing a cycle of change that presents specific geopolitical, economic, and demographic risks. Addressing these risks is beyond the purview of the PCS; however, understanding the dynamics and direction of these factors can be critical to assessing both global and country specific situations.

Geopolitical Risks: Political volatility has led to multiple fragile or failing states which are often beset by chronic insecurity or active conflict. These situations can result in weakened or non-functional health systems and displaced or inaccessible populations, and other fractures or fault lines, such as the denial

[11] In April 2017, a Dutch vaccine manufacturer reported a containment breach in which two workers were exposed to WPV 2 after a spill at the plant, with one worker becoming infected. See 13th IHR Emergency Committee statement, 2 May 2017. http://www.who.int/mediacentre/news/statements/2017/13th-ihr-polio/en/.

of services based on ethnic or cultural discrimination.[12] Health workers, specifically vaccination workers, become vulnerable and service delivery or surveillance can become severely compromised.[13]

Economic Risks: Slowed economic growth and shifting national priorities in donor countries can lead to greater scrutiny and even decreasing amounts of foreign aid. Overall, these trends translate into reduced support for country level health services, whether it is bilateral country funding or through multilateral and multi-sectoral organizations.

Demographic/Environment Risks: The impact of particularly high rates of fertility in low-income countries translates into a burgeoning number of infants and children requiring vaccination. Placing further stress on the health system is a worldwide increase in the political and economic migrants who often end up living in urban areas and slums without access to clean water. Climate change also presents increasingly problematic access to water through extreme weather conditions and rising temperatures. This may not only contribute to disease spread and geographic changes in disease distribution; it also produces famine and malnutrition, thereby weakening population immunity.

3. Risks to Implementing Post-Certification Strategy

In addition to the epidemiological and global risks above, there are some operational risks that might also impact the capability of countries and agencies to implement the guidelines outlined in the PCS. While specific risks and challenges to specific mitigation measures are detailed under each goal, multiple cross-cutting factors present generic risks to implementing PCS strategies, particularly after the dissolution of the GPEI partnership. They are highlighted here as known risks that merit attention by implementing agencies, countries, and donors, even as solutions or mitigating measures fall outside of the PCS scope.

Insufficient financial resources—global, regional, national: The Ministries of Health in countries that will self-finance ongoing polio-essential functions might divert resources away from polio since it is no longer a looming threat, and other critical needs will likely arise. While resources might wane and in-country priorities may shift, maintaining the core functions of the PCS will require strong national level leadership and regional support from WHO and UNICEF, to leverage financial resources and ensure adherence to strong data practices and monitoring activities.

Lack of enforcement measures: Implementing immunization, surveillance, or containment recommendations at the national level as proposed by the PCS or other global guidelines essentially rests with compliance by national health ministries, private- and public-sector agencies, and other partners. Enforcement is primarily through widely sharing of national progress in global forum. For example, GAPIII expects national authorities to submit reports on containment status which are then open for discussion at the World Health Assembly.

[12] In response to these changes in the geopolitical landscape, the Gavi Alliance has developed a new policy on fragility, emergencies, and refugees and has extended support for IPV coverage to 2020. For more, see the June 2017 press release: http://www.gavi.org/library/news/press-releases/2017/gavi-to-help-protect-millions-more-children-against-polio/

[13] GPEI. Ending Polio in Conflict Zones. 21 June 2017. http://polioeradication.org/news-post/ending-polio-in-conflict-zones/

Operational Risks

Continued generic issues inherent in weak infrastructure and or capacity can result in systemic gaps which can impact effective and efficient operational implementation of surveillance and vaccination programs.

- Insufficient and inadequately trained staff
- Inadequate information/data quality and analysis
- Poor coordination/management without centralized oversight
- Complacency, lack of commitment by global partners, countries, and donors
- Inadequate resources and/or infrastructure (e.g., vaccine, cold chain, and transport)

B. Goal Summaries

Goal One: Contain Poliovirus Sources - Ensure that polioviruses are properly contained or removed in laboratories, vaccine manufacturing and other facilities by: (1) validating containment of OPV/Sabin virus after bOPV cessation and after use of OPV for outbreak response, and (2) monitoring and supporting long-term adherence to containment of poliovirus-essential facilities with appropriate safeguards.

Goal Two - Protect Populations - Protect populations from vaccine-associated paralytic poliomyelitis (VAPP) and vaccine-derived poliovirus (VDPV) by effectively preparing and implementing the globally synchronized withdrawal of bOPV. Additionally, provide access to safe, effective vaccines for long-term protection from polioviruses for global populations by (1) implementing relevant future immunization policy, and (2) ensuring proper procurement and supply of affordable IPV vaccine.

Goal Three - Detect and Respond - Promptly detect any poliovirus re-emergence through a sensitive surveillance system by (1) redefining the polio surveillance paradigm, and (2) sustaining adequate and technically qualified laboratory and surveillance infrastructure (including human capacity) and information systems. Additionally, develop and maintain adequate global and regional capacity and resources to support national efforts to respond to any poliovirus emergence by: (1) identifying future outbreak risks; (2) developing response strategies and preparedness plans; (3) sustaining trained human capacity to appropriately implement these strategies and plans; and (4) creating, maintaining, and managing an adequate stockpile of polio vaccine and antivirals for an appropriate response.

Enabling and Cross-Cutting Areas

Propose the ongoing polio functions that should be embedded in existing institutions and new approaches to sustain the goals of polio post-certification (includes governance model, financial model, monitoring framework, research activities, etc.)

C. Scope

Mainstreaming Polio-Essential Functions

The GPEI has identified those polio-essential functions that must continue in the post-certification period after the closure or dissolution of its partnership. They include: containment, immunization with appropriate polio vaccines, poliovirus surveillance, and outbreak response. The PCS provides detailed recommendations based on the development of financial scenarios and technical infrastructure needed to adequately support international coordination of these functions at the global and regional levels. It does not, however, identify the owners of those activities. Partner agencies and national governments will be responsible for transitioning or mainstreaming these essential functions and personnel to the agreed upon future governance and management structure.

Providing Global and Regional Guidelines

The PCS provides guidance on the necessary polio-essential functions, regional and global reporting requirements, and the regional and global structures that country programmes can expect to interact with after the closure of the GPEI. The PCS will not, however, provide detailed guidance or recommendations for how polio essential functions should be mainstreamed or funded within national health systems at the country level. Similar to other existing global guidance documents, such as the *Global Strategy to Eliminate Yellow Fever Epidemics*, the PCS will provide strategic recommendations that country programmes will be expected to implement using their own resources.

The budget for country transition plans will be developed and refined at the country level as part of their individual country planning processes. Because country plans are expected to focus on building national capacity to take on key public health functions, securing domestic financing for transition execution and sustained programme implementation should be a priority. Some country governments may choose to seek external funding, however, to support transition.

The GPEI recognizes that a number of countries currently receiving GPEI support for polio-essential functions may not currently have the capacity to fully mainstream polio-essential functions in the absence of donor financial and partner agency technical support, particularly those with the lowest income level, fragile health systems, emergencies, and conflict. Consequently, country transition plans should be aimed at identifying strategies for mainstreaming and financing these functions through progressively greater percentage of a country's health budget in national systems over time and/or long-term capacity building. Implementation of these long-term mainstreaming strategies should begin as early as possible to allow for gradual, high-quality transitions to take place over 3-10 years (timeframe to be determined in the country transition plan). A critical goal of these plans should be to ensure that national management of polio-essential functions within integrated surveillance and outbreak response systems is strong enough to adopt and implement the high-level guidance provided in the PCS, as is expected of all countries globally.

Identifying Post-Certification Strategies, Not Implementation

The PCS presents strategies identified by experts on the activities, functions, and mechanisms required to maintain a polio-free world. Though it provides global-level financial scenarios, the PCS does not include an estimated budget for country-level implementation of the recommended strategies. Based on the content of these recommendations, however, relevant stakeholders at the country, regional and global levels should develop implementation budgets as global certification of eradication and the execution of the recommendations draws closer. The implementation of PCS recommendations at the global and regional levels is expected to be funded through the regional and global bodies/stakeholders with jurisdiction over the areas covered in the recommendations, with financing provided by international donors. At the country level, implementing activities in compliance with PCS recommendations will be the responsibility of national governments.

Goal One: Contain Poliovirus Sources

Contain Poliovirus Sources		
Main Objectives	Major Activities	Outcome Indicators
Objective 1.1 - Achieve and sustain containment of polioviruses in laboratories, vaccine manufacturing and other facilities	• Activity 1.1.1 - Achieve and validate containment of OPV/Sabin virus after OPV cessation and after any OPV use for outbreak response • Activity 1.1.2 - Monitor and support long-term adherence to containment of poliovirus-essential facilities with appropriate safeguards	• Containment of all OPV/Sabin viruses achieved XX months after bOPV cessation • Containment of all OPV/Sabin viruses achieved within XX months after mOPV use for outbreak response • % PEFs with containment certificate (target 100%) • % PEFs renewing CC every 3 years (>80%)?
Monitored by GCC with regular reports presented to WHA		

A. Introduction

After the global interruption of WPV transmission and cessation of bOPV use, certain laboratory and manufacturing facilities will continue to store and handle polioviruses as necessary to perform essential functions related to vaccine production, quality control, diagnostics, and research. Accidental or intentional release of poliovirus from any of these facilities may re-establish circulation in the population.

The risk of poliovirus release will depend on: the number of facilities handling polioviruses; and the biorisk and biosecurity standards applied during storage and manipulation of poliovirus-containing materials.[14] Although polioviruses are considered a low-threat agent for a biological weapon because they cause low morbidity and mortality, deliberate release of wild, vaccine- or genetically-engineered polioviruses is possible.[15]

The risk of poliovirus being released from facilities, spreading in the surrounding communities, and causing outbreaks will depend on factors such as the type of poliovirus (i.e., WPV and VDPVs have much higher infectivity and transmissibility than OPV/Sabin); the amount of poliovirus in the materials handled (i.e., vaccine production and cell cultures for poliovirus testing have >10,000-fold higher

[14] Dowdle W, van der Avoort H, de Gourville E, et al. Containment of polioviruses after eradication and OPV cessation: characterizing risks to improve management. Risk Anal 2006;26:1449-69

[15] Cello, J., A. V. Paul and E. Wimmer (2002). "Chemical synthesis of poliovirus cDNA: generation of infectious virus in the absence of natural template." Science 297(5583): 1016-1018.

concentration than stools or respiratory samples); time since WPV eradication or homotypic OPV cessation; population density and growth, levels of vaccination-induced immunity, sanitation infrastructure, climate, and local surveillance and response capabilities.[16]

To minimize the risks posed by known poliovirus-infected materials and potentially infected materials (e.g., clinical stool and respiratory samples) stored in public and private research, laboratories, and vaccine production facilities, the GPEI made containment of polioviruses a goal for the endgame strategic plan. The plan outlines a timeline for containment-related activities phased in parallel to the certification of the world as polio-free. Identifying all facilities that may harbor poliovirus in any kind of material, developing guidelines to ensure that facilities handle those materials under appropriate biorisk and biosecurity standards, and monitoring compliance with adherence to containment standards will continue to be a critical function in the post-eradication era.

B. Description of the Goal

Goal One aims to institute effective poliovirus containment practices to mitigate the risks and consequences of re-introducing poliovirus from laboratory or vaccine manufacturing facilities into a polio-free world. The overriding objective is to minimize the number of facilities that will store or handle poliovirus. The major principles of poliovirus containment are: 1) minimal storage and handling of poliovirus infectious and potentially infectious materials in laboratories; 2) minimal risk of exposure for the worker or community during operations; 3) minimal susceptibility of workers to poliovirus infection; and 4) minimal susceptibility to spread in the community.

C. Objective 1.1: Achieve and sustain containment

1. Context

Global Action Plan for containment of poliovirus in facilities (GAP)

The Global Action Plan (GAP) for the containment of poliovirus in laboratory facilities developed in 2000 proposed several strategies and mechanisms for implementation of containment of poliovirus before and after the certification of poliovirus eradication. The original plan was modified to incorporate changes in polio eradication policies and to improve efficiency of implementation. The third edition of the containment plan (GAPIII) was endorsed by the World Health Assembly in May 2015.[17]

[16] See Dowdle W, van der Avoort H, de Gourville E, et al. Containment of polioviruses after eradication and OPV cessation: characterizing risks to improve management. Risk Anal 2006;26:1449-69; Fine PE, Ritchie S, Fine PEM and Ritchie S. Perspective: determinants of the severity of poliovirus outbreaks in the post eradication era. Risk Anal 2006;26:1533-40

[17] WHO Global Action Plan to minimize poliovirus facility-associated risk after type specific eradication of wild polioviruses and sequential cessation of OPV use. Geneva: World Health Organization, 2014. http://www.polioeradication.org/Portals/0/Document /Resources/PostEradication/GAPIII_2014.pdf; Accessed on January 2017.

General strategies to achieve poliovirus containment according to GAPIII

Although the risk of intentional or unintentional release of poliovirus cannot be completely eliminated, effective containment is technically and operationally feasible with the following strategies outlined in GAPIII.

- **Risk elimination** through the destruction or transfer of materials known to contain poliovirus in facilities where the handling of poliovirus is non-essential. Materials that are potentially infectious (e.g., clinical samples) will be destroyed or inactivated depending on the risk of containing poliovirus. These facilities also need to implement secure working practices while handling new specimens potentially contaminated with poliovirus (e.g., new samples from areas using any OPV or with cVDPV outbreak), and implement a non-retention policy after testing the samples.

- **Biorisk management** through the implementation and adherence to several levels of containment safeguards in a small number of poliovirus-essential facilities (PEFs) that perform crucial vaccine production, surveillance, or research activities *(See **Table 1**: GAPIII Containment Safeguards).*

    - Primary safeguards reduce the risk of accidental or intentional release of poliovirus from a facility or personnel infection after exposure. They include appropriate facility construction principles; strict biosafety and biosecurity procedures during manipulation, storage, and transport of potentially contaminated materials; immunization of facility personnel; and existence of plans to respond to an environmental release or occupational exposure.
    - Secondary safeguards decrease community vulnerability by establishing vaccine-induced immunity requirements that would minimize spread of poliovirus.
    - Tertiary safeguards, required only for facilities manipulating WPV/VDPV, minimize the potential for released poliovirus to survive in the environment and reach humans at infectious doses. They include placement of facilities in countries with good hygiene standards, closed sewage systems, and appropriate treatment of effluents from the facility.

Safeguards are stricter for facilities handling WPV/VDPV than for those using Sabin/OPV virus because of differences in their infectivity and ability to spread.

Safeguards	Poliovirus type 2 biocontainment (phases IIa and IIb)	Final poliovirus biocontainment (phases IIIa and IIIb)	
	All type 2 polioviruses	All OPV/Sabin polioviruses	All wild polioviruses
Primary safeguards: prevention of infection with and release of contaminated materials			
Operator protection*	Yes	Yes	Yes
Decontamination of materials/equipment	Yes	Yes	Yes
Dedicated effluent treatment plant	No†	No†	Yes§
Air/exhaust treatment	No	No	Yes¶
Secondary safeguards: population immunity in country hosting facility			
Number of IPV doses	≥1	≥1	≥3
IPV coverage	= DTP3 coverage**	= DTP3 coverage**	>90%
Tertiary safeguards: environment and location			
Situating facilities in areas with low transmission potential for wild polioviruses	No	No	Yes

* Because the operator is considered to be one of the sources of release of poliovirus from the facility, specific measures of protection are required, including use of personal protective equipment, use of primary containment devices, and vaccination.
† Untreated release into a closed sewage system with secondary effluent treatment in facility location (Note: all waste from facilities, potentially containing live poliovirus, should be inactivated before release through adequate and validated inactivation procedures. For facilities without a dedicated effluent treatment plant, this would normally be done through the application of heat or chemicals as part of a validated treatment process. Under no circumstances should raw poliovirus containing effluents be discharged to drains, unless the effluent treatment plant has been designed and validated to handle such effluents, effectively acting as part of the primary containment system).
§ Facility effluent treatment before release into closed sewage system with secondary or greater effluent treatment in facility location.
¶ HEPA (high efficiency particulate arresting) filtration on exhaust air.
** Diphtheria-tetanus-pertussis (DTP3) vaccine third dose coverage; available at http://www.who.int/gho/immunization/dtp3/en/.

Table 1: GAPIII containment safeguards (source GAPIII document)

Implementation of GAPIII

GAPIII defines several actors responsible for the implementation of poliovirus containment: national polio containment coordinators (NPCC); poliovirus-essential facilities (PEFs) authorized to harbor polioviruses; national authorities for containment (NACs); and an international oversight body, the Global Commission for the Certification of Poliovirus Eradication (GCC).

National polio containment coordinators (NPCC), designated by the Ministry of Health or an equivalent authority, must survey all facilities in the country which may harbor poliovirus and identify those which will become PEFs. Then the NPCC will follow-up and validate that facilities not designated as PEFs destroy, transfer, or "inactivate" infectious and potentially infectious materials following specific guidelines,[18] before the phased containment for each poliovirus serotype. The inventories of facilities holding poliovirus materials and the validation of the fate of these materials will be shared with WHO and the GCC through periodic reports. Some Regional Certification Commissions are also involved in the validation of these reports before sharing with the GCC.

Those facilities that want to become PEFs to store or handle polioviruses indefinitely are responsible for implementing the primary safeguards described above and providing both access to auditors for inspections and necessary documentation to obtain certification against GAPIII requirements, following a process described in the Containment Certification Scheme (GAPIII-CCS). PEFs must also periodically renew their certificate of containment and report relevant issues that could jeopardize containment to the national authorities and international oversight body.

[18] *Guidance for the completion of Phase I of GAPIII – Assignment of samples to high, moderate, or negligible likelihood categories of being contaminated with poliovirus type 2 & recommended conditions for their handling and storage (under pilot testing at the time of writing this report)*

Countries hosting PEFs will need to establish a national authority for containment (NAC). The NAC will ensure that PEFs implement primary safeguards and undergo periodic inspections and will issue, suspend, or revoke certificates of containment in coordination with an international oversight body (the GCC-CWG explained below). The NAC will also oversee the country implementation of secondary and tertiary safeguards.

The GCC will act as the global oversight body to confirm global containment of polioviruses based upon reports on progress on containment activities supplied by the NPCCs and RCCs. Under the GCC, the Containment Working Group for the Global Certification Commission (GCC-CWG) will review and approve/endorse containment certificates submitted by PEFs and NACs as per the GAPIII-CCS process (*see **Figure 3***).

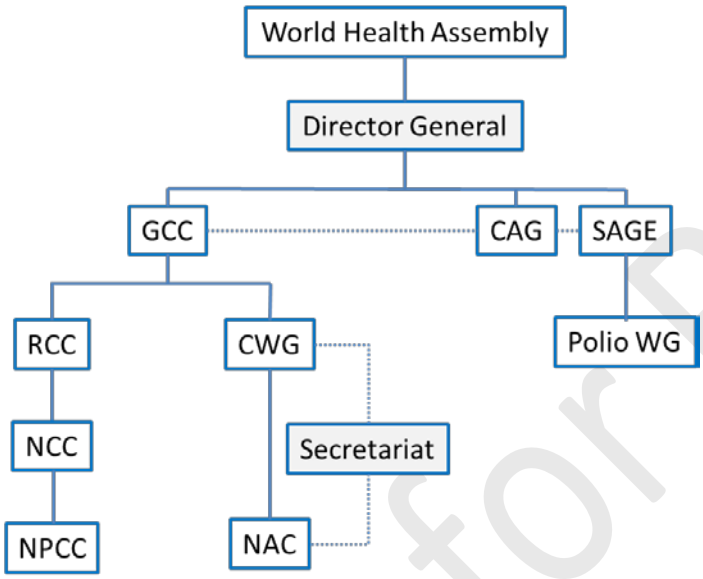


Figure 3: Oversight structure of containment activities

Current status of containment activities

GAPIII was aligned with the phased-OPV cessation and divided in three phases. Phase I involves a worldwide inventory of facilities containing polioviruses; Phase II refers to containment of type 2 WPV (IIa) and Sabin/OPV viruses (IIb); and Phase III refers to containment of all polioviruses *(see **Figure 4**: Phased poliovirus containment by type of facility)*.

Phases I and II of containment were planned to be implemented around the certification of WPV2 eradication in 2015 and after tOPV withdrawal in 2016. Phase III was planned for implementation after global certification of WPV eradication and bOPV withdrawal *(See **Figure 4**)*.

As of 7 April 2017, all 195 countries had sent reports on containment activities for Phase Ia (WPV2/VDPV2). Based upon these reports, 178 countries reported no WPV2/VDPV2 retained, and 30 countries reported retention or intention to retain type 2 poliovirus (WPV2/VDPV2/Sabin 2) materials in poliovirus-essential facilities. Reports from Phase Ib activities are still under preparation in most of the countries.

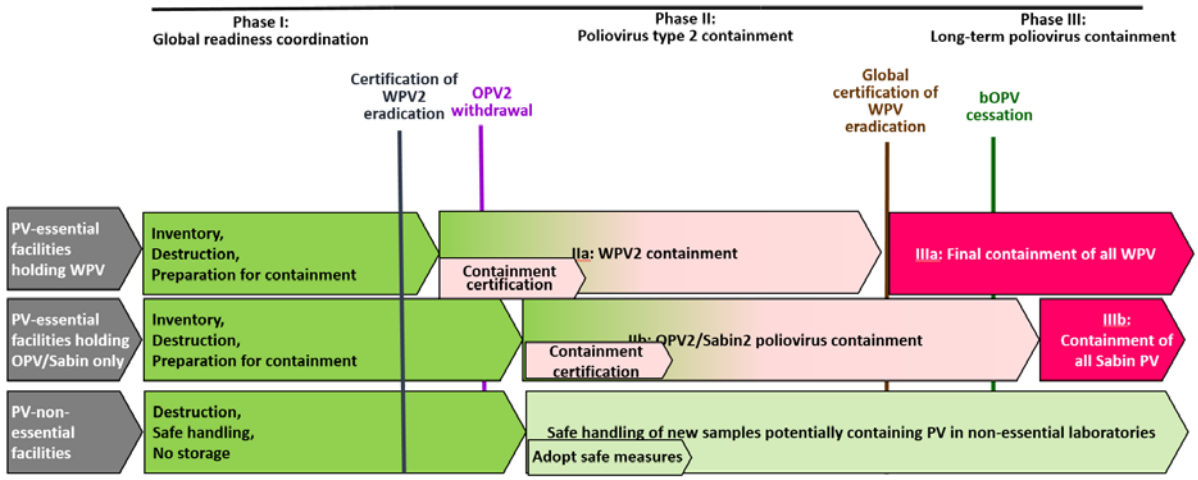


Figure 4: Phased poliovirus containment by type of facility (updated from GAPIII)

Several challenges delayed implementation of Phases I and II, including: 1) slow acceptance and elicitation of technical questions from the biomedical community of the strict containment measures requested by GAPIII for clinical samples and materials; 2) insufficient communications and advocacy around the regulatory changes needed to ensure that national and international biosafety standards for handling poliovirus and for vaccine manufacture match GAPIII requirements; and 3) lack of time and resources for PEFs and the countries hosting them to implement the structural and operational changes required to be compliant with GAPIII and complete the process of certification.

To advance the implementation of containment during the endgame, the GPEI has increased technical support and funding for communications, advocacy, and training of national authorities and future PEFs. In addition, the Containment Advisory Group (CAG) has been established to advise the WHO Director-General on potential revisions to the GAPIII document and annexes to address technical concerns slowing implementation (*see **Figure 3** with oversight structure*). Because of the different speed at which containment activities can be completed in countries with or without designated PEFs, Phases I and II will likely progress in parallel until certification.

2. Risks

A. General

As explained in the introduction, following eradication of WPV circulation and withdrawal of oral poliovirus vaccines, the accidental or intentional release of poliovirus from facilities conducting clinical testing, research or vaccine production will pose a risk for re-introduction of poliovirus into the population. The risk can be minimized, but not eliminated, by reducing drastically the number of these facilities, by ensuring strict safeguards in the facilities, and by providing adequate immunity to the surrounding communities.

B. Challenges to developing mitigation measures

There are several risks to the implementation of poliovirus containment strategies that reduce the risk and potential consequences of poliovirus releases from facilities:

- Facilities not certified as PEFs and lacking appropriate safeguards might not to comply (intentionally or unintentionally) with declaring the existence of poliovirus materials or with destroying or transferring those materials.
- Facilities harboring poliovirus might not implement safeguards in compliance with GAP (for lack of resources or other reasons).
- National authorities might not have mandate to enforce compliance of PEFs or other facilities with containment requirements.
- National authorities in countries with PEF might not be able to ensure the presence of secondary (i.e. adequate population coverage with IPV) or tertiary safeguards.
- IPV supply might be insufficient to ensure the coverage required by GAPIII in countries holding PEFs.
- The international oversight body (i.e., GCC, GCC-CWG) might not be able to enforce compliance with containment requirements by all countries because of insufficient recognition or authority and/or inadequate resources to conduct assessments (especially if the number of PEFs is high).

3. What Will Be Done

Strategic Priorities

The central strategies to achieve and sustain poliovirus containment in the post-certification period are: the reduction of the number of facilities that handle polioviruses to the minimum necessary to provide essential functions; the application of strict safeguards in those facilities retaining polioviruses and in the populations that surround those facilities; and the monitoring of facilities compliance with containment requirements through periodic certification by national and international oversight bodies.

Goal One of the PCS assumes that certain prerequisites will have been fulfilled and containment activities for Phases II and IIIa will be completed by the time of certification *(See **Annex B**: PCS Prerequisites and Assumptions)*.

Activity 1.1.1 - Achieve containment of OPV/Sabin virus after bOPV cessation and after any OPV use for outbreak response

Cessation of bOPV use is essential to maintain a polio-free world after the eradication of WPV types 1 and 3, as is the containment of all OPV/Sabin materials following bOPV cessation (*see also **Goal 2***). The following containment activities will need to be planned around bOPV cessation (currently scheduled for around one year after the global declaration of WPV certification):

- Countries need to update the facility inventory to take account of facilities holding any infectious or potentially infectious OPV/Sabin materials, including those holding bOPV stocks. These reports will be supervised by the NPCCs in each country in coordination with other teams coordinating removal of bOPV (*See **Goal 2***), standardized, and shared with WHO for consolidation.
- Those facilities not designated as PEFs (including laboratories in the GPLN) must destroy or transfer all OPV/Sabin infectious materials and proceed according to the GAPIII guidelines for handling potentially infectious OPV/Sabin materials. NPCCs will need to validate the implementation of containment activities, and submit a standardized country report to WHO and international oversight bodies. As with the tOPV switch, WHO will provide guidelines for collection and

destruction of all bOPV stocks in health facilities and storage depots, and coordination between NPCCs and immunization staff responsible for bOPV withdrawal will be established.

- Poliovirus-essential facilities (PEFs)—including research or reference laboratories, Sabin-IPV and OPV production facilities, and stockpile depots—will need to have in place the appropriate primary and secondary safeguards. The NAC established in each country with PEFs, will certify that each facility adheres to GAPIII requirements, following an inspection, and will update the current certificate or issue a new certificate to include containment of all Sabin poliovirus types. The containment certificate will also be reviewed and endorsed by the GCC-CWG. WHO will update the global inventory of PEFs containing WPV or Sabin polioviruses.
- The GCC will review country reports of containment activities and progress in certification of PEFs, and then use this documentation to validate that all polioviruses, including OPV/Sabin virus, are appropriately contained (Phase IIIb). Once Phase IIIb begins, facilities that have not received appropriate containment certification will no longer be permitted to handle or store OPV/Sabin materials. OPV/Sabin containment requirements may be temporarily suspended in areas where mOPV needs to be used to respond to re-emergence of WPV/VDPV transmission.

Following bOPV cessation and achievement of containment to all poliovirus strains, the presence of an outbreak and the use of OPV (monovalent types 1, 2 or 3 of Sabin or other novel strains) to stop the outbreak will result in a temporary breach of containment principles. The outbreak and its response will require that a number of facilities, without the extensive safeguards of PEFs, handle infected and potentially infected poliovirus materials for surveillance and diagnosis activities, in addition to storage, transport, and delivery of vaccine. Once active poliovirus circulation is interrupted and provision of any type of OPV stops, it is necessary to ensure that containment of poliovirus in facilities is re-established.

The following activities are expected to be implemented in coordination with the outbreak response:

- Notification of the outbreak and the type of response planned, to the country focal person for poliovirus containment (NPCC, NAC if available). The focal containment person can ensure that laboratories and other facilities use secure working practices while handling new specimens potentially contaminated with poliovirus and implement a non-retention policy after testing the samples as per GAPIII guidelines.
- When the outbreak is considered closed, the outbreak response team will coordinate with the containment focal person to ensure that all facilities that may have stored poliovirus materials (e.g., laboratories, vaccine depots, health facilities storing and delivering vaccine) destroy these materials following the guidelines specified in the outbreak response and GAPIII (*see **Goal 3***).
- The GCC (or equivalent oversight body created in the long term) will review country reports that outline activities done to survey facilities with potential poliovirus materials and destroy those materials. The GCC will use this documentation to certify that containment of all polioviruses has been "re-established" in the country/countries affected by the outbreak.

Activity 1.1.2 - Monitor and sustain poliovirus containment in essential facilities with the appropriate safeguards

Because the risks of poliovirus re-introduction from containment breaches within PEFs persists, and the potential severity of the consequences increases with time after bOPV cessation, it will be necessary to

maintain long-term national and international mechanisms that periodically monitor adherence of poliovirus-essential facilities to containment requirements, and retain technical and functional capacity for addressing new questions or challenges and for responding efficiently to potential breaches.

Potential functions related to this activity at different levels are as follows:

At the national level

- The PEFs will need to maintain the primary safeguards required by GAP III and periodically submit the appropriate documentation to be reassessed by auditors and NACs and renew their containment certificate.
- The NACs will need to implement certification procedures to regularly (annually) assess compliance of facilities. Every three years, the NAC will coordinate with the PEF a new full-scope audit for renewal of the containment certificate. Based upon the results of the audit, the NAC will renew, modify, suspend, or withdraw the certificate of containment in coordination with the GCC-CWG (or equivalent body).

At the global level

- The GCC-CWG will oversee the issuance of new containment certificates and periodic re-certification of existing PEFs in coordination with NACs.
- The CAG will continue to advise the WHO on technical questions and issues related to poliovirus containment that may be elicited by vaccine manufacture, vaccine or diagnostic research, or others.
- The following tasks must also be maintained:
    - Develop and regularly update guidelines and technical materials on poliovirus containment for laboratory or research communities, governments, and regulatory agencies (revisions of GAPIII, guidelines for implementation of GAP, guidance for responses to containment breaches, etc.).
    - Maintain a global inventory of PEFs that is updated when new facilities apply for a certificate, when certificates are expired or withdrawn, etc.
    - Provide updated training on the containment certification processes and mechanisms to auditors, NACs, and focal persons in PEFs.
    - Support the GCC-WG activities, including periodic training of members, organization of meetings, and preparation of documentation necessary for review of containment certificates requests, among others.
    - Provide secretariat functions to the CAG and GCC-CWG.
    - Provide technical assistance to PEFs and country health officials for investigating and responding to containment breaches, ensure that response plans adhere to guidelines, help with the investigation, and coordinate the potential response with polio outbreak response teams.
    - Provide technical assistance to countries that need to use OPV in response to an outbreak, to ensure the implementation of appropriate guidelines that minimize risks in new facilities handling polioviruses infected materials; to follow up activities to destroy remaining vaccine and poliovirus materials; and to ensure that reports of these activities are validated by the national and international oversight body (e.g., NPCC and GCC).

D. Who Oversees the Goal

(To be edited in coordination with the Governance section)

The Global Certification Commission (GCC) will oversee achievement of containment in the precertification stages (as per the PEESP), and it is expected that the GCC will continue high-level oversight until it needs to be adjusted. The GAPIII assigns the responsibility of compliance with containment principles from essential and non-essential facilities to national authorities, which periodically will need to report progress in containment activities and potential breaches to the GCC. To facilitate enforcing of containment principles by all countries, the GCC will present a status report of containment activities to the WHA regularly.

The GCC-CWG will to continue to oversee and endorse the provision of certificates of containment post-certification, for as long as PEFs exist. The number of PEFs is not expected to decrease significantly post-certification until IPV is no longer required for routine immunization.

Finally, considering the need for continued vaccine manufacture, diagnostic capacity, and research, it is expected that the CAG will be needed long-term to provide technical expertise to the Director General on new issues related to poliovirus containment.

Goal Two: Protect Populations

Protect Populations		
Main Objectives	Major Activities	Outcome Indicators
Objective 2.1 - To protect populations from VAPP and VDPV by effectively preparing and implementing the globally synchronized withdrawal of bOPV	• Activity 2.1.1 - Develop and implement plans (including pre-cessation SIAs) to withdraw bOPV from routine programmes and SIA	• Globally synchronized withdrawal of bOPV within 12 months after certification of WPV eradication
Objective 2.2 - To provide access to safe, effective vaccines for long-term protection from poliovirus for global populations	• Activity 2.2.1 – Implement future immunization policy to protect population against poliovirus • Activity 2.2.2 – Support the procurement and supply of affordable IPV vaccine and for its effective, efficient delivery to facilitate high immunization coverage	• Post-OPV immunization schedule recommended by SAGE (April 2017) implemented in all countries (date TBD) • >90% coverage with ≥3 IPV doses achieved in all countries with PEF containing WPV.
Monitored by SAGE, GCC		

A. Introduction

The *Polio Eradication and Endgame Strategic Plan* and *Midterm Review* provided a vision to protect populations through strategies to interrupt transmission and optimize the management of the immediate and long-term risks of poliovirus. These strategies are based on the core assumption that a polio-free world means not only complete interruption of wild poliovirus (WPV) transmission, but also the elimination of poliovirus infections associated with the use of oral polio vaccines (OPV). Although OPV has been the key tool in stopping WPV transmission, its use can also cause vaccine-associated paralytic poliomyelitis (VAPP) in vaccine recipients and close contacts, or it can mutate and lead to circulating vaccine-derived polioviruses (cVDPVs) in populations with low immunity. Additionally, individuals with B-cell related primary immunodeficiencies who are exposed to OPV can continue to excrete poliovirus (i.e., immunodeficiency-associated VDPV, or iVDPV) and potentially introduce the live virus into the community.

Even after eradication is certified, the world's population will still require protection from a possible re-emergence of poliovirus for a number of years. Individuals and communities must remain protected

from the immediate post-cessation era risks of VAPP and VDPV from bOPV, the intermediate risk from iVDPV, and the continued long-term risk from WPV or other polioviruses due to a containment breach or intentional release. Unless and until other safe, effective, and affordable options are developed, this protection will rely on IPV (plus mOPV stockpiles in case of outbreaks, *see **Goal 3***).

B. Description of the Goal

The goal of eliminating all paralytic polio disease and achieving polio eradication ultimately requires stopping all use of OPV globally and continuing to immunize with other safe and effective polio vaccines. These dual efforts of bOPV cessation and extended widespread use of IPV in routine immunization to reach 90% seroconversion will mitigate the risks from VAPP, VDPVs, and possible re-emergences of WPVs.

C. Objective 2.1: Protect populations from VAPP and VDPVs

1. Context

The GPEI has already successfully implemented strategies to eliminate WPV in most of the world and has initiated sequential steps to withdraw OPV along with the widespread introduction of inactivated poliovirus vaccine (IPV) to continue protecting populations from polioviruses. Following the declaration of type 2 WPV global eradication in September 2015, the GPEI coordinated an intermediate step to globally withdraw trivalent OPV (tOPV) and switch to bivalent OPV (bOPV) in April 2016. The corollary plan to additionally introduce at least one dose of IPV in all 126 OPV-only using countries has been only partially implemented due to severe global constraints on IPV supply. To offset these supply constraints, some countries have utilized fractional dosing and others have had to either defer IPV introduction altogether or interrupt providing IPV, as supply was no longer available.

2. Risks

A. General

After all WPVs have been eradicated, a critical impediment to establishing a truly polio-free world will be a failure to protect populations from the development of cVPDVs 1 and 3 or a failure to fully stop all use of live vaccine. Emergence of cVPDV 1 or 3 can best be prevented by ensuring maximum population immunity against these types prior to bOPV cessation. The withdrawal process itself can present significant logistical challenges and lead to further risks if not implemented effectively. While intensive global planning and support will be provided to assist countries to withdraw bOPV, experience from the switch in 2016 demonstrates there is still a risk of residual live vaccine remaining in the community either in storage or even continued use in routine EPI. This residual vaccine presents a potential risk for development of VAPP or VDPVs. These risks can also persist if mOPV is required to be widely re-introduced for an outbreak response *(see **Goal 3**)*.

B. Challenges to developing mitigation measures

Inherent system characteristics

- Although bOPV and mOPV represent the best option for stopping poliovirus transmission in the first stages after certification, like all live polio vaccines, they can result in VAPP or cVDPVs (especially if population immunity is low). Giving IPV before OPV can substantially reduce VAPP. However, limited IPV supply may preclude many children from receiving an RI dose prior to receiving bOPV or mOPV.

Implementation

- Sustaining high levels of immunity to types 1 and 3 from the time of WPV interruption until bOPV cessation in all countries is dependent on national commitment, quality of vaccination activities (both RI and SIAs), and adequate resources (both financial and vaccines). Although proper global planning should assure availability of bOPV supplies, due to competing priorities following the last global case of WPV, countries may have difficulties meeting the other requirements.
- The readiness criteria for bOPV cessation may be dependent on all countries achieving global surveillance and containment standards. Experience to date has demonstrated these standards may be difficult to attain for some countries, especially if sub-national benchmarks are expected.
- Adequate lead time is required prior to cessation so the withdrawal is globally synchronized and effectively implemented. However, assurance that all persistent cVDPV transmission has stopped so final plans can be implemented will be dependent on halting any ongoing transmission and confidence in poliovirus surveillance systems in high risk areas.
- Although comprehensive guidelines are available, fully verifying that all remaining bOPV vaccine from thousands of local sources is collected and destroyed at the country level post-withdrawal can be problematic. Environmental surveillance tracking Sabin viruses may be the most efficient way to supplement on-site monitoring of the vaccine cold chain, but the number of sampling sites is limited.

3. What Will Be Done

Strategic Priorities

Populations will be protected by providing high levels of type 1 and 3 immunity prior to bOPV withdrawal. The GPEI will balance the need for high confidence of WPV eradication with necessity to withdraw bOPV as soon as feasible after interruption to sustain these high levels. As supplies permit, some countries currently using bOPV may switch to an IPV schedule before certification. For other countries still relying on bOPV for use in RI and/or SIAs at the time of certification, planning for withdrawing this vaccine will be initiated as soon as feasible in order to have a globally synchronized process. Global support will be provided to assist countries to meet the readiness factors for initiating the withdrawal. Additionally, as was the case for the switch from tOPV to bOPV, a well-organized global coordination effort along with sufficient regional and national level funding, staff, and monitoring are required to effectively implement the cessation plan.

Activity 2.1.1 Develop and implement plans (including pre-cessation SIAs) to withdraw bOPV from routine programs and SIA use

The principles, strategies, planning process, and implementation of the withdrawal of bOPV will be similar to the withdrawal of tOPV. However, withdrawing bOPV will occur in the context of global certification and represent complete cessation and not simply a switch of live polio vaccines. Furthermore, while bOPV use is a risk for VAPP or VDPVs, the vaccine's withdrawal can present a risk due to potential gaps to the protection provided against poliovirus types 1 and 3.

Framework for bOPV cessation: principles, readiness factors, and risk management strategies

The general framework for OPV cessation after global polio eradication has already been established by the GPEI. [19] Further principles for bOPV withdrawal are patterned on those employed for the tOPV switch, but reflect lessons learned and the specific post-certification situation:

- Readiness factors should be established which mitigate the risks involved with cessation. Special attention should be directed to ensuring all populations have affordable access to IPV and polio outbreak response OPV stockpiles.
- Complete cessation of the remaining use of bOPV at the time of certification should be globally synchronized within a fixed two-week period. This ensures that no country is inadvertently put at risk of importing Sabin OPV or a VDPV from a country that continues to use OPV in routine immunization.
- All remaining stocks of bOPV outside of outbreak response OPV stockpiles and manufacturers' stocks should be collected and destroyed at the time of cessation. The withdrawal and destruction of all bOPV should be confirmed through a comprehensive validation process. The GPEI will explore with relevant countries whether manufacturers should retain any remaining bOPV stocks until expiration.

Guidance for bOPV withdrawal will consider these principles by establishing five key readiness factors:

1. Pre-cessation immunity for types 1 and 3
2. IPV supply and status of global introduction
3. Poliovirus surveillance
4. Outbreak response capacity (e.g., vaccine stockpiles, availability of response guidelines)
5. Containment of poliovirus

By April 2018 the SAGE is expected to establish specific expected parameters for each factor as well as a timeline and triggers for activating the withdrawal process relative to certification. Achieving these standards reflects the strategies required to minimize and manage the risks associated with final OPV cessation as well as the overarching objective of sustaining a polio-free world. While the actual withdrawal of bOPV will not take place until after global certification, the GPEI will regularly monitor country progress to meeting the expected readiness factors and provide technical assistance as

[19] See WHO. Cessation of routine oral polio vaccine (OPV) use after global polio eradication: Framework for national policy makers in OPV-using countries. Geneva, 2005. GPEI. Polio Eradication & Endgame Strategic Plan 2013-2018. WHO: Geneva, 2013

appropriate to ensure timely achievement in each category. Considerations for these readiness factors include the following:

1) Maintaining high population immunity for types 1 and 3 prior to cessation is essential to maximize protection against future VDPVs. While IPV should be available for high-risk countries, under-vaccinated subpopulations remain particularly at-risk and should be specifically targeted for bOPV SIAs. Other countries which have not been able to obtain adequate IPV supplies will also be vulnerable. Several options exist for these pre-cessation SIA (e.g., annual and/or intensified campaigns just before withdrawal). Approaches will need to be tailored to match specific country-risk profiles based on vaccination and immunity status, assessed risk for emergence of different categories of poliovirus, and appropriate level of granularity to target need. The scope, timing, and number of SIAs should be chosen to maximize quality of implementation and achieve the highest levels of immunity possible just prior to bOPV withdrawal. The GPEI is expected to establish a detailed strategy and pre-cessation SIA calendar no later than two years prior to certification.

2-5) Specific strategies for IPV supply and introduction *(see **Objective 2.2**)*, surveillance *(See **Objective 3.1**)*, outbreak response *(See **Objective 3.2**)*, and containment *(see **Objective 1.1**)* are outlined elsewhere, as provided, in the PCS.

Operational considerations for withdrawal planning

In addition to the meeting the readiness factors, there are substantial operational, logistical, communication, and programmatic challenges to implementing the withdrawal. Some key lessons learned from the successful tOPV switch which will help guide the operations of bOPV cessation

- Early engagement and intensive coordination among global, regional, and national levels was important for successful implementation. Country and regional leadership and ownership should be augmented by global support, potentially including financial support.
- Providing options and minimum standards for implementation permitted local flexibility.
- Although advanced planning with countries was a challenge due to low motivation to commit to concrete switch plans, beginning the process 18-24 months in advance of the anticipated withdrawal was required to complete the process.
- Planning was further complicated by uncertainties in the global capacity to meet the switch preconditions for containment, absence of cVDPV2s, and IPV supply.
- Extensive training on required planning and implementation for country representatives, as well as communication materials on the switch, facilitated cooperation and maximized technical compliance. Messages related to bOPV withdrawal can potentially be simpler since all regular use of OPV will cease, instead of one form of OPV being switched for another.
- Early and transparent engagement with the manufacturers can result in timely changes in vaccine production plans, potentially allowing sufficient supply of vaccine to be available to meet demand.
- Global-level task monitoring promoted accountability and timely progress. Validation relied on leveraging in-country monitoring mechanisms supplemented by international observers in some key areas.
- Subsequent discovery of tOPV remaining in the cold chain in several countries highlighted the gaps in the validation process. Incorporating checks for OPV into routine immunization

supervisory and evaluation visits indefinitely after OPV withdrawal can complement efforts to confirm that all OPV has been withdrawn immediately after the withdrawal date.

These lessons can help SAGE and the GPEI in establishing the recommended timeline for implementation by balancing operational and epidemiologic considerations. To maximize the population immunity for types 1 and 3, country-level withdrawal of bOPV should take place as soon as feasible after global certification (ideally <12 months). Global preparatory planning for this operationally-challenging event should begin 24 months prior to the scheduled implementation. Final country-level planning should be initiated when there is high confidence of the date of global certification and at least 12-18 months prior to withdrawal. Specific markers such as certification milestones (e.g., date of last regional certification) and/or epidemiologic achievement (e.g., global lack of persistent cVPDVs for at least 6 months) will need to be designated to activate both pre- and final planning.

A well-organized global coordination effort along with sufficient national-level funding, staff, and leadership will be essential to effectively implement the plan. Relying on lessons learned during the switch process, updated guidelines for national implementation of the bOPV withdrawal will be developed and disseminated well in advance. Given the risks to containment and VAPP/VDPVs from failure to identify and destroy any remaining bOPV, further emphasis will be placed on aggressive and comprehensive monitoring and validation measures conducted during the withdrawal. Additional guidelines for tracking and destroying remaining OPV used in SIA are already available.[20] Direct communication should be provided to both the general public and health care providers on the need to stop all regular OPV use.

D. Objective 2.2: Provide access to safe, effective polio vaccines for long-term protection

1. Context

A. Population protection: polio vaccines, policy, RI use, and supply

Vaccine formulations

Significant progress has been made in interrupting WPV transmission using live attenuated OPV due to its low cost, ease of administration, and effectiveness in generating mucosal immunity. Initial formulations contained Sabin strains of all three poliovirus serotypes (tOPV), but type-specific vaccines have been developed to contain either types 1 and 3 (i.e., bivalent or bOPV) or single strains (i.e., monovalent OPV or mOPV). Because OPV can cause rare paralytic disease, many developed countries have transitioned to IPV soon after their last case of polio. IPV is highly effective in inducing individual protection and therefore has a critical role in routine immunization. However, it has limited effect on providing community protection (i.e., mucosal immunity) and its role in eradication is less evident. Clinical studies have shown that it may aid in stopping WPV or VDPV transmission by reducing the

[20] See GPEI. Technical Guidance: Additional verification of withdrawal of tOPV or mOPV2. WHO: Geneva, 13 June 2017

prevalence and duration of fecal shedding, but this effect depends on coverage, OPV status (naive vs. OPV-vaccinated with waning intestinal immunity), OPV take, and adequacy and timing of OPV use.

Delivery

IPV has historically been delivered by intramuscular (IM) injection. However, due to severe supply shortages, the GPEI has evaluated the use of fractional (i.e., 1/5 of the full IM dose) dosing of the vaccine delivered intradermally (ID) using a standard bacillus Calmette–Guérin (BCG) syringe and several innovative delivery devices (*see **Research** in Enabling and Cross-Cutting Areas*). A significant body of evidence shows that two ID fractional IPV (fIPV) doses at the appropriate age and interval are more immunogenic than one full IM dose and provide equivalent protection as two full IM doses of IPV. Further research is ongoing to determine the length of protection provided by fractional dosing.

Policy

In 2005 the GPEI concluded that ultimately all countries would need to stop using OPV in order to achieve a polio-free world. As an initial step in this plan, in November 2012 the Strategic Advisory Group of Experts on Immunization (SAGE) recommended that at least one dose of IPV should be introduced into all EPI programs prior to the switch from tOPV. Severe global supply constraints precluded full implementation of this recommendation and required prioritizing available vaccine by tiers of countries based on their risk of PV transmission.

By April 2017, 176 countries had introduced at least one dose of IPV into their RI schedules and the remaining 18 countries had committed to do so. However, due to lack of IPV vaccine, these 18 countries have delayed the introduction of IPV and 17 additional countries' supplies have been interrupted leading to intermittent or prolonged stockouts. Given the ongoing severe global IPV shortage, SAGE further recommended that in the short term, countries should use two fractional IPV doses in their national routine immunization schedule where practical, and that IPV supply should be prioritized for use in routine immunization. Catch-up immunization was recommended for all missed cohorts as soon as supply becomes available.

Status of routine polio immunization

Table 2. Summary of polio vaccine use in RI (June 2017)

Vaccine	*# of countries*	*Comment*
bOPV only	TBD	All have committed to introducing IPV once supply is available
bOPV + IPV		Includes x with fI dosing in some or all of the country
IPV only		Includes multiple formulations (single or combination)

Table 3. Summary of estimated vaccination coverage w/ 3 doses of polio vaccine (POL3), by WHO region (2015) and last endemic countries (2016)

WHO Region *(selected country*)*	*% POL3 coverage*
AFRICA	76
Nigeria	49
AMERICAS	91
EASTERN MEDITERRANEAN	80
Afghanistan	60
Pakistan	72
EUROPE	94
SOUTH-EAST ASIA	86
WESTERN PACIFIC	96
GLOBAL (n=194)	86

*Last endemic countries; Source: regional estimates from MMWR[21]; country estimates from latest WHO/UNICEF data[22]

Table 4. No. (%) of countries reaching 90% coverage w/ 3 doses of polio vaccine (POL3), by World Bank income category, 2015

Income category* (no. of countries)	No. (%) of countries with 90% POL3 coverage
High (57)	54 (95)
Upper-middle (54)	35 (65)
Lower-middle (50)	23 (46)
Low (31)	8 (26)
All income categories (192)	120 (63)

* World Bank income category based on countries' per capita gross national income (GNI) in 2015.
Source: MMWR[23]

The global POL3 coverage attained through routine immunization (RI) has remained stable between 84-86% from 2010-2015. Seventy-two countries (37%) have not yet met the Global Vaccine Action Plan 2011–2020 target of 90% national POL3 coverage. Coverage varies widely among and within WHO regions, countries, and communities. The low RI coverage in the last two remaining regions with endemic polio transmission, the African Region and the Eastern Mediterranean Region, and the most likely to face cVDPV emergence, indicate the challenges ahead to providing long-term protection from polio in the post-certification era. Average POL3 coverage also remains troublingly low in many of the upper-middle and lower-middle income countries, which may be the most likely at risk for iVDPVs in the future.

[21] Casey RM, et al. Global Immunization Coverage, 2015. MMWR November 18, 2016 / Vol. 65 / No. 45, 1270-1273.
[22] See: http://apps.who.int/immunization_monitoring/globalsummary/timeseries/tswucoveragedtp3.html (accessed 28 July 2017)
[23] Casey RM, et al. Global Immunization Coverage, 2015. MMWR November 18, 2016 / Vol. 65 / No. 45, 1270-1273.

Supply

bOPV

Sufficient bOPV vaccine supply is available through XXX to meet the projected SIA and routine immunization requirements for the 70+ countries which procure through UNICEF. UNICEF is currently finalizing the procurement process aiming to secure adequate stocks to cover these needs through cessation. Several large countries which are currently self-procuring from the global market or have national vaccine production, including India, Indonesia, and China, have adequate stocks for their own requirements but will also be expected to withdraw bOPV by the time of global cessation.

IPV

All the high-risk tier 1 and 2 countries have introduced at least one full or two fractional doses of IPV into their routine schedules. Provided supply continues to be available, the latest allocation principles recommended by the GPEI assures these countries of an uninterrupted supply. Because of the continued constrained supply availability, the 18 countries securing vaccine through UNICEF which have not been able to introduce IPV into their routine programme will probably not be able to do so until XXX. For the other 18 countries which have experienced stockouts, further vaccine to cover their missed cohorts with one fractional dose could be made available based on their assessed risk tier. Any of these countries willing to change to administration of fractional dose of IPV (fIPV) will be prioritized as supply becomes available.

B. Population protection: global immunization

Although polio eradication has often relied on supplemental immunization and represents a focused objective within EPI, its long-term sustainability remains highly dependent on the capacities of national routine immunization and overall health systems. From the global perspective, the GPEI's program accomplishments as well as challenges are closely linked to broader immunization goals and stakeholders under the Global Vaccine Action Plan (GVAP).[24] Polio eradication is an integral part of all the GVAP goals for the decade to: 1) improve routine immunization to meet vaccination coverage and equity targets; 2) eradicate polio, eliminate measles, rubella, and maternal and neonatal tetanus; 3) introduce new and improved vaccines; and 4) spur research and development for the next generation of vaccines and technologies.

2. Risks

A. General

Sustaining a polio-free world in the post-certification era is put at risk if there is a failure to provide access to IPV, which can generate long-term individual protection against a possible poliovirus re-emergence. This access is dependent on supply, affordability, and effective delivery to the community through RI. Deficiencies in any one of these requirements jeopardizes attaining the high coverage required by Goal Two. Failure to achieve the goal leaves individuals vulnerable to infection and potentially to paralysis, and leaves communities and the world susceptible to wider transmission.

[24] See http://www.who.int/immunization/global_vaccine_action_plan/en/

B. Challenges to developing mitigating measures

- Long-term protection depends on IPV, which requires at least two doses to meet the 90% seroconversion target recommended by SAGE, is relatively expensive (compared to OPV), and provides only limited community protection to stop transmission. Duration of protection with a two-dose schedule remains unknown. Development of more affordable IPV formulations depends on overcoming multiple technical challenges. Expanding use of ID fIPV faces regulatory issues, uncertainties about costs and availability of suitable delivery devices, lack of staff trained to effectively use ID techniques, and challenges with acceptance of new approaches in many countries. Global supply of IPV is still precarious. Multiple cohorts could be left unprotected indefinitely if new interruptions to IPV supply result in further delays in supplying the 35 countries now without a dependable source of IPV.
- The unpredictability of long-term demand for IPV may adversely affect manufacturers' willingness to enter the market and thus market stability. Multiple countries may shift to fIPV, and middle-income countries in particular may question whether to adopt IPV after balancing costs, risks, and other health priorities.
- There is currently not a clear commitment from the donor community to support IPV after 2018. There are significant benefits but also opportunity costs associated with continued long-term use of IPV given other competing demands for their investments in public health. Strengthening RI, particularly in the highest-risk countries, faces chronic programmatic problems (e.g., reaching marginalized populations, lack of trained staff, and poor governance) as well as daunting systemic challenges (e.g., weak health systems, substantial income inequalities, and intractable humanitarian emergencies).

3. What Will Be Done

Strategic Priorities

Implementing a future polio vaccine immunization policy, including a schedule which is programmatically feasible and provides at least the required minimum immunity, will be the cornerstone of the strategy to ensure long-term protection. This policy cannot be fully implemented unless there is an adequate supply of affordable IPV for all countries. Adequate supply depends on both production capacity and positive market forces. Affordability will be addressed by exploring new formulations or delivery options to lower the cost of the vaccine to make it more attractive, especially for middle-income countries. Additional medium- to long-term financing strategies are needed to support low-income countries.

IPV will be delivered through routine immunization implemented by national EPI programs under the global strategic umbrella of GVAP. In the context of sustaining eradication, the priority for immunization programs is not only ensuring high levels of coverage of a polio vaccine among the general populations through effective and efficient delivery, but particularly targeting the most susceptible populations.

Activity 2.2.1 Implement future immunization policy to protect population against poliovirus

Based on available evidence, in April 2017 SAGE recommended that after global OPV withdrawal:

1. Countries should include at least two doses of IPV in their routine immunization schedule, the first at or after 14 weeks (i.e., with the second or third dose of diphtheria-tetanus-pertussis or DTP-containing vaccine) and the second dose ≥4 months after the first dose, administered either as full or fractional doses.
2. Countries without poliovirus-essential facilities (PEFs) should maintain IPV in their routine immunization schedule for at least 10 years after global OPV withdrawal, to address: immediate (VDPVs), intermediate (iVDPV) and longer-term (e.g., containment failure) risks.
3. Countries with PEFs should continue to use IPV as long as mandated by GAPIII to minimize poliovirus facility-associated risk.

While specifics may change prior to certification based on additional research *(see **Research** in Enabling and Cross-Cutting Areas)* or changes in GAPIII containment recommendations, this establishes the global immunization policy for future polio vaccination and sets the expectations for national EPI programmes.

The proposed schedule is designed to achieve durable individual immunity through providing at least 90% seroconversion and robust antibody titers to all three poliovirus serotypes. The designated age at first dose and dosing interval will offer maximum vaccine efficacy and accommodate existing EPI contacts for DTP and measles.

SAGE also acknowledges the programmatic equivalency of fractional or full-dose IPV. This recommendation provides long-term options for countries which could reduce costs and stretch vaccine supplies. Further research will be needed to determine the eventual effectiveness and duration of immunity delivered by each approach.

The recommendation to use IPV for 10+ years addresses the need to provide long-term global protection against the small but continuing risk of residual circulation of poliovirus and may provide some signal to vaccine manufactures about the potential future demand of IPV.

Containment considerations expand the expected duration of IPV use and set coverage levels to be achieved. After the OPV cessation, GAP III requires that countries with PEFs containing OPV/Sabin materials provide at least one dose of IPV (=DTP 3 coverage) and countries with PEFs containing WPV materials provide at least three doses of IPV (greater than 90% coverage). The SAGE recommendations require all countries to have at least two doses of IPV but do not establish coverage expectations which are tied to DTP3 goals set by GVAP. As additional countries with large populations such as China, India, and Indonesia establish PEFs, SAGE and the Global Certification Commission, may choose to further refine the parameters and expected geographic scope of these recommendations.

Activity 2.2.2 Support the procurement and supply of affordable IPV vaccine and for its effective, efficient delivery to facilitate high immunization coverage

Attaining and sustaining high immunization coverage with IPV in the post-certification era will require extensive inputs at global, national, and ultimately, community levels, including: 1) global capacity and willingness to produce sufficient vaccine supply; 2) national commitment, finances, and infrastructure capacity to purchase and deliver the vaccine; and 3) community desire for their children to be vaccinated. Meeting these conditions will require broad support and systemic inputs from multiple

stakeholders that are beyond the scope of the PCS. The strategies noted below are targeted to IPV but should be part of a coherent set of activities which promote high coverage with all vaccines and overall sustainability of the immunization efforts. These strategies include:

- Determine demand for IPV and facilitate adequate long-term supply of appropriate IPV products
- Advocate for sustainable financing of IPV
- Facilitate effective and efficient delivery of IPV

Determine demand for IPV and facilitate adequate long-term supply of appropriate IPV products

Demand —

Key clarifications that have been sought by industry regarding the demand of IPV refer to the following issues: 1) at the time of OPV cessation, should countries adopt least two doses of IPV in their schedule; and 2) should countries without PEFs continue to immunize for at least 10 years following bOPV withdrawal. These points have been discussed and addressed in the April 2017 SAGE recommendations (See Activity 2.2.1).

However, there are still several critical factors pending clarification which could have a significant impact on demand:

1. Timing of bOPV cessation. Current assumptions are that bOPV cessation will happen globally within 12 months after global certification, with global certification happening three years after the last WPV is identified. The factors below need to be confirmed before a more precise demand forecast can be established:
   a) Timing of when countries should introduce a two-dose schedule (i.e., at the same time as bOPV withdrawal or six months prior, similar to the switch from tOPV to bOPV)
   b) Will there be 12 months between certification and bOPV withdrawal? Or will withdrawal be during the "low transmission season" (i.e., April, similar to the bOPV, tOPV switch)?
   c) Will global certification happen three years after the last WPV, following regional certification?
2. Future financing mechanisms and costs of IPV (or IPV-containing vaccines)
3. Use of full or fractional doses
4. Perceived risk of polio by countries, especially those that will not have introduced IPV more than two years after the switch due to lack of supply.

Aside from countries with PEFs which are expected to meet IPV use requirements under GAPIII, other countries may take the SAGE recommendation into consideration, but will need to make their own decision to use IPV based on a cost/benefit analysis. Some expectations of this demand have already been made based on broad-based scenarios and assumptions (See ***Figure 5***). Post bOPV cessation, unless all current OPV-using countries adopt fIPV, from 170 million to 230 million IPV doses will be required to meet global demand. A more comprehensive understand of the expected global demand for IPV should be generated by conducting investigations of individual country on their 'willingness to pay,' perceived future risk of poliomyelitis for their population, and intended dosing-type (e.g., full or fractional).

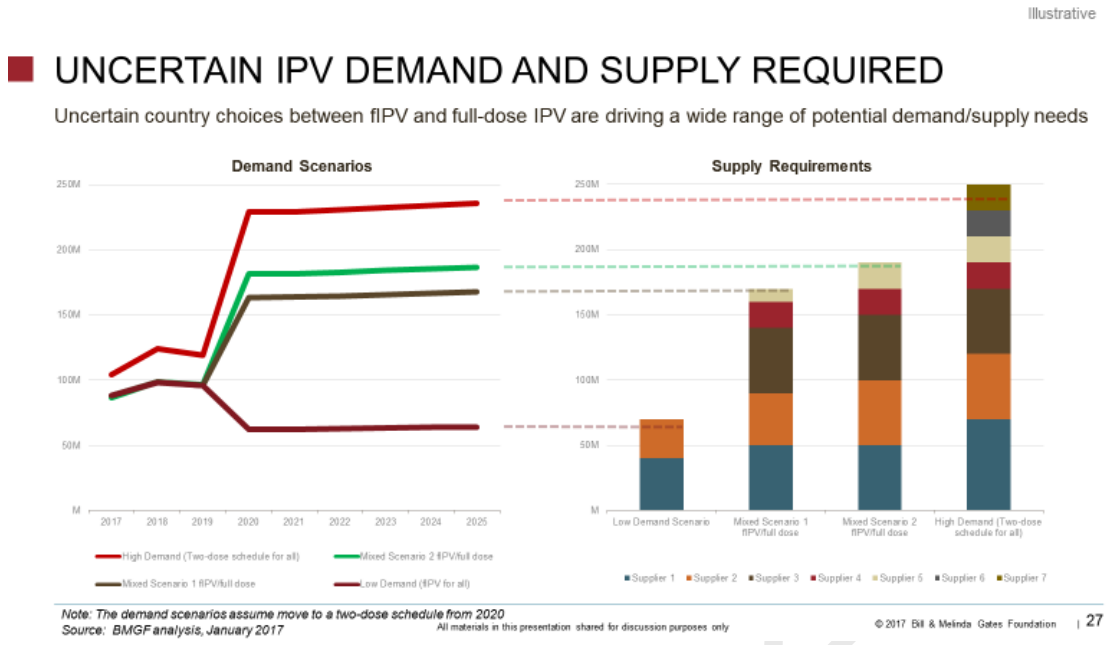


Figure 5. Future IPV demand scenarios and supply requirements

Supply. (to be expanded based on IPV Road Map being developed by GAVI and other partners)

IPV products—Introducing IPV into all low- and low-middle income countries will require volume procurement of existing IPV single-antigen formulation and development of low-cost alternatives. Alternative options include:

- Broader use of fractional dosing
- Development of adjuvanted and antigen-sparing IM IPV products
- Development of low-cost, IPV-containing combination vaccines, such as hexavalent

Although fractional dosing has already been introduced in multiple countries primarily as a method to stretch limited supplies, this option can provide a valuable means for cost savings. Active engagement with global and national regulators will be required to address the challenges associated with the current off-label use. However, the primary challenge with the use of fractional dosing by many countries is due to the necessity of using ID delivery. Studies are underway to determine the efficacy of fractional IM dosing. Wider availability of ID delivery devises which are simpler to use than standard ID syringes could also perhaps spur wider acceptance. *(See **Effective and Efficient Delivery** below.)*

Development of adjuvanted vaccines is being pursued; however, in the long-term combination vaccines containing IPV may be the most attractive option. According to WHO/UNICEF Joint Reporting Forms in 2016, many upper-income countries already widely use IPV containing formulations in their EPI schedules: 42 countries use hexavalent (DTaP-Hib-HepB-IPV) and 39 use pentavalent (DTaP-Hib-IPV). These formulations are currently more expensive than single-dose IPV, however IPV combination vaccines using whole cell pertussis are under development could be cheaper while still providing equivalent efficacy to stand along IPV. Combining antigens can stimulate community demand and improve efficiency of delivery. Since age of first dose, interval, and number of doses of combination

vaccines are usually dictated by antigens other than IPV, additional investigation will be needed to ensure that any recommended schedule still provides the necessary minimum seroconversion standards for polio protection. *(See **Research** in Enabling and Cross-Cutting Areas for further details.)*

Advocate for sustainable financing of IPV

X countries are expected to receive GAVI-funding through 2020 to support a single IM dose or two fractional doses of IPV for routine EPI. Decisions for funding from 2021 onward are anticipated by 2018. There is consideration to include IPV as a 'global public good' under a new Vaccine Investment Strategy. The number and type of dosing, length of funding, etc. all remain to be determined.

Facilitate effective and efficient delivery of IPV

By the time of certification, IPV will no longer be a "new vaccine" for any country; however, depending on when adequate supplies are available, some countries may still be in the process of fully integrating the vaccine into regular use. Key steps which are important for any change to the EPI schedule should be undertaken well in advance, including: training of health workers, developing and implementing a comprehensive communication strategy for caregivers and parents, instituting any required changes in cold-chain and vaccine management, revising immunization records, etc. These activities should be fully integrated with implementing the withdrawal of bOPV.

Widespread experience to date in India and Sri Lanka has already demonstrated the feasibility of using ID fIPV in routine immunization settings. The multi-dose vial policy for IPV and availability of five-dose vials have also resulted in lower wastage rates and vaccine requirements. However, despite evidence of effectiveness and potential savings in supply and cost, countries have been slow to adopt fractional dosing for IPV primarily due to concerns over ID delivery. Several alternatives to BCG syringes have already been developed and widely tested. *(See **Research** in Enabling and Cross-Cutting Areas)* These options are still relatively expensive and some require intensive re-training of health care workers. Nevertheless, they may present viable methods to increase the efficiency of ID delivery. Additional field experience and collaboration with manufacturers should provide ways to bring down costs and increase acceptance among policy makers and workers.

The transition planning process that the GPEI currently supports at the country level aims to identify how polio resources, human capacity, and knowledge can be directed to achieving GVAP and broader public health goals. Overall strengthening of RI must be a critical priority for attaining these broader goals, as well as sustaining the functions essential to protecting populations from future polio emergences. As partners develop the next GVAP 2021-2030, sustaining polio eradication should be included as a core objective.

E. Who Oversees the Goal

(To be expanded later)

Development and implementation of both objectives will require technical and operational monitoring. Technical monitoring will most likely depend on SAGE, etc. Operational monitoring will need to incorporate similar capacities as required under the tOPV-bOPV switch, as well as long-term oversight of EPI delivery.

Goal Three: Detect and Respond

This goal is currently the longest because the team is still very much in the data-gathering phase but we will further edit and shorten this section.

Detect and Respond		
Main Objectives	Major Activities	Outcome Indicators
Objective 3.1 - To promptly detect any poliovirus in a human or in the environment through a sensitive surveillance system	• Activity 3.1.1 - Redefine poliovirus surveillance paradigm • Activity 3.1.2 - Sustain adequate and technically qualified laboratory and surveillance infrastructure (including human capacity) and information systems	• AFP and ES indicators (TBD) • >80% of identified PIDs have stool test • Accreditation criteria (aggregate of performance indicators) are met by X% of GPLN laboratories
Objective 3.2 - To develop and maintain adequate global and regional capacity and resources to support national efforts to rapidly and effectively contain any new poliovirus detection from a containment breach or other source or stop any new poliovirus transmission	• Activity 3.2.1 - Identify future outbreak risks, develop response strategies and preparedness plans, and sustain trained human capacity to appropriately implement these strategies and plans • Activity 3.2.2 - Create, maintain, and manage an adequate stockpile of polio vaccine and antivirals for an appropriate response	• Appropriate SIA response to any new poliovirus detections within 14 (?) days (SIA quality indicators) • Any new poliovirus outbreak stopped within (?) 120 days • Adequate mOPV stockpile available to meet expected requirements prior to cessation
Monitored by IHR, SAGE, others?		

A. Introduction

Detecting circulating polioviruses through a comprehensive global surveillance system and responding rapidly with effective vaccination campaigns have been core strategies for polio eradication efforts since the inception of the GPEI. Detection and response strategies will continue to play a critical role in the post-certification era. While every effort will be made to prevent the re-emergence of poliovirus from any source through containment measures and immunization, after the milestone of certification is

achieved, the world must also sustain a sensitive surveillance system and the capacity, capability, and commitment to rapidly respond if such an event does occur.

Missed transmission of poliovirus or a delayed/inadequate response could dramatically threaten the sustainability of a polio-free world. If a poliovirus circulates undetected for a prolonged period or the response is not of sufficient timeliness and quality, there is a high-risk transmission could be quickly re-established, leading to multiple cases of poliomyelitis and negating the hard-won efforts of the GPEI over the last several decades.

Minimizing this risk requires building on current capacity and adapting proven strategies. Although the GPEI in its current form will dissolve after polio eradication is certified, the essential capabilities to detect and respond to polioviruses which it has developed must be maintained by public health systems at the global, regional, and national levels. Polio detection and response capabilities at the national level can be included in the core surveillance and emergency operation core capacities which all countries are required to establish and maintain under the IHR. Additional activities should be targeted to the areas and populations most vulnerable for a poliovirus emergence.

B. Description of the Goal

In the long term, the third goal of the PCS is to ensure quality surveillance and adequate response capacity in order to provide confidence that any poliovirus that emerges will be rapidly detected and effectively contained.

The overarching principle of the PCS is that detection of any poliovirus will come under the IHR as a public health event of international concern (PHEIC) and should be treated as a threat to global health security. Within this context, surveillance for poliovirus in the post-certification era will take a risk-based approach which involves identifying risks, clarifying risk tolerance, and developing corresponding risk mitigation measures.

Using this risk-based approach, the general surveillance goal in the post-certification era will be twofold:

1. For high-risk areas (i.e., those most likely to experience a poliovirus emergence and concomitantly most likely to have the potential for rapid transmission), the PCS surveillance strategies are designed to detect any poliovirus and/or low-level transmission.
2. For areas at lower risk and limited consequence of detection, the goal of surveillance will be to detect clusters of poliovirus and/or relatively higher levels of transmission.

As the expected probability of a poliovirus emergence further decreases over time, lower levels of surveillance sensitivity and modified strategies may be appropriate in all areas, but minimal levels of vigilance must be sustained due to ongoing risks from a containment breach. In the post-certification era, the ultimate objective of surveillance will be not only to detect any cases of poliomyelitis in a population but also to detect even low-level human-to-human transmission or a break in PEF biosecurity prior to the virus reaching the community.

Ensuring global, regional, and national public health system readiness to respond to any detection is also critical. While any initial assessment and response must be primarily implemented at the national level,

given the wider implications of any detection and possible spread, these efforts in the post-certification period should be supported by the regional and global levels which should also be prepared to provide technical assistance and access to vaccines should they be required to stop transmission.

C. Objective 3.1: Prompt detection and sensitive surveillance

1. Context

A. Polio surveillance

The gold standard for detecting poliovirus transmission has been to identify all acute flaccid paralysis (AFP) cases among children under 15 years of age and to test their stools in a laboratory accredited by the Global Polio Laboratory Network (GPLN) to verify the diagnosis of poliomyelitis. AFP cases have usually been identified through either active facility-based surveillance or an extensive network of informants using standards and guidelines developed by the GPEI.[25] There is a well-established system for reporting and analyzing the data at the national, regional, and global levels. This system of syndromic surveillance with laboratory-based confirmation to identify poliovirus has proven to be robust and has supported the certification of four WHO regions. Although some polio-free countries (particularly in Europe and the U.S.) now use other surveillance methods, most countries in both polio-endemic and non-endemic areas still rely on AFP surveillance to detect poliovirus transmission and to guide program interventions. Countries in non-endemic WHO regions primarily rely on passive reporting and have already successfully integrated syndromic AFP into either vaccine-preventable disease (VPD) or other broader communicable disease surveillance.

Environmental surveillance (ES), which involves the testing of sewage samples for polioviruses, has been added in selected locations to aid in detecting silent community circulation of poliovirus and to track the presence of Sabin viruses in areas using OPV. Eighteen countries report ES results in 2017 and an ambitious global expansion plan targets 34 additional countries to begin implementing ES between 2017-2019.[26]

In addition to AFP and ES, a third method for detecting poliovirus among the general population is through community stool surveillance. This approach usually includes testing stool samples from individuals without paralysis but who may otherwise be considered at risk for transmitting poliovirus, including contacts of AFP cases or healthy children in known high-risk areas.

Although currently limited in scope, another supplemental surveillance system has been developed to specifically track immunodeficient individuals with prolonged (i.e., ≥6 months) excretion of vaccine-related polioviruses. WHO maintains a global inventory of individuals with VAPP or iVDPV detected through the AFP surveillance database, case reports of VAPP, or literature reports of children with iVDPV isolation. This approach usually identifies prolonged or chronic poliovirus excretors only after the patient is already paralyzed. Another approach is being piloted in selected countries with high rates of primary immunodeficiencies (PID) in which children diagnosed with PID are tested for PV. The practicality of broadly implementing this approach and its sensitivity and specificity remain to be determined.

[25] WHO. WHO-recommended surveillance standard of poliomyelitis. Geneva: WHO, 2015.
[26] WHO. Global Expansion Plan

The GPLN is a comprehensive network of 146 national, regional, and global laboratories which support diagnostics on stool isolates submitted through the surveillance systems. The GPLN provides accreditation and ongoing training to ensure quality control. All 146 laboratories can conduct initial virus isolation (VI), 103 provide intratypic differentiation (ITD), and 27 also have capacity to do genetic sequencing of polioviruses.

B. Other relevant surveillance systems

In order to provide the rapid, case-based detection required in an eradication program, most countries which have experienced sustained poliovirus transmission within the last couple of decades have established AFP surveillance as a separate, vertical structure alongside other indicator-based surveillance (IBS) systems. While these other systems may not have been the most efficient approach to reach eradication, they will be relevant for future poliovirus surveillance post-certification. The scope of these other IBS systems can range from traditional comprehensive surveillance tracking trends of all communicable diseases to more targeted detection of vaccine preventable diseases, high-threat pathogens, or enteroviruses. (*See **Annex D** for further details on these systems.*)

C. Surveillance under IHR

The IHR prompts Member States to "develop the capacities of their surveillance systems to detect, assess, notify and respond to all acute health events or health risks that may constitute a threat to human health."[27] Given the acute nature of these threats, the priority is to provide early warning and response (EWAR). This capacity is expected to rely on both conventional IBS for infectious diseases from routine or sentinel site surveillance, as well as event-based surveillance (EBS). EBS gathers information on health events from ad-hoc sources (e.g., local informants, general public, and media rumors). (*See also **Annex D***.) At the global level, EBS relies on detecting raw, unverified data from formal or informal sources such as direct communication, internet, hotlines, and literature reviews. Raw data is triaged and verified along with a risk assessment of the event prior to formal communication and response planning.

2. Risks

A. General

A critical risk to sustaining a polio-free world in the post-certification era is the potential failure to detect the emergence of a poliovirus. While global certification will only be declared when there is high confidence that WPV has been eradicated around the world, the potential remains for a vaccine-related poliovirus to emerge or wild poliovirus to be re-introduced (See *Risks of Poliovirus Re-Emergence*, p. 10). Extensive efforts will be made to mitigate the risks of these occurrences *(see activities under **Goals 1** and **2**)*. Two aspects of these risks should be understood: 1) The probability of a vaccine-related emergence is low and declines over time, yet the consequences may increase over time due to declining population immunity; and 2) regardless of time since certification, the consequence of late detection will be high in areas with poor population immunity.

Fully appreciating these scenarios and implementing sensitive surveillance to detect any emergence early must be a core strategy in the post-certification era. Several challenges to this strategy to mitigate the risk of missed detection should be recognized.

[27] WHO. Early detection, assessment and response to acute public health events. Geneva. WHO/HSE/GCR/LYO/2014.4

B. Challenges to developing mitigation measures

1. Inherent system characteristics

- As the vast majority of poliovirus infections are asymptomatic, AFP surveillance may miss low levels of transmission which can continue with IPV use, particularly for polioviruses with a low paralysis-to-infection ratio such as cVDPV2. Furthermore, the sensitivity of case-based AFP surveillance will dramatically decline as poliovirus disappears and the primary risk for emergence shifts to different sources (i.e., from OPV to containment breach).
- AFP surveillance gaps can readily occur in situations where large groups of people cannot be regularly accessed (due to mobility, conflict, remoteness, etc.) or may not be visible to local health workers (e.g., urban slums).
- ES may provide additional valuable information and can be useful to detect even low-level ongoing transmission particularly in large urban areas. However, ES cannot identify specific individual cases or precisely pinpoint affected neighborhoods; and, as yet, the sensitivities of the system remain to be determined.
- Confirmatory diagnostic testing for polioviruses relies on specialized laboratory techniques and reagents. Tests developed for other pathogens generally will not detect polioviruses.
- The overall sensitivity and specificity of enterovirus surveillance to detect poliovirus has not been fully determined. Any poliovirus detected through this system must to be referred to a GPLN laboratory for confirmation, intratypic differentiation, and possible sequencing.
- Current methods of identifying iVDPV patients miss most PID individuals with subclinical poliovirus infection or detect these individuals only after they have been excreting virus for a prolonged period.

2. Implementation

- Experience from polio-free regions demonstrates the challenges to sustaining high standards of AFP surveillance in non-endemic areas, especially as time passes since elimination. As other diseases become priorities, the awareness of polio among healthcare providers wanes and there is an inevitable drop in diligence to search for AFP. Maintaining the skillset of polio virologists in all laboratories will also be difficult in the face of decreased workload and funding in some areas. In the medium- to long-term, poliovirus surveillance will need to be highly targeted and/or linked to other national or global priorities to be sustained.
- While it will be important to coordinate and link current surveillance and laboratory functions and structures with other systems, there is a simultaneous need to sustain resources and qualified staff dedicated to polio at the global level and in high-risk regions and countries for several years as long as the risk of poliovirus emergence remains above a “risk tolerance” threshold.
- Implementing ES is particularly challenging. The system is only effective in areas with confluent community sewage systems; there is no globally standardized information system to monitor quality or track results; the geographic scope and resource requirements for implementation in highest risks locations remain to be determined; and processing samples puts high workload requirements on polio laboratories.
- Due to the lack of commercial assays, all polio labs are expected to remain exclusively dependent on CDC for molecular diagnostic reagents. While laboratory diagnostics and new algorithms have markedly decreased time required to obtain definitive results from stool samples, transport

difficulties and laborious procedures can still necessitate a lengthy process from initial suspicion to virus confirmation. Enhanced containment requirements may generate further challenges for both the laboratories and sample collection.

- High non-polio acute flaccid paralysis (NPAFP) rates may give a false level of perceived sensitivity and lead to an over-reliance on imperfect surveillance, especially if many non-AFP cases are included and/or estimates of the population <15 years of age are inaccurate.
- Epidemiologic data, particularly for cases detected through EV surveillance, is often incomplete or missing.

3. What Will Be Done

Strategic Priorities

Developing an appropriate global poliovirus surveillance system includes: a) establishing strategies and standards to meet the post-certification objectives; b) defining the capacities and functions required to implement these strategies; and c) providing possible options for the structures to sustainably manage these functions.

The baseline global strategies and standards established by the PCS will reflect the surveillance expectations set by the GCC and RCCs leading up to certification. (Date for establishing these "certification quality surveillance standards" is to be determined.) The PCS also encompasses a longer-term perspective which considers that risks for re-emergence and potential consequences will change over time and vary according to category of virus (e.g., WPV, cVDPV, iVDPV).

Different functions and capacities will be required at global, regional, and national levels depending on the expected strategies to be implemented. Cross-cutting, multi-disease surveillance systems (i.e., covering all or selected communicable diseases) and generic surveillance capacities may be sufficient in medium- to low-risk settings. However, even within integrated surveillance systems, polio-specific capacities and technical expertise should be maintained for some period after certification at global and high-risk regional/country levels. Polio-specific laboratory capacity accessible to all countries will also need to be maintained.

The appropriate structure to manage these functions should similarly match the required functions. Since the current GPEI structures will no longer be operational, suitable efficient and effective options will need to be identified for the future.

Strategies and standards

Activity 3.1.1 Redefine the polio surveillance paradigm

Like what occurred with smallpox, the global intensity of surveillance for poliovirus can be expected to decline after certification. However, the last countries to be affected by smallpox (i.e., Bangladesh, India, Ethiopia, and Somalia) continued intensive active surveillance in high-risk areas for several years post-eradication.[28] Poliovirus will be an eradicated pathogen but will have the potential to re-emerge and

[28] Fenner. P. 1118

cause low-level transmission or even disease, which could rapidly spread if not detected early. Therefore, the minimum objective of future poliovirus surveillance is to provide confidence that a poliovirus emergence can be detected. Since sustaining sensitive surveillance universally will be extremely difficult, if not impossible, the proposed paradigm will be focused on balancing the intensity of effort and risk of emergence over time.

Table 5. Current and re-defined paradigms for poliovirus surveillance

	Current paradigm	Re-defined paradigm
Approach	Global application of similar strategies (except in high income countries); standards based on endemic vs non-endemic status	Risk-based approach with strategies and standards designated by risk and changing over time
Standard strategy	Primarily AFP syndromic surveillance supplemented by ES	Initial reliance on AFP but increasing use of ES; mix of strategies evolving over time
AFP surveillance system attributes	Vertical, active, case-based, multiple facility & community reporting sites	Integrated, mix of active & passive, shifting to focus on sentinel sites & CBS
Polio laboratory	Separate tiered network with designated capacities	Separate polio labs may be maintained at global/regional levels, but combined or integrated at national level; potential for improved, faster diagnostics
Key expected additional strategies		Develop surveillance for PID and containment breaches

AFP= acute flaccid paralysis; ES= environmental surveillance; CBS= community based surveillance; PID=primary immunodeficient individuals

To reach certification, polio surveillance will rely on effective implementation of the standard steps for identifying and controlling all communicable disease outbreaks: detection, confirmation, notification, risk assessment, and response.[29] While polio surveillance in the future will continue to rely on this same core approach, the system will need continual refinements to address the challenges of the post-certification environment *(see **Section B**. Challenges to developing mitigation measures)* and mitigate the risk of missing a poliovirus detection.

To address these challenges, the post-certification polio surveillance paradigm seeks to provide rapid detection and confirmation of poliovirus through five essential strategies:

[29] Note: Detection and verification are covered under Objective 3.1; notification, risk assessment, and response are covered under Objective 3.2.

1. Sustain sensitive surveillance for poliovirus through an appropriate mix of AFP, environmental, and enterovirus surveillance.
2. Utilize event-based surveillance (EBS) to provide early warning of potential poliovirus circulation
3. Develop targeted PID surveillance to sustainably detect and treat poliovirus excretors
4. Develop specific plans to detect any containment breach both within PEFs and the community
5. Maintain core polio laboratory capacity from global to national levels and enhance laboratory innovations to support rapid and reliable confirmation of potential poliovirus detected through any of the above strategies.

The core strategies of AFP, environmental, and enterovirus surveillance (and the necessary laboratory capacity) are already used by GPEI to identify poliovirus circulation and outbreaks, but after certification of polio eradication new innovations will be required and the relative importance of each strategy will change over time. Additional strategies to address potential new risks (e.g., PIDs and containment breaches) will need to be developed. Utilizing informal sources such as EBS also have the potential to increase overall poliovirus surveillance system sensitivity. Underlying all these strategies is the necessity to maintain data quality, critical analysis, and wide reporting of results.

Country risk assessment. Prior to certification all countries should assess their future risk both for emergence and consequences of detection for each category of poliovirus. *(See **Annex C**: **Country Risk Classification*** for details on proposed methods and criteria for conducting his assessment*)*. Countries are recommended to employ a variable mix of strategies appropriate to their assessed risk and reflective of the changing potential re-emergence of poliovirus post-certification (*See Figure 2*). Depending on circumstances, a country may be assessed as high-risk for one category (e.g., VPDV) yet low-risk of another (e.g., iVDPV). Countries should adopt the strategy proposed for their highest risk category. However, in some large countries this assessment may apply to only certain provinces or geographic areas (usually population blocks of at least 10 million). In addition to their own national circumstances, countries will need to understand the risks imposed by bordering populations and work with regional offices to implement a multinational approach to surveillance applicable for a concentrated high-risk area (e.g., Lake Chad). Assessments should be re-evaluated as each post-certification stage (*See Table 6*) is passed to determine how the risk has evolved.

Essential strategies by risk category. Table 6 summarizes how the proposed global approach and the recommended strategies which should be implemented for each risk category by the stage after certification. Further details of the recommended strategies are provided below.

Table 6. Summary of surveillance standards & operational strategies by post-certification time periods

	Stage I	Stage II	Stage III	Stage IV
	Certification to bOPV cessation (0-1 year post certification)	Immediate post-cessation (2-5 yrs. post certification)	Intermediate post-cessation (6-9 yrs. post certification)	Longer term (≥10 years post-certification)
Primary global risk	VDPV 1 or 3	VDPV1 or 3	iVDPV1 or 3	Containment breach (WPV, VPDV, or Sabin)
Secondary risks	VDPV2, Containment breach (WPV, VDPV, or Sabin)	Sabin 1 or 3, iVDPV1 or 3, Containment breach (WPV, VDPV,	Containment breach (WPV, VDPV, or Sabin)	

		or Sabin)		
Global – General overview				
Strategies	Mix of indicator-based and event-based strategies—all countries expected to implement Early Warning surveillance per IHR; countries at high-med risk to maintain AFP surveillance with intensity and scope to evolve over time and risk status; increasing reliance on ES.			
Minimum Standards	1. Targets/indicators as articulated under IHR for the expected core capacities for lab, surveillance, and response will continue for all countries. 2. Additional standards specific to polio (primarily based on NPAFP + stool adequacy rates) will vary by time and risk.			
Laboratory	Maintain coordinated global polio lab network with standardized QA/QC, accreditation system, and defined pyramid of responsibilities for viral isolation (VI), intratypic differentiation (ITD, and sequencing (S).			
Polio High Risk				
Strategies	• Active AFP • ES • CBS (especially for hard to reach populations) • Nat'l PID/iVDPV	Stage IIA (years 2-3) • Active AFP • Enhanced efforts among high risk populations or areas Stage IIB (years 4-5) • Passive AFP + active sentinel site surveillance in specific areas All stage II • ES • CBS (especially for hard to reach populations) • Nat'l PID/iVDPV	• Passive AFP • ES • CBS (especially for hard to reach populations) • Nat'l PID/iVDPV + enhanced in specific areas	• Passive AFP • ES • CBS (especially for hard to reach populations) • Nat'l PID/iVDPV
Minimum Standards	NPAFP rate 2/100K + stool adequacy ≥80% at first admin level (For 12 months post any outbreak, NPAFP rate ≥ 3/100k) ES: TBD	NPAFP rate 2/ 100K + stool adequacy ≥80% at national level and for selected sentinel site districts (For 12 months post any outbreak, NPAFP rate ≥3/100k) ES: TBD	NPAFP rate 2/100k + stool adequacy >80% at national level ES: TBD	NPAFP rate 1/1000k + stool adequacy ≥ 80% at national level ES: TBD
Laboratory	Continue current cell culture algorithms. Polio laboratories with at least VI and ITD capacity should be maintained in (or as close as possible to) all high-risk countries along with efficient referral system for sequencing, if necessary.			
Polio Medium Risk				

Strategies	• Active and passive AFP • ES	Stage IIA (years 2-3) • Passive AFP • Include active sentinel site AFP surveillance in subnational areas of risk • ES Stage IIB (years 4-5) • Passive AFP • ES	• Passive AFP • ES	• Passive AFP • ES
Minimum Standards	NPAFP rate 2/100K + stool adequacy ≥ 80%rate at national level ES: TBD	NPAFP rate 1/100K + stool adequacy >80% at national level ES: TBD	NPAFP rate 1/100K + stool adequacy >80% at national level ES: TBD	NPAFP rate 1/100K + stool adequacy ≥80% at national level ES: TBD
Laboratory	Potential for initial testing for polioviruses to shift to direct detection (if validated) unless processing ES samples. Depending on anticipated demand and national resources, maintain ≥1 laboratory with VI and ITD diagnostic capacity integrated into multi-disease platform along with efficient referral system for sequencing, if required. Countries (especially with small populations) may rely on neighboring country laboratories to process stool samples.			
Polio Low Risk				
Strategies	Mix of passive AFP, EV, ES	Mix of passive AFP, EV, ES	Mix of passive AFP, EV, ES	Mix of passive AFP, EV, ES
Minimum Standards	NPAFP rate 1/100k + stool adequacy >80% at national level ES: TBD	NPAFP rate 1/100k + stool adequacy ≥80% at national level ES: TBD	NPAFP rate 1/100k + stool adequacy ≥80% at national level ES: TBD	NPAFP rate 1/100k + stool adequacy ≥80% at national level ES: TBD
Laboratory	Countries with labs could potentially use direct detection methods (if validated) for initial testing for polioviruses. Countries (especially with small populations) may rely on neighboring country labs to process stool samples. Countries with labs maintain VI and ITD diagnostics as part of IHR core national laboratory capacity.			

CBS= community-based surveillance; ES = environmental surveillance; EV = enterovirus surveillance; NPAFP= non-polio acute flaccid paralysis

1. Sustain sensitive surveillance for poliovirus through an appropriate mix of AFP, environmental, or enterovirus surveillance.

Efforts to broadly sustain sensitive poliovirus surveillance include:

- Maintain minimum core capacities for AFP surveillance as envisioned under IHR for all countries and enhanced capacities based on risk

- Implement targeted environmental surveillance as an increasingly important source for poliovirus detection
- Continue selective use of enterovirus surveillance in appropriate areas

To increase the sensitivity to detect both poliomyelitis cases or circulation, these broad strategies will need to be supplemented by additional activities targeted at hard-to-reach populations or areas.

AFP surveillance

Acute flaccid paralysis (AFP) surveillance has been the cornerstone in detecting cases of poliovirus infection and will continue to remain an important strategy after certification. However, the sensitivity and thus utility of AFP surveillance will decline over time. Therefore, the parameters for implementation (e.g., active vs. passive, population-based vs. sentinel sites, community- vs. facility-based, integrated vs. single-disease structure) will also need to evolve and should be appropriately tailored to individual country situations. Similarly, the expected surveillance standards (e.g., NPAFP rate and stool adequacy percent) will evolve by time and country risk category.

While global and regional coordination and support will remain available, the primary responsibility for implementing AFP surveillance will be national. The IHR envision that all countries should have a core capacity for "real-time surveillance conducted according to international standards to be able to detect at least three core syndromes indicative of potential public health emergencies."[30] The three syndromes are to be chosen depending on national disease control priorities.[31] Although the priority for AFP surveillance will vary depending on risk of poliovirus emergence, all countries should maintain a minimum core capacity for AFP surveillance given the global significance of maintaining poliovirus detection capacity.

AFP, along with a standardized syndromic definition, should remain as a priority disease/condition under any comprehensive routine[32] or early warning surveillance system.[33] As a priority condition, a single case of AFP should be an immediately notifiable event. Although AFP has already been included as a reportable condition in most national integrated disease surveillance systems, health workers have often relied on polio surveillance officers under GPEI to be responsible for detecting and reporting this condition. As vertical AFP surveillance networks will be transitioned to more sustainable systems, all health providers and surveillance officers should appreciate the necessity to immediately report any case of AFP or suspected poliomyelitis to national health authorities. Any suspected case will need to be further investigated and reported to a designated regional surveillance focal point. (*See also Activity 3.1.2 under Information Management*). Clinicians will need to be efficiently linked to central public

[30] WHO. Joint External Evaluation Tool. Geneva, 2016.

[31] Internationally recognized standards for syndromic surveillance are available for the following five syndromes: severe acute respiratory, syndrome, acute flaccid paralysis, acute hemorrhagic fever, acute watery diarrhea with dehydration, and jaundice with fever. See WHO. Joint External Evaluation Tool. Geneva, 2016

[32] For regional example, see Technical guidelines for integrated disease surveillance and response in the WHO African Region, 2nd edition. World Health Organization, Regional Office for Africa, 2010.

[33] Criteria for priority diseases include: epidemic potential; ability to cause severe morbidity or death; international surveillance requirements (IHR/PHEIC); availability of prevention and control measures; availability of reliable and meaningful case definitions and simple laboratory tests. See WHO. Outbreak surveillance and response in humanitarian emergencies: WHO guidelines for EWARN implementation. Geneva, 2012.

health infrastructures to report their suspicions of AFP. New innovations in mobile health (e.g., "mHealth") should be fully utilized to facilitate this communication which will become increasingly important wherever passive AFP is the primary mode of surveillance.

High-risk countries. Countries assessed as high-risk for future poliovirus re-emergence should expect to continue active AFP surveillance at least for two years after bOPV cessation. Regular health facility reporting sites should continue to be supplemented by 'non-routine' sources (e.g., community health workers, traditional medicine practitioners, private health providers, and NGOs) outside the government health system. During the period immediately after cessation when the risk from VDPV will be the highest, surveillance sensitivity can be enhanced by increasing the age range of contacts sampled, expanding number and geographic scope of community informants, and increasing frequency of visits to high-priority sites.

As overall sensitivity of AFP surveillance declines along with the inevitable challenges to sustain the effort required for active surveillance, surveillance activities during the later periods of Stage II (e.g., 4-5 years post-certification) should revert to passive surveillance but continue an active focus on sentinel sites within the subnational areas identified as known areas-of-risk. Even if the frequency of field visits becomes more sporadic, active surveillance can be maintained through mobile contact.

Reporting from the 'non-routine' sources has usually been dependent on active engagement from polio surveillance medical officers which will be unlikely to continue in all areas. Structured community-based surveillance can provide an alternative. However, since AFP will be a relatively rare event, passive reporting from these sources will be difficult to sustain. Using some structured form of community investigation and reporting may be of most utility in targeting high-risk populations for specific periods of time *(See Strategy 3 below, implement supplemental surveillance activities)*.

Medium- to Low-risk Countries. Countries assessed as medium- to low-risk for future poliovirus re-emergence should also continue AFP surveillance but the expected parameters will vary *(see **Table 6**)*. Countries at medium-risk should continue active AFP surveillance through global certification. After that period, surveillance can switch predominantly to a passive mode, supplemented by active sentinel sites during the immediate post-bOPV cessation period when the potential for VDPVs is greatest. Low-risk areas should continue a mix of surveillance strategies appropriate for their situation.

Environmental surveillance (ES). (Section to be expanded)

ES has been utilized for many years by some countries, particularly in Europe, as their primary approach to poliovirus surveillance and has been increasingly introduced to supplement AFP surveillance in many other areas. Studies from Pakistan and India have presented evidence that ES can provide earlier and more sensitive detection that AFP surveillance alone. Recent experience from Israel has also demonstrated that ES can detect subclinical transmission in areas that predominantly use IPV.

The need for ES will increase as the detectable paralysis-to-infection ratio decreases. Especially in high-risk areas ES should be a core component of surveillance strategies to aid in early detection of poliovirus circulation, monitor geographic extent of a detection, and verify the fadeout of vaccine strains. A comprehensive plan for placement of ES sites in different countries based on a thorough risk analysis can increase the overall sensitivity of global polio surveillance provided that suitable sampling sites are available. Similarly, ES sites within a specific country should be selected based on a number of factors

associated with increased sensitivity of detection. Although there are some possible markers that can aid in this process, it is not clear at present how to evaluate ES sites and identify those most suitable to monitor poliovirus circulation. Further analysis to determine appropriate site selection and interpretation of ES results are ongoing.

Additional topics to be included in future drafts—

- Define incremental benefits to PV surveillance: Sensitivity of ES and interpretation of ES findings, including what role, if any, for deep sequencing, whole genome sequencing, "next-generation" sequencing, etc.
- Criteria for future country and site selection
- Long-term vision of the objectives of ES
- Measures to mitigate implementation challenges or limitations of ES (i.e., ES has a high probability of detecting polioviruses in a targeted population, but has a lower probability of identifying an index case or initial excretor so may be of limited utility in high risk areas.

To ensure sustainability and take full advantage of established ES sites, countries could consider expanding detection to other enteric diseases of interest or tracking antimicrobial resistance patterns. Benefits would include increased understanding of the burden of diarrheal diseases in the country and early detection of outbreak-prone pathogens, such as cholera.

Although no other disease control program currently utilizes an extensive ES network as part of routine surveillance, there is a Global Sewage Surveillance Program (GSSP) which attempts to identify and track antimicrobial resistance by sampling sewage from urban areas in more than 100 countries, two to four times per year. Using this cross-sectional testing would not provide timely or sensitive detection of poliovirus, but could give additional information.

Enterovirus Surveillance

Although not specific for detecting poliovirus, enterovirus (EV) surveillance can be a useful auxiliary surveillance system in certain situations. To be an effective tool for polio surveillance, an EV surveillance system should have known sensitivity and specificity based on several key variables:

- Known proportion of the total population that is under surveillance by the system
- Known proportion of patients with specific clinical illness that are tested for enteroviruses
- Standardized laboratory procedures used to test specimens and the quality management of those laboratories[34]

Given the challenges in meeting these criteria, the widespread future use of EV surveillance will most likely continue to be restricted to countries with relatively well-established health systems. However, this system may be advantageous in other areas to target specific urban populations or subpopulation groups. In these defined high-risk areas, using EV surveillance to screen for aseptic meningitis for example could be a useful adjunct as AFP sensitivity declines.

[34] WHO EURO and US CDC. Enterovirus surveillance guidelines. Copenhagen, 2015

Supplemental surveillance activities to specifically target high-risk populations and areas

Geographic, political, and social constraints present constant challenges for detecting poliovirus using traditional methods among certain populations who either cannot chose not to access health services. These groups include: populations inaccessible due to insecurity or geographic isolation; ethnic minorities; migrants or nomads; internally displaced persons or refugees; or those living in densely populated urban areas, particularly slums. These same populations who are poorly reached by surveillance and lack access to health facilities are also a high-risk for undetected circulation due to low immunization rates, poor sanitation, etc.

Although high-risk countries are most likely to contain these vulnerable populations, all countries should periodically conduct their own internal assessments to determine groups or geographic areas most likely to be missed by routine strategies and require intensified surveillance. These assessments should be conducted at least annually through two years post-cessation and triggered if an emergence occurs or routine surveillance performance indicators are not met. This should be a dynamic process, requiring not only updates on formal population data (e.g., immunity), but also informal information such as community and media sources on mass population movements, etc. Border areas require specific attention for surveillance and necessitate joint multi-national reviews.

Further identifying areas most at-risk for re-emergence will not only aid in efficiently targeting surveillance resources, but should also maximize the chance to detect low-level transmission. Many supplemental strategies are already being implemented in the pre-certification era, but these efforts will need to be intensified as part of the risk-based surveillance approach.

Targeted supplemental surveillance. AFP surveillance (either as a vertical or integrated system) should still be attempted among hard-to-reach populations, but the challenges to reach and enumerate these groups will further limit the value and sensitivity of this approach.[35] Additional surveillance strategies have been used to improve polio surveillance and should be considered viable options either where traditional AFP surveillance and ES cannot be supported, or as supplemental strategies to increase sensitivity of findings. These strategies have the most utility in high-risk areas but can be useful elsewhere as required to maintain confidence in the surveillance system. In all situations, these strategies should be implemented as part of a comprehensive plan to utilize multiple sources of information and not as standalone approaches. Results from these complementary strategies will need to be interpreted carefully in the context of other data.

Additional efforts to target hard-to-reach populations include:

a) Collect stools from a sample (or even all) healthy children under 5 years of age to detect subclinical PV infections. These "healthy child stool samples" can be used in "silent districts" (i.e., districts where the NPAFP rate is zero or far below expectations) but they should be used judiciously and are not a substitute for adequate AFP surveillance. A positive result is helpful, but given the low probability of detection among healthy children, a negative result does not rule out PV transmission.
b) Periodic serosurveys can also be conducted in high-risk areas as long as they are carefully targeted and avoid sampling only easy-to-reach children who are more likely to be immunized. Although results from serosurveys cannot be used to assess if sampled individuals have

[35] See WHO. Outbreak surveillance and response in humanitarian emergencies, Geneva, 2011.

poliovirus infection, they provide important and valuable information on population immunity. and especially gaps, which will be important in the years leading up to bOPV cessation.

c) Perhaps even more than with settled populations, community-based surveillance (CBS) can be a critical strategy to gain health information from isolated, mobile, or insecure groups. While formal CBS structures attached to government health systems may not be viable either for political or logistic reasons, those run by independent NGOs (such as the IFRC), can provide regular or at least periodic contact. In Syria, a network of Village Polio Volunteers (VPVs) have proved instrumental in detecting a VDPV outbreak in the middle of an intense conflict zone.
d) Other key informants who regularly interact with isolated communities can also be valuable sources. For example, seeking health reports from veterinary health providers who care for animals of nomads and traditional healers who treat migrant or refugee populations. Mapping known areas of migrant or nomadic movement will help identify key informants and potential sites to interact. If any immunization campaigns (e.g., for measles/rubella) target these populations, vaccinators can also be instructed to conduct active case search for AFP in the community during the SIA.
e) ES may be particularly useful in densely populated urban areas with convergent sewer systems, although identifying individual cases will still be problematic. Unfortunately, there is generally an inverse relationship between practical ES sites and locations of other high-risk populations. Environmental sweeps (i.e., the collection of sewage from select locations in an area without an established ES site), has been introduced as an approach to detect poliovirus transmission in areas recently accessible around Borno, Nigeria. While this may be attempted in intermittently accessible high-risk areas, the effort did not yield any positive results in Borno. The overall cost-benefit and sensitivity of this approach remain to be determined. Any use of this approach will need to carefully consider laboratory capacity.
f) Develop targeted language and culturally appropriate communication and outreach to ethnic minorities or others who may chose not to access health services due to either actual or perceived barriers. Specific CBS outreach should be made to these communities. Additional efforts may be required to foster collaborative environments among all health staff.
g) As currently being done in Syria and Iraq, enhance the integration with EWARN in the security compromised areas and ensure that AFP or suspect poliomyelitis is included in the list immediately reportable conditions.

2. Utilize event-based surveillance (EBS) to provide early warning of potential poliovirus circulation

Broadening the sources of information through inclusion of informal sources can help to detect signals of acute public health events such as an AFP case at the earliest possible stage. Polio surveillance has already utilized one form of EBS, community informants, to report suspect AFP. The benefits of including relevant poliovirus-specific signals in other non-traditional information sources at both global and national levels remain to be proven but potentially will provide an additional surveillance tool. Regardless of source, any signal of possible poliovirus emergence will need further investigation and laboratory confirmation.

Event-based surveillance (EBS)—global and regional levels. At the global (and potentially regional) level, the primary sources of EBS will be formal and informal media and internet reports from official and unofficial websites. Technologically advanced tools to track these sources can identify emergence, and more so, the amplification of infectious disease outbreaks. Although the sensitivity of EBS to detect a single AFP case is low, the system has the potential to assist with early detection of clusters of AFP cases.

The Epidemic Intelligence from Open Sources (EIOS) system is being developed which will include global scanning of social media, aggregated news sources (PROMED, Global Public Health Intelligence Network-GPHIN, etc.), and both official and unofficial health reports. To be useful for polio surveillance, specific poliovirus triggers relevant to potential emergence (including clusters of AFP, etc.) will need to be introduced into the EIOS and specific confirmation filters identified to avoid overwhelming the system with false-positive signals.

Event-based surveillance--national level. Depending on resources and risk assessment, countries may establish their own EBS systems either through high-tech scanning of social media, establishing a national hotline number, or more informal methods. After smallpox eradication, a low-tech approach using local 'rumor registers' was implemented in countries that previously had a large number of cases, such as India, to collect local information from the community on re-emerging suspect cases. However, as discovered in India, additional technical confirmation by epidemiologists (from the global or regional levels, if necessary) with polio expertise may be required to identify which signals are relevant and warrant a more comprehensive local risk assessment.

3. Develop targeted PID surveillance to sustainably detect and treat poliovirus excretors

(Section to be expanded)

In the post-certification era, the role and importance of iVDPVs and their potential to seed a VDPV outbreak increases in the years after eradication and bOPV cessation while other polio risks decline. However, iVDPV surveillance is only recommended for countries where prolonged vaccine virus excretion among PID individuals is suspected and the potential subsequent community transmission is high. This would include countries that stopped bOPV use prior to certification, have high co-sanguinity rates, and experienced improvements in survival of PID patients.

Additional topics

- Initial lessons learned from pilot PID screening projects
- Implications for practical implementation
- Expected scope for future PID surveillance, including retrospective and prospective identification of PID patients.

4. Develop specific plans to detect any containment breach both within PEFs and the community

(Section to be developed)

5. Maintain core polio laboratory from global to national levels and enhance laboratory innovations to support rapid and reliable confirmation of any potential poliovirus detected through the above strategies.

Identification of a future poliovirus will still require confirmation by an accredited polio laboratory. The desired outcome in the post-certification era is to build on the significant contributions of the current polio laboratory network for virus confirmation and seek to find any poliovirus even faster than currently.

GPLN will continue to improve sensitivity, specificity, and efficiency through utilizing more efficient testing, conducting tests closer to patients, and adopting new technologies. All polio laboratories should continue to follow WHO-validated and standardized methodologies, but additional procedures and algorithms may be developed depending on risk of poliovirus re-emergence in the sample area.

Principal field and laboratory strategies to enhance identification of future poliovirus include:

- Improve sample collection and transport
- Improve processing methods, including diagnostics and testing algorithms to reduce time from case identification to confirmation
- Continue global accreditation process to ensure quality control

Improve sample collection, transport, and processing methods. The GPLN network currently processes >200,000 stool samples a year, but <5% are of potential programmatic importance. Post-certification, the number of stool samples from AFP cases may decline; however, the workload imposed by expansion of ES will likely increase as this system gains in importance. Since many polio labs will most likely be further integrated with those diagnosing other diseases, identifying mechanism to improve efficiency of poliovirus detection will be important.

Probably the most gains in laboratory efficiency will come in concentration and processing of ES samples. Processing ES isolates remains reliant on cell culture and is particularly labor intensive, although it has the advantage of detecting live viruses compared to molecular methods. Multiple projects are under way to improve methods for ES sampling and handling (*see **Enabling and Cross-Cutting Areas: Research***). However, a fine balance should be maintained between methods improvement and implementation in the field.

Post-certification, the inactivation of potentially infectious clinical materials and viral isolates will become prerequisites. Only 18 (primarily at the global or regional levels) of the 146 current polio laboratories are expected to become poliovirus-essential facilities (PEFs) with the required containment capacity to verify poliovirus. Viral inactivation techniques and FTA (Flinders Technology Associates) cards which are already in use due to prohibitions on transport of infectious materials in some areas, will become even more critical mechanisms for national laboratories to transport polio isolates to these PEFs for molecular testing. However, processing of FTA cards takes additional time and provides opportunity for cross-contamination. Collaboration among laboratory, containment, and transportation regulators will be required to ensure efficient transport of isolates.

Improve diagnostics and testing algorithms. Providing rapid, reliable diagnostic results may be complicated by several factors: stool samples are often of low quality or are delayed in transport, there are many programmatically unimportant viruses, and virus mixtures are common (particularly with ES samples). However, several initiatives can be considered to accelerate the detection of a suspected emergence and to rapidly confirm poliovirus. *(See **Enabling and Cross-Cutting Areas: Research**.)*

Algorithms for testing stool samples can be simplified and tailored to risk. Cell culture provides the highest diagnostic sensitivity and must be retained for processing samples in high risk areas. Other methods have been considered for other areas. Direct detection methods have the potential to provide faster results and simpler processing. However, these methods remain to be validated, are more expensive, and slightly less sensitive than cell culture so their long-term use remains to be determined. Labs processing ES samples will need to continue using cell culture for the foreseeable future.

A critical diagnostic challenge with significant programmatic implications is the capacity to distinguish iVDPV from cVDPV during the early phase of divergence. Methodologic challenges remain in improving the laboratory assays which directly target VPDVs. Research is ongoing to differentiate iVDPVs from cVDPVs, but resolution may not be possible except in highly divergent viruses. The definition of "VDPV" itself is empirical and subject to change. The bias of the current definition is toward sensitivity while retaining reasonable efficiency about laboratory workload. In the future, the definition of VDPV could be made even more sensitive, but the programmatic implications for response will also need to be considered.

Continue global accreditation process to ensure quality control. Confidence in the results from GPLN laboratories has been dependent on a rigorous accreditation process required for all laboratories. Annual on-site reviews based on standardized accreditation and performance indicators are performed to ensure quality assurance and control. This process should be continued in the post-certification period to sustain the confidence in the GPLN network.

Functions, capacities, and structure

Activity 3.1.2. Sustain adequate and technically qualified surveillance and laboratory infrastructure capacity, including information systems

Global/regional surveillance

Although surveillance must be implemented primarily by countries, support for these activities will need to be maintained at the global as well as regional level. Specific expectations are outlined in Table 6.

Key points to highlight:

- A core group of epidemiologists with polio expertise should be maintained at the global level to provide a wide range of monitoring and support functions. The number of staff and scope of responsibilities of this group will gradually decrease over time, but should be sufficient to ensure a prioritized focus on PV detection through at least Stage IV.
- Capacity will also need to be maintained at the global level to provide quality assurance and expert advice on multiple aspects of surveillance and laboratory management. Ambiguous AFP cases which use to be evaluated by National Expert Review Committees will all be referred to a

single global committee. Laboratory accreditation reviews should continue to be conducted by a global roster of expert virologists.

- All regions should retain general epidemiologist who include poliovirus detection as part of their overall responsibilities. Regions with high-risk countries should continue to maintain substantial polio technical expertise at least through the end of Stage II and may be required to have sufficient staff to directly support active sentinel site surveillance in both high- and medium-risk countries. Regions with multiple high-risk countries may require this cadre of staff at the sub-regional (e.g., IST) level to support countries and pay particular attention to cross-border areas.
- As part of the early warning and response mechanism, a generic capacity and structure for EIOS and EBS should be maintained at the global level which incorporate 'signals' for detecting poliovirus.

National level surveillance

In keeping with the expectation articulated under the IHR that each country should have a core capacity for "real-time surveillance," primary responsibility for poliovirus surveillance lies at the national level. However, in the post-certification era, the scope and intensity of poliovirus surveillance required beyond the core capacity will depend on the individual country risk assessment. Again, specific expectations are outlined in Table 6, but key points include:

- Since sustaining AFP surveillance will be problematic especially after certification, to the extent possible, countries should seek opportunities where AFP surveillance can be combined with ongoing surveillance activities for other VPDs, communicable diseases, and/or supplemented by other strategies. Linking AFP surveillance to other health priorities (e.g., GVAP targets such as measles elimination and MCH targets under SDG3.) can help to sustain the effort.

- Although the functions and the poliovirus surveillance as a whole should be integrated within other systems in all countries, the number of surveillance officers and/or portion of their time dedicated to poliovirus detection will vary depending on the expected surveillance standards (and ultimately the assessed country risk category.) Sustaining active AFP surveillance through the second year of Stage II in high-risk countries will undoubtedly still require a considerable portion of an individual officer's time. The percentage of their time focused on poliovirus surveillance should gradually decrease as the strategies shift to selected sentinel sites for the later part of Stage II and ultimately to passive surveillance. The expected portion of time dedicated to poliovirus surveillance in middle- and low-risk countries should similarly reflect the mix of strategies and expected minimum standards. Regional or sub-regional staff with primary polio responsibilities should be available to provide support or even implement sentinel site surveillance if necessary.

- Countries at all risk levels with environmental sites will need to ensure adequate qualified staff to maintain routine (or if required post-outbreak, expanded) field and laboratory operation of ES. Sustaining this capacity will be critically important as poliovirus surveillance becomes more dependent on ES over time the priority of this polio-specific activity may potentially diminish under integrated systems.

National level health system capacity building

Regardless of a country's assessed risk, AFP surveillance will be integrated into either VPD or broader communicable disease surveillance systems and depend on maintaining local health worker engagement. Alert clinicians and health workers have long been key to the initial identification of disease outbreaks, especially involving rare or unusual pathogens. Training for both medical and surveillance staff at tertiary- (and maybe even district-) care levels to clinically diagnose AFP and properly follow stool collection protocols must be continued. Periodic training will be particularly essential in areas deemed to be at high-risk for poliovirus transmission. Maintaining relevant diagnostic skills will require mainstreaming this training while still highlighting its singular importance as a critical expertise. Ongoing efforts to strengthen country core capacities for communicable disease or VPD surveillance to meet the IHR goal of public health workforce development for field epidemiologists should include training in AFP surveillance.[36] Additional training for healthcare providers may be channeled through the recently established WHO Emerging Diseases Clinical Assessment and Response Network (EDCARN). Although this network focuses on enhancing early diagnosis and clinical care of rare, but deadly emerging infectious diseases, the same training for frontline health workers could include a focus on polio as a similar high-threat pathogen.

Laboratory capacity and infrastructure

(To be expanded)

Additional analysis will be necessary to fully define the future scope of the GPLN. At a minimum, the post-certification GPLN must retain the capability to sustain polio eradication by conducting poliovirus testing and providing a wealth of molecular epidemiological data around the world. All countries should have ready access to laboratories with capacity to confirm a poliovirus either through national laboratories or efficient transportation channels. Capacity for sequencing will be increasingly importance, but will not be required in all locations. Economic, epidemiological, and, to a lesser extent, containment considerations will influence the number, location, and diagnostic capacities required at the global, regional, and national levels. General guidelines are outlined in table 6.

As with surveillance capacity, specific polio focus and virologic expertise should be sustained at global and regional levels to ensure technical competence, standardized approaches, and overall confidence in the quality of the results provided through an accredited system. Maintaining a global polio lab network which provides critical technical expertise and even basic supplies such as reagents which are not commercially available will be critical to sustaining polio eradication.

Simultaneously linking the GPLN to other relevant laboratory networks can be mutually beneficial. Several other VPD control programs have already used the GPLN model to establish tiered networks of laboratories with close epidemiologic connections to guide programmatic actions. The GPLN thus has obvious synergies and assets that can potentially be integrated with other VPD networks or specialized virologic laboratories for diagnosis of emerging and re-emerging diseases. However, in the post-certification era polio laboratories will no longer be dealing with 'routine' surveillance but samples potentially containing an eradicated pathogen with high potential for transmission. In this sense, the GPLN will face some of the same challenges as other laboratories focusing on high-risk pathogens. Although it normally deals with 'high consequence' pathogens such as Ebola or MERS-CoV, the Emerging

[36] E.g. at least 1 trained field epidemiologist per 200,000 population. See JEE…

and Dangerous Pathogens Laboratory Network (EDPLN) can provide evidence-based strategies, tools, and practices for rapid detection and containment that will be relevant for polio laboratories. Similar generic training on biosafety, biosecurity, and managing laboratory preparedness will become even more important for the GPLN in the future.

Ultimately, the location of national polio laboratories will be a country-driven process based on their perceived risk, available resources, and national capacity. However, maintaining reliable, rapid access to a quality laboratory with polio specific expertise is necessary for all high-risk countries at least through Stage III. In other areas, capacity for poliovirus detection should be maintained either through a local lab or the capacity to efficiently transport samples to other countries. Although PCR testing for polio is fully integrated with other VPDs only where labs are in the same department (or in a single lab), in the future, poliovirus detection is likely to be merged with other diagnostic platforms. Capacities developed for direct detection and other molecular testing for polioviruses can also be transferred to other pathogens where this is not the norm.

Information management

(section to be expanded)

Case-based AFP surveillance, laboratory, and environmental surveillance data are available to GPEI partners through the web-based polio information systems (POLIS). The full breadth of this comprehensive system will not be sustainable or even necessary under integrated surveillance systems after certification. Nevertheless, access to reliable and high-quality surveillance data in near real-time will continue to be an important priority not only to detect infections but also to monitor surveillance performance to ensure sensitivity of detection. Options for meeting this requirement are still under consideration. Incorporating POLIS into an already existing surveillance infrastructure would help to ensure continued technical and financial support for polio data while extending the benefit of a rich and well-maintained information system to global and country partners. As countries begin to adapt different surveillance approaches to detect polio, it will be important to incorporate these data into electronic information systems so they may also be available for use at national and global levels. This will be a critical step when countries develop polio surveillance plans.

High-risk countries should be able to continue reporting case based AFP data to regional and global levels. (further expansion on potential for case based vs aggregate reporting).

Table 7. Functional detection capacities required at global, regional, and national levels (unless noted, capacities should be sustained through Stage IV)

	Surveillance-Detection	**Laboratory**
Global	In addition to generic capacity for EIOS and implementation of EBS Maintain core staff of polio expertise with capacity to: • Provide TA/training • Develop updated guidance on PV surveillance • Conduct risk forecasting on countries or areas that require priority monitoring	Maintain global specialized labs plus polio virologists with capacity to: • Provide TA/training • Prepare & distribute reagents • Perform viral isolation, ITD, and sequencing, while safely containing polioviruses • Conduct QA/QC along w/ accreditation • Conduct research • Develop guidance, procedures, and

	• Conduct regular analysis of AFP of ES data and manage global data information • Evaluate significance of ambiguous AFP cases (e.g. Global Expert Review Committee) • Monitor quality & periodically evaluate national systems • Conduct research to guide operational and policy changes	recommendations to maintain the coherence and safety of the Network (planning, standardization, Information systems) • Coordinate with other WHO-led laboratory networks
Regional	All regions should have staff with general epidemiologic capacity to: • Assist w/ TA, training, updated surveillance guidance, risk forecasting, data analysis and information management, monitoring, In addition, regions w/ high-risk areas should maintain polio specific technical expertise at regional and/or sub-regional level through Stage III w/ capacity to: • Coordinate and monitor surveillance in high risk cross border areas. • Conduct or assist national staff with active AFP surveillance in sentinel sites or conducting case/event investigations	Maintain regional reference laboratories and polio virologists with capacity to: • Assist w/ TA, training, analysis, monitoring (depending on regional requirements) • Perform VI, ITD, and sequencing while safely containing polioviruses • Assist w/ QA/QC • Coordinate with other regional laboratory networks
National—The expected scope and intensity of surveillance will depend on the assessed risk; however, all countries regardless of assessed risk for emergence, should maintain a core capacity to detect a PV emergence and reliable access to a laboratory accredited to test for PV.		
High Risk	Integrate polio surveillance with VPD or communicable disease surveillance but maintain polio specific technical expertise at national level through Stage II with capacity to: • Identify subnational high-risk areas or populations • Implement case-based, event-based, and special surveillance as required by stage—including AFP case or event investigation • Conduct polio-specific data analysis and information management from AFP, ES, or EBS, including monitoring performance indicators. • Conduct operations research as required to develop streamlined surveillance	Depending on anticipated demand, maintain >1 accredited national polio laboratory with at least VI and ITD capacity along with efficient referral system for sequencing.
Medium	Integrate polio surveillance with VPD or communicable disease surveillance but	For all countries, depending on anticipated demand, maintain, or have access to ≥1 lab with

	maintain polio specific technical expertise at national level through Stage I with capacity to: • Implement appropriate mix of strategies depending on stage • • Conduct polio-specific data analysis from AFP, ES, or EBS, including monitoring performance indicators. • After Stage 1, may rely on global or regional support to conduct AFP case or event investigations	VI and ITD diagnostic capacity along with efficient referral system for sequencing if required.
Low	Integrate polio surveillance with VPD or communicable disease surveillance with capacity to: • Implement appropriate mix of strategies depending on stage • Identify potential polio outbreaks based on surveillance or EBS data • May rely on regional support for AFP case or event investigations if necessary	Countries (especially those with small populations) may rely on neighboring country laboratories to process stool samples. Countries with laboratories maintain VI and ITD diagnostics.

D. Objective 3.2: Adequate response capacity

1. Context

A. Polio Outbreak Preparedness & Response

The GPEI outbreak preparedness and response activities evolve from three core strategies: 1) prior planning; 2) early notification and rapid risk assessment after a poliovirus has been detected; and 3) reactive vaccination and enhanced surveillance once an outbreak or high-risk event has been verified.[37]

Planning. All countries are now expected to develop polio-specific outbreak preparedness plans which include detailed steps for notification (both internal and global), response management, risk assessment, vaccination, and enhanced surveillance that would be undertaken if a poliovirus is detected.[38] Plans are intended to be updated annually. Additionally, some polio-free countries have periodically conducted "polio outbreak simulation exercises" to test the robustness of their plans.

Notification. In addition to notification protocols established for sharing information on poliovirus detections within the GPEI, the IHR (2005) require all countries to alert WHO within 24 hours of identifying any WPV case.[39] In recognition of the threat posed by ongoing WPV transmission to global health security, the Director General declared polio a "public health event of international concern" (PHEIC) in May 2014. The designation has been periodically renewed, the latest in April 2017. Since the declaration of type 2 eradication and the removal of type 2 containing vaccines for routine

[37] For extensive national operational parameters and guidelines, see http://polioeradication.org/tools-and-library/resources-for-polio-eradicators/gpei-tools-protocols-and-guidelines/
[38] GPEI. Guideline for developing a national preparedness plan for a polio outbreak. Geneva, December 2015.
[39] See WHO. International Health Regulations (2005), Annex II. 3rd edition. Geneva, 2016.

immunization in April 2016, the Emergency Committee established under the designation of polio as a PHEIC has extended the reporting requirement to include the isolation of wild or vaccine-derived poliovirus from any human or non-human sources (i.e., from persons without paralysis or from environmental samples) as well as Sabin2 isolates detected more than four months after the last use of tOPV or mOPV2.

Risk Assessment. After a poliovirus has been identified, a rapid risk assessment determines the appropriate further response measures for additional surveillance and vaccination. Based on the initial case investigation and other laboratory and epidemiologic data, the risk assessment qualitatively evaluates multiple factors in three categorical areas: virologic characterization, population and health system context, and international spread.

Vaccination. Supplementary Immunization Activities (SIAs) implemented in response to a poliovirus outbreak are tailored to type and classification of the poliovirus, underlying population immunity, local situation, and findings of the initial epidemiologic investigation. For OPV-using countries in the pre-cessation era, confirmed outbreaks of types 1 and 3 (e.g. WPV or cVDPV1 or 3) require a rapid vaccination response with bivalent OPV; detection of a cVDPV2, an aVDPV2 deemed at high-risk for transmission require vaccination with mOPV2. [40]

Beginning in 2009, the GPEI secured global stockpiles of monovalent vaccine bulk of types 1, 2, and 3 (total of 1.19 billion doses) to use for outbreak response after OPV cessation. Due to the withdrawal of type 2 containing vaccine (i.e., tOPV) from routine use in 2016, a total of 269 million doses of type 2 bulk have either been converted or are in the process of being converted to finished product (i.e., mOPV2). As of May 2017, around 76 million doses of mOPV2 had been shipped to countries to respond to type 2 outbreaks. Additional vaccine in the global stockpile may be needed for type 2 outbreaks in the near future. Vaccine bulk of types 1 and 3 will be converted to finished product in time for use post-bOPV cessation if necessary. *(Also see **Activity 3.2.2** below.)*

Surveillance enhancement. Regardless of whether a vaccination response is initiated post-PV detection, countries are expected to evaluate their current surveillance quality, increase their surveillance sensitivity for at least the next year, and consider increasing or initiating supplemental environmental surveillance.

B. Other communicable disease outbreak preparedness & response

Although technical capacity, infrastructure, and logistical resources vary widely, most countries have already developed a response system for communicable disease outbreaks. WHO has developed generic Investigation and control measures[41] as well as specific protocols for outbreak prone diseases[42] to assist national efforts.

Vaccine preventable diseases. In addition to polio, multiple other VPDs which have control targets (e.g., measles/rubella) and/or are epidemic prone (e.g., meningitis) utilize vaccination campaigns as a core outbreak response strategy. However, most responses to outbreaks of these VPDs also rely heavily on

[40] GPEI. Standard operating procedures: responding to a poliovirus event and outbreak. Geneva, May 2017.
[41] See WHO. Early detection, assessment and response to acute public health events: Implementation of Early Warning and Response with a Focus on Event-Based Surveillance. Geneva, 2014
[42] For example, see

other control measures such as case management (e.g., for measles/rubella) or vector control (e.g., for yellow fever). Except for measles/rubella, these other VPDs also face vaccine supply constraints which can limit a vaccination response. Global stockpiles have been established for meningitis, yellow fever, and cholera vaccines under the control of the International Coordinating Group (ICG). The ICG has developed specific criteria to prioritize supply allocations during epidemics.

C. Preparedness and Response under IHR

The IHR (2005) and Global Health Security Agenda place the primary responsibility for responding to events of public health concern on the countries. To implement this responsibility, countries are expected to develop a wide ranging 'all hazard' response capacity to deal with any relevant biological, chemical, radiological, or nuclear hazard. This capacity is envisioned to include national and subnational preparedness plans along with the necessary infrastructure and policy frameworks to facilitate an effective response.

Some regions (e.g., the South-East Asia Region) have established their own disease control strategies to supplement the IHR by providing mechanisms for information sharing, technical support, and monitoring of national preparedness and response efforts for their member states.[43] These regional initiatives can be of particular utility in coordinating public health emergencies affecting multiple countries and/or international border areas.

The IHR specifically obligates countries to identify and report events threatening global public health and for WHO to assess their significance, assist affected states in investigation and control, and inform others of the situation.[44] Generic risk assessment methods[45] are supplemented by disease specific analysis as required. Information about verified events and response actions should be recorded in the WHO Event Management System (EMS). Once an event has been identified as likely reportable under IHR and assessed as exceeding local response capacity, the Global Outbreak Alert and Response Network (GOARN) can mobilize, deploy, and coordinate international support from multiple partners to assist with outbreak control. Large-scale events with a severe global health impact are also reportable to the UN Inter-Agency Standing Committee (IASC) which can activate a wider global humanitarian response.

2. Risks

A. General

Prevention of a poliovirus emergence through adequate containment and widespread population protection measures represents the best risk management strategy to remain polio-free *(See **Goals 1 and 2**)*. However, there remains a non-zero probability of at least one poliovirus outbreak post-certification. If comprehensive global and national preparedness plans are not already established prior to the outbreak detection, there is a high risk that an ad-hoc response will be delayed and ineffective. Furthermore, once a poliovirus has been identified, inability to quickly implement an aggressive outbreak response to stop transmission represents a significant risk of failing to contain the emergence and making it difficult to re-establishing a polio-free world. Mitigating this risk depends on ensuring a

[43] WHO. Asia Pacific Strategy for Emerging Diseases: Advancing implementation of the International Health Regulations beyond 2016. Manila, 2016.
[44] For further details see: WHO. Emergency Response Framework, 2nd edition. Geneva, 2017.
[45] See WHO. Rapid Risk Assessment of Acute Public Health Events. Geneva, 2012.

high-quality response through thorough preparation and implementation of proven control strategies with sufficient resources and effective management. Challenges to developing and implementing these mitigation measures should be identified and addressed.

B. Challenges to developing mitigation measures

1. Inherent system characteristics

- All currently available polio vaccines have limitations for stopping post-bOPV cessation outbreaks. Responses will need to rely on type-specific mOPV; however, these vaccines also present a risk for VAPP and VDPVs in any low-immunity setting such as may occur after certification *(see **Goal 2**)*. Although IPV is highly effective in protecting individual recipients through humoral immunity, it has a limited role in stopping transmission in most settings due to it its low efficacy in generating intestinal mucosal immunity.
- Although there are ongoing intensive efforts to develop alternative polio vaccines (preferably oral) which prevent PV transmission without the risks of current Sabin vaccines, progress has been slow and success is not guaranteed. *(See **Enabling and Cross-Cutting Areas: Research**)*.
- Development of safe, effective, and non-resistant antivirals has proven similarly problematic. These compounds are essential to treat iVDPV excretors and ensure they do not pose a risk for transmission within their community. *(See **Enabling and Cross-Cutting Areas: Research**)*.

2. Implementation

- Recent difficulties initiating and implementing responses to polio outbreaks in areas that have been polio-free for multiple years demonstrates the challenge to maintain national commitment to preparedness and retention of qualified staff with experience to conduct field investigations, enhanced surveillance, or SIA campaigns.
- Ensuring adequate quality in the SIA response in the post-certification era will be further challenged by the almost certain future increase in marginalized populations including those living in conflict/inaccessible areas and urban slums.
- Developing adequate supplies of appropriate type vaccines to respond to potential outbreaks depends not only on availability of sufficient funding and production capacity, but also realistic assessment of the number and scope of future outbreaks in order to develop sufficient stockpiles far in advance of need. Predicting future outbreak risk (and thus stockpile needs) is exceedingly complex due to multiple unknowns on long-term population immunity, variability of population mixing, etc. in the post-certification era. Final decisions on stockpile requirements will need to integrate a wide range of needs predicted by forecast models.
- Maintaining and managing stockpiles of vaccines for an eradicated pathogen can be problematic. OPV vaccines in the stockpile may expire since there is no opportunity for rotating stocks through ongoing production and routine use. Similarly, if stocks are depleted, there may not be production capacity or manufacturer interest to rapidly replenish the reserve. In the long term, ongoing stockpile management costs may be high and difficult to justify.

3. What Will Be Done

Strategic Priorities

Adequate preparedness and response capacity to address these challenges and mitigate the risks of failing to stop any future transmission requires the following:

- An estimation of future outbreak risks
- Determination of response strategies and parameters, including identification of appropriate vaccine type, scope, number of rounds, etc., and recommendation of steps to enhance surveillance;
- Sustained technical, operational, and management capacities at global, regional, and national levels, and
- An adequate stockpile of appropriate polio vaccines and antivirals.

Current experience and strategies for preparedness and outbreak response can be instructive but must be adapted to wider unknowns of future population immunity and poliovirus behavior, as well as the realities of evolving health system priorities and capabilities. Knowledge gained from predicting and addressing VDPV2 outbreaks after the withdrawal of tOPV will be relevant for the post-bOPV cessation period; however, types 1 and 3 have distinctly different transmission profiles from type 2. Future response protocols should retain the core principles of current proven strategies while providing innovative approaches tailored to the evolving poliovirus risks and immunity profiles. As with sustaining capacity for polio surveillance, some polio-specific expertise will need to supplement the generic capabilities of global and national public health systems to respond to communicable disease outbreaks. In addition to the polio-specific human resources, material resources in terms of supplies of safe and effective vaccines and antivirals dedicated for polio outbreak response must be available at the global level for distribution to wherever they are needed.

Activity 3.2.1. Identify future outbreak risks, develop response strategies and preparedness plans, and sustain trained human capacity to appropriately implement these strategies and plans

A. Future outbreak risks

The projected primary risks for a poliovirus emergence over time after certification are presented in the PCS *Plan Overview & Rationale: Risks (see **Figure 2**)*. These general assumptions help determine the required surveillance, preparedness, and response priorities for each of the post-certification milestones. Further elaborations, including type specific risks, trends, and even quantification of potential numbers of emergences can provide additional guidance on future program priorities and resource requirements.

VDPV

Models and prior experience with VDPV emergences can provide imperfect estimates of the future number of VDPVs yet are still important contributions to strategic planning. Uncertainties surrounding all the factors which determine the risk of VDPV emergence (e.g., poliovirus dynamics, type-specific population immunity, population mixing and mobility, and local environmental factors influencing the propensity for fecal-oral transmission) translate into wide ranges for the quantity of predicted future

emergences. Even these ranges can be instructive to determine vaccine stockpile needs *(see Activity 3.2.2 below)* and other response strategies and requirements.

The numbers of type 2 emergences in the first year post-tOPV withdrawal have been at the high end of what models anticipated within this timeframe. The number and geographic distribution of these emergences have highlighted the importance of sustaining high quality surveillance, fully implementing pre-cessation SIAs to mitigate risk, and the continued susceptibility of populations in insecure or inaccessible areas. Intensive efforts will be required to stop these outbreaks. Nevertheless, the risk for further type 2 emergences should rapidly decline and the probability of further such outbreaks by the time of certification should be very low.

Experience to date with type 2 can help guide estimations of future risk from types 1 and 3; however, there are distinct differences among the serotypes in terms of virulence, reversion patterns, and transmissibility which need to be considered. Since VDPVs were first characterized in 2000, 86% of cVDPVs detected through June 2017 have been type 2 with only 12% type 1 and 1% type 3.[46] However, prior to the shift from tOPV to mOPV and bOPV for SIAs starting in 2005, the majority of VDPVs was type 1. In addition to this modification of vaccination strategy which most likely resulted in a drop in type 2 population immunity levels, the historical predominance of type 2 VDPVs may be attributed to differences in OPV reversion rates (OPV2>OPV1>OPV3) and improved VDPV surveillance accompanied by the change to a more sensitive case definition of type 2 VDPVs. While specific numbers of future outbreaks are uncertain, the risk of cVDPV 1 and 3 emergences post-bOPV cessation is predicted to be much smaller than the relevant risk for type 2 after tOPV withdrawal. Still, pre-cessation SIAs and outbreak response planning remain critical risk mitigation strategies.

iVDPV

The global prevalence of B-cell related primary immunodeficiency disease (PID) patients is uncertain due to wide variabilities in diagnosis, reporting, and survival rates. Only a small portion of PID patients become infected with poliovirus and fewer still (estimated range 0.1% to 20%) become long term iVDPV excretors. PID patients have low survival in low income countries which tend to use OPV so while their OPV use would put these countries at the highest risk for the emergence of iVDPV, decreased survival of these patients greatly reduced the risk of persistence. PID patients in high-income countries have much better survival rates but as these countries primarily use IPV, which does not lead to VAPP or VDPV, the risk for developing iVDPVs is exceedingly low. The primary risk for iVDPVs and the source of most reported cases since 2005 has been from middle-income countries.

The vast majority of iVDPV cases are thought to spontaneously stop excreting PV in less than 6 months. Projections on the number of iVDPV cases with prolonged (e.g. >6months to 5 years) or chronic (e.g. ≥5 years) excretion are difficult to estimate. The number of chronic excretors in the post-certification period could be quite small (e.g. <30) but more precise predictions will depend on further data from ongoing PID surveillance.

Experience gained from tracking cVDPV2 and iVDPV2s in the pre-certification period will be critically important in estimating the risks for additional emergences post-certification.

[46] See… Full citation to be added.

B. Preparedness and response strategies

Preparedness

To mitigate the risk that a required polio outbreak response will be delayed or ineffective, preparedness activities that will be initiated at the global level include:

- Developing innovative statistical tools for identifying and monitoring future risk for PV outbreaks, containment breaches, surveillance gaps, etc. *(See Risk Forecasting under **Activity 3.1.1**)*
- Based on experience and changing epidemiology, periodically updating the technical guidelines for preparing and responding to a PV outbreak or event at the national level. Updated guidelines will be available at the time of certification.
- Training additional staff in high-risk countries as well as a cadre of public health workers at the global and regional levels to conduct PV risk assessments and implement outbreak responses
- Developing and regularly updating polio-specific plans for global support to an outbreak
- Periodically monitoring regional and high-risk country response capacity
- Creating and maintaining appropriate polio vaccine and antiviral stockpiles *(See **Activity 3.2.2**)*

These global activities will supplement the generic preparedness planning and training that strive to develop broad global and national capacities for preventing, detecting, and responding to public health emergencies. For example, the Joint External Evaluations (JEE) which are used to monitor progress in the development of IHR Core Capacities can be valuable tools to assist countries not only with transition planning of polio resources to support other public health goals, but also to identify any key areas that need to be strengthened in high risk countries. Polio-specific guidance can also be included in broader training on disaster risk management, vulnerability assessments, and readiness.

Regardless of assessed risk for a poliovirus emergence, all regions should continue to periodically monitor their countries' response capacity and have a preparedness plan for a regional response to poliovirus detection. In collaboration with global efforts, regions which have one or more countries assessed to be at high-risk for an emergence should consider conducting periodic trainings in polio-specific assessments and responses to ensure updated technical competence.

All countries should include polio as a possible scenario in their communicable disease outbreak preparedness response plans. Countries assessed as high-risk should develop and regularly review more detailed polio-specific guidelines and periodically conduct polio outbreak simulation exercises (at least through two years post-bOPV cessation). High-risk countries and medium-risk countries should also ensure polio-specific training on a regular basis at least for a core group of staff at the national level through this same period.

Response

Detection of any human or environmental source of poliovirus in the post-certification era will most likely require an immediate and comprehensive response. Although some of the tactical implementation will change, the response will generally include the current core strategies of notification, risk assessment, vaccination, and surveillance enhancement.

Notification. Post-certification, all countries will be required under the IHR (2005) to alert WHO within 24 hours of identifying any WPV. The full scope of the reporting requirements remains to be determined, but as an eradicated pathogen, detection of any category or presentation of poliovirus would most likely constitute a 'public health event of international concern' and require global notification. An Emergency Committee established under the IHR will be tasked with establishing and monitoring broad response parameters to prevent international spread which could include extensive measures such as vaccination of travelers and cross-border checks.

Risk assessment. Guidelines proposed for conducting risk assessments and situational analysis following a sudden onset public health emergency can provide generic strategies which are relevant following detection.[47] While these tools may be useful for outlining general assessment management steps and recognizing the international context, polio-specific guidance will be needed to determine explicit data requirements for evaluating the risk and identification of potential control measures.

The current general and type-specific guidelines for obtaining relevant data following poliovirus detection[48] provide approaches for determining the virologic characterization, population and health system context, and risk of international spread. These approaches will be updated to include innovative laboratory detection measures, new tools for assessing population numbers and movement, etc. *(See **Enabling and Cross-Cutting Areas: Research**).* Risk assessments provide information not only for judging appropriate response strategies, but also the potential need for external human resources or vaccine supplies to rapidly contain an outbreak (*see also C. Functional Capacities*).

Vaccination Response. Post-certification, poliovirus introduction may or may not lead to an actual case depending on population immunity, local environmental conditions impacting transmission, and source of the virus (e.g., containment breach or PID individual). Nevertheless, even in the absence of a human case, the general recommendation—assuming the availability of appropriate vaccine—will be to initiate a rapid and robust vaccination response due to the potential for an uncontrolled outbreak. Revised standard operating protocols for responding to a poliovirus detection will be developed no later than one year pre-certification.

Key requirements for an effective vaccination response in the post-certification period are the same factors which have been critical to achieve eradication. However, dealing with an eradicated pathogen presents new considerations and priorities. Further details and standard operating procedures for responding to future poliovirus detections will be provided prior to certification based on updated epidemiology and vaccine supply information. However, it is possible to delineate the critical strategic and operational decisions required, including:

- Selecting appropriate vaccine(s)
- Establishing aggressive operational parameters (timing, target population, geographic scope, number of rounds, etc.)
- Maximizing SIA quality with special efforts to access hard-to-reach populations

[47] See WHO. Rapid Risk Assessment of Acute Public Health Events. Geneva, 2012; and Inter-Agency Standing Committee. IASC Reference Module for the Implementation of the Humanitarian Programme Cycle. Geneva, 2015.
[48] See WHO. Standard Operating Procedures for responding to a poliovirus event or outbreak, Parts 1 and 2. Geneva, 2017; and WHO. A guide for investigation of Sabin Like 2 (SL2) poliovirus in a human or in the environment. Geneva, 2017

1. Vaccine selection. The appropriate vaccine for an outbreak response will depend on a multitude of factors (e.g., time since cessation, detected serotype, and prior local vaccine use), but predominantly on the assessed transmission characteristics.

Although unlikely to occur (except through a containment breach), detection of a poliovirus in a country with good sanitation, where the primary route of transmission is expected to be oral-oral, should be responded to with IPV. While IPV's primary impact is to generate humoral immunity, it does contribute to oropharyngeal mucosal immunity and should be sufficient to provide both individual protection and stop transmission. However, as the situation in Israel in 2013 demonstrated, low-level transmission of PV can continue in the environment even in the face of a generally highly IPV-vaccinated population if there are sufficient pockets of vulnerable individuals particularly if they are susceptible to fecal-oral transmission. While there will be understandable reluctance to re-introduce a live vaccine into an IPV-only using situation, local assessment of risk will need to determine the appropriate response vaccine in such cases.

Where poliovirus is detected in situations where the primary transmission modality is fecal-oral, the vaccine of choice will be the homotypic mOPV related to the detected poliovirus even if IPV has already been introduced into RI. IPV in RI can prevent paralysis for polio outbreaks and OPV use, but will have limited direct impact on transmission in settings with poor transmission. Vaccine safety, efficacy, and effectiveness of all mOPV types have been proven. However, by five years post-cessation, as a live vaccine mOPV does present a risk of seeding additional outbreaks if high immunity levels are not achieved. Using IPV as a 'ring' or to vaccinate high-risk subpopulations adjacent to outbreak areas can be effective to preemptively mitigate this risk by raising individual humoral immunity and may also bolster mucosal immunity among individual who have previously received OPV. Co-administration of mOPV and IPV can be operationally challenging yet should be considered as a key vaccination strategy as long as this approach does not adversely jeopardize achieving high coverage.

Creating and maintaining large stockpiles of mOPV and IPV for use in outbreak response will be essential *(see **Activity 3.2.2**)*. However, due to the long-term risks of using mOPV and the limitations of IPV for stopping transmission in settings of poor sanitation, developing alternative response vaccines is imperative for the long-term stability of polio eradication. *(See **Enabling and Cross-Cutting Areas: Research** chapter.)*

2. Operational parameters. Given the implications of uncontrolled transmission and expected declines in population immunity over time, outbreak control measures post-bOPV cessation will need to be more aggressive than current strategies.[49] While further modeling and experience will help to refine the recommendations, it is expected that controlling future outbreaks may require four to six SIAs of anywhere from 2-10 million target population depending on time since cessation and local risk factors. Initial target age groups should be 0-5 years of age; however, including older children or even adults may be required in the future due to potential for transmission to be sustained by IPV vaccines in these age groups. Initiating a vaccination response within 14 days of poliovirus confirmation should still be a primary objective.

[49] For current strategies, see WHO. Standard Operating Procedures for responding to a poliovirus event or outbreak, Parts 1 and 2. Geneva, 2017

3. Maximizing SIA quality. The core strategies to enhance campaign quality outlined in the PEESP[50] and further expanded in the midterm review[51] (e.g., effective management/supervision, social mobilization, focusing on missed children, and objective monitoring) have proven to be effective. However, implementation of these strategies has often remained challenging, particularly in insecure areas or among nomadic and other mobile populations. Achieving the necessary SIA quality in the future will depend on attaining high coverage among these hard to reach populations. Many of the same strategies which target these populations for surveillance are relevant for vaccination as well. *(See Activity 3.1.1.)* Quality can be maximized by ensuring that all high-risk country have adequate preparedness plans in place and maintain the necessary response capacity.

Surveillance enhancement. Following any PV detection, surveillance will be enhanced by:

- Ensuring strict attention to completeness and timeliness of all AFP reporting.
- Increasing the minimum standards for the affected country and first administrative level to three non-polio AFP cases per 100,000 children less than 15 years of age for 12 months following outbreak confirmation.
- Increasing frequency of available environmental surveillance, and establishing or expanding local environmental sampling sites. Given the expanded role of environmental surveillance in the post-certification era, specific steps have already been developed to monitor for SL2 and VDPV2 pre- and post-outbreak response with mOPV2. Based on this experience with type 2 outbreak surveillance, additional guidelines will be developed to monitor in the post-bOPV cessation era.

Special considerations (To be expanded)

Response to PID patients and iVDPV

Response includes surveillance, antiviral deployment (procurement, storage, release, regulatory oversight, and administration) as well as outbreak assessment and mOPV use, if appropriate. Will differ by source (e.g., iVDPV case vs. iVDPV in environment), consequences (e.g., risk of further spread based on local force of infection and population immunity), time since cessation, etc.

Containment breach

All PEFs should have comprehensive plans for responding to a containment breach in their facilities. GAPIII (or further additions) as well as national regulatory authorities should provide clear expectations for the speed, scope, and type of activities required. All countries with a PEF should also include comprehensive plans for the community response that would also be necessitated in the event of a containment breach *(see also **Goal 1**)*. Elaborate on response criteria (depends on type of PV, location, circumstances of the breach, etc.)

C. Functional capacities

Eradication achievements to date have already demonstrated that effectively implementing the required preparedness and response strategies requires resources and collaborative efforts from the global, regional, and national levels. Similar collaboration and synergistic capacities will be required in

[50] GPEI. Polio Eradication & Endgame Strategic Plan 2013-2018. Geneva: WHO, 2013.
[51] GPEI. Polio Eradication & Endgame Strategic Plan 2013-2018 Midterm Review. Geneva: WHO, July 2015.

the post-certification period. To a large extent these efforts can depend on generic capacities for mitigating and responding to all communicable disease threats. However, to ensure technical quality in implementation, polio-specific components will be needed for selected responsibilities, time periods, and geographic areas.

Table 7 outlines the functional capacities required to implement the preparedness and response activities at the global, regional, and national levels, as well as where and when polio technical expertise will be needed to supplement the standard operations envisioned under IHR.

As with addressing all threats, the primary responsibility for addressing the risks to sustaining a polio-free world lies at the national level. To prepare and respond to events of public health concern, the IHR (2005) and Global Health Security Agenda expect all countries to develop a wide range of core capacities, including:

- Mechanisms for timely and accurate disease reporting according to WHO requirements
- Availability of skilled and competent health personnel for sustainable and functional public health surveillance and response at all levels of the health system
- Development and maintenance of national, intermediate, and local or primary response level public health emergency response plans
- Establishment of a public health emergency operation center (EOC)
- Development of a national framework to allow for the rapid cross-border deployment and receipt of medical countermeasures and public health and medical personnel among international partners
- Development of multi-level and multi-faceted risk communication capacity

In addition to these generic capacities expected of all countries, those countries assessed as being at high-risk should retain polio-specific capacities in their Rapid Response Teams and for critical responsibilities (such as planning and implementing an SIA) through Stage IV. Medium-risk countries should retain similar capacity through Stage II. The breadth of this capacity and how it will be organized depends on individual country situations. Countries with a PEF should also have designated capacity to monitor GAPIII compliance as well as human resources in place to implement an aggressive emergency response plan.

Global and regional levels will play a supportive role to national efforts as required. Given the critical importance of sustaining the global achievement of polio eradication and the technical expertise required for certain responsibilities such as advising the incident management system in the case of a poliovirus outbreak, some polio-specific capacity should be maintained within the previous GPEI partner agencies at the global level for at least 10 years after certification. Regional capacities should generally mirror the global level; however, the requirements for polio specific capacity should be based on regional assessment of national capacities, especially of high risk countries. Regions will have specific leadership and operational responsibilities for multi-country or border outbreaks.

In addition to global and regional core staff who work to sustain various polio essential functions, a global roster of public health experts with polio eradication field experience will be established. Experts from this roster will be able to provide surge capacity as required for all countries but particularly medium-risk countries in stages III-IV and low-risk countries for all stages.

Further analysis of expected need for global and regional support will be conducted by 2018 to further identify the specific number and expertise for core polio staff in GPEI partner agencies, specifics of developing an external roster, etc.

Table 8. Functional preparedness and response capacities required at global, regional, and national levels (unless noted, capacities should be sustained through Stage IV—10 years post certification)

	Generic capacity	***Polio specific capacity***
Global	• *Leadership* (incident management, security, external relations, EOC management	• Technical input to incident management system and EOC
	• *Partner coordination/liaison* (GORAN, etc.)	
	• *Information & planning* (generic preparedness tools, global communication and planning in response situations)	• Technical guideline development or revisions; surge capacity for rapid assessment (global roster
	• *Health operations & technical expertise* (risk communication, technical guidance, training)	• Training, surge capacity for outbreak response (global roster)
	• *Operational & logistic support*—including vaccine & antiviral stockpile management; syringe deployment	• TA to polio vaccine stockpile management as required
	• *Finance & administration (*budget, procurement, HR)	• Vaccine and antiviral procurement as required
	• *IHR monitoring and administration*	• Monitor outbreak response
Regional—depends on risk	Mirrors global level	Mirrors global level based on regional assessment of national capacities, especially of high risk countries. Specific leadership and operational responsibilities for multi-country or border outbreaks.
National depends on risk	Countries have primary responsibility for preparedness/response and should develop minimum capacities recommended by IHR. All countries should have Rapid Response Teams. Global or regional level to provide surge capacity as required for all countries but particularly Medium Risk countries in Stages III-IV and Low Risk countries for all Stages.	
High risk	• *Leadership* (activate EOC, etc.)	• Technical input to incident management system and EOC
	• *Partner coordination*	
	• *Information & planning*	• Preparedness planning & periodic simulation exercises; Conduct rapid assessment;
	• *Health operations & technical expertise*	• Plan, organize, and implement outbreak response;
	• *Operational & logistic support*	• Polio vaccine management, including collection/destruction of residual mOPV doses
	• *Finance & administration*	
	• *IHR monitoring and administration (*monitor development of minimum core capacity; notify WHO of verified PV detection)	
Medium	Should at least develop IHR minimum expected	Mirror High Risk capacity for Stage I-II; utilize

risk	capacities, including notification to WHO if PV detected	global and/or regional surge capacity if required for outbreak support in Stages III-IV
Low risk	Should at least develop IHR minimum expected capacities, including notification to WHO if PV detected	Utilize global and/or regional surge capacity if required for outbreak support.

Activity 3.2.2. Create, maintain, and manage an adequate stockpile of polio vaccine and antivirals for an appropriate response

Polio vaccine stockpile
(Section to be added following completion of Report from the Polio Vaccine Stockpile Working Group

Antivirals
(See Research chapter)

E. Who Oversees the Goal

(To be expanded)

While specific agency responsibilities have yet to be determined, the effective monitoring and oversight of this goal should include two relevant capacities: technical competency to understand specifics of polio virology and epidemiology; and operational competency to understand the requirements of outbreak response. Potential options are:

Objective 3.1: Monitoring and Oversight of Polio Surveillance

Overall surveillance: Annual report to WHA? Joint External Evaluations under IHR?
Lab: GPLN, Global Lab Alliance for Detection of High Threat Pathogens?

A critical adjunct to risk forecasts will be ongoing monitoring of surveillance indicators and periodic assessments of surveillance system capacity in high-priority areas. Meeting surveillance quality standard indicators (e.g., NPAFP rate and adequate stool) will become increasingly problematic as AFP surveillance sensitivity and dedicated commitment decline (see challenges to mitigating factors above). Additional indicators (i.e., for environmental surveillance) to track surveillance quality are under development. These assessments may include desk reviews as well as on-site visits to selected high-risk areas.

Monitoring of ES sites will be critical to determine suitability of a site and the overall quality of processing samples. For the pre-certification period, indicators of quality ES surveillance that are being tested include: >50% non-polio enterovirus (NPEV) recovery rate and detection of Sabin or Sabin-like viruses at least once within six weeks of an OPV SIA. Indicators for use during the post-certification era will be further defined once additional data on ES sensitivity is available.

Objective 3.2. Outbreak Preparedness & Response

Preparedness: Joint External Evaluations under IHR?

Response: IHR Secretariat? Other global emergency response monitoring (WHO Health Emergencies [WHE])?

Enabling and Cross-Cutting Areas

The overview for this section will be added with the third draft.

A. Governance and Management Model

To be added with the third draft

B. Research Activities

Polio-related scientific inquiry and new product development will, by necessity, continue through and beyond certification and contribute to each of the post certification goals, in addition to informing the development of relevant public health policies.

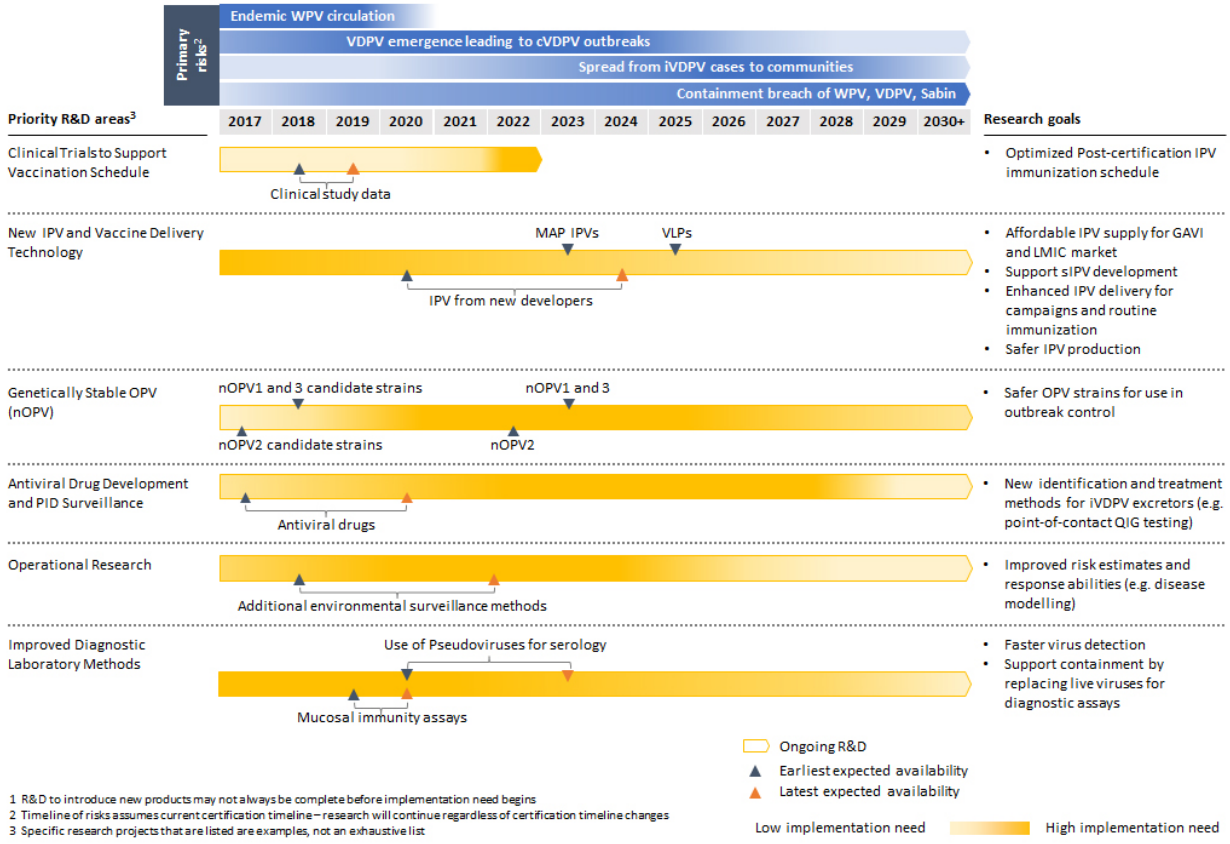
Within the GPEI partnership, WHO, CDC and BMGF have independent but highly collaborative polio research programs. Unlike most GPEI activities, there is no formal oversight or reporting relationship for the research programs other than within their parent organizations. The Polio Research Committee (PRC), which includes the GPEI partners and ex-officio representatives from the National Institutes of Health (NIH), Food and Drug Administration (FDA), the Program for Appropriate Technology in Health (PATH) and WHO regional offices, serves as a forum to identify research needs and review current research activities. The PRC also supports extramural research under a competitive program funded by Rotary International. In addition to twice annual PRC meetings, research updates are shared on the monthly Research Call and, for communications and operational research, the monthly Interinstitutional Working Group (IIWG) call.

The GPEI partners and the PRC interact with an extensive network of other organizations including academic and government investigators, clinical research organizations, multinational and developing country vaccine developers and infectious disease modelers, many of which are grantees of one or more of the GPEI partners.

Broad areas of research focus and collaboration include serological surveillance to assess population immunity; infectious disease modelling to estimate post-cessation risks and support environmental surveillance deployment; development of new laboratory assays to speed virus detection, comply with containment requirements, and measure mucosal immunity; new IPV development to reduce costs and improve production safety; non-infectious production processes for IPV (i.e., virus-like particles); development of IPV with mucosal adjuvants; new platforms to enhance IPV delivery; new OPV development to respond to post-cessation VDPV outbreaks and provide a safer vaccine in the event routine use of OPV is reintroduced; antiviral drug development to reduce risk from iVDPV excretors; operational research to improve post-cessation planning and outbreak response; and clinical research on new vaccines, vaccine schedules, and antiviral drugs to inform public health policy.

The polio research agenda is forward-looking, includes projects that may take years to complete, and generally does not distinguish between pre-certification and post-certification objectives. However, for planning purposes, it is useful to delineate the research requirements needed to support each of the PCS goals, recognizing there may be broad applicability across goals, for example with modeling, surveillance, and assay development. *(See **Figure 6** for more on polio research and development.)*

Figure 6: Polio Research and Development



Goal 1: Contain Polio Sources

Poliovirus-essential facilities (PEF) include vaccine manufacturers, public health testing facilities, and academic laboratories who maintain stocks of wild and attenuated viral material for vaccine production, vaccine quality control, and clinical assay requirements. In PEFs, the risks from inadvertent exposure or a breach of containment can be reduced by replacing live polioviruses with non-replicating viral antigens or safer live viruses in laboratory protocols, reducing the need to maintain laboratory stocks of wild and attenuated viral material.

Post-certification, the use of all wild and attenuated polioviruses in clinical research will be effectively prohibited unless manipulated under proper containment conditions in compliance with GAPIII requirements. These restrictions will bar the human OPV challenge studies now used to assess post-immunization mucosal immunity and antiviral efficacy. New assays for mucosal immunity that rely on "neutralization" of pseudo viruses or on IgA detection have been developed, but require further validation.[52] Also, if nOPV viruses prove to be safe to use in the community (i.e., deliberate release) that could avoid containment requirements, they may be permitted in human challenge research.

[52] Wright PF, Connor RI, Wieland-Alter WF, et al. Vaccine-induced mucosal immunity to poliovirus: analysis of cohorts from an open-label, randomised controlled trial in Latin American infants. Lancet Infect Dis **2016**; 16:1377-8410.1016/S1473-

Goal 2: Protect Populations

Protecting the global population against a re-emergence of poliomyelitis will require ongoing risk assessment, optimization of individual protection with marketed vaccines, development of new vaccines designed to reduce costs, enhance coverage, and reduce transmission of live polioviruses through induction of mucosal immunity, and development of antiviral drugs to clear infection in long-term, immunodeficient iVDPV excretors.

Risk assessment — Forecasting of short- and long-term risks will require development of models to predict the absolute and relative risks from wild type (WT), cVDPV and iVDPV viruses in all regions and over time until all credible threats to eradication are irreducible. For example, KidRisk has developed an integrated dynamic poliovirus transmission model to simulate potential risks from 2013 to 2052 and the quantities of stockpile mOPV required to mitigate these risks.[53] Post-certification, it will be critically important to continuously re-evaluate assumptions and update models based on past and current experience.

Periodic, targeted serological surveys in high-risk countries may be needed to better inform the models and improve risk assessment. Continued development and validation of a standardized EIA assay for global use (currently in progress at CDC) should improve timeliness, reduce costs, and mitigate the containment requirements of the serum neutralization assay.

Optimize individual protection with currently marketed IPV vaccines — SAGE has recently recommended a 2-dose IPV schedule for the post-certification period and suggested that fractional dose IPV (fIPV) is equivalent to full dose for routine immunization. However, additional clinical research is necessary to have confidence in this recommendation. Studies supported by BMGF and CDC, which are underway in Uruguay and Bangladesh, respectively, will provide more information on the optimal full dose and fractional dose IPV schedules for primary immunization by late 2018 or early 2019. These studies are complemented by current operational research on delivery, feasibility and costs associated with intradermal IPV administration supported by PATH and WHO.

New IPV vaccine development — Post bOPV cessation, unless all current OPV-using countries adopt fIPV, from 170M to 230M IPV doses will be required to meet global demand (see ***Figure 5****: Future IPV demand scenarios and supply requirements, page 39*). Several new IPV development programs that deploy different strategies to reduce costs (enhanced production technology, improved viral yield, antigen sparing) are in progress. Other manufacturers have started Sabin strain IPV (sIPV) development programs designed to enable developing country vaccine production, including five companies who have adopted Intravacc methodology through WHO supported technology transfer agreements.[54]

3099(16)30169-4; Wright PF, Wieland-Alter W, Ilyushina NA, et al. Intestinal immunity is a determinant of clearance of poliovirus after oral vaccination. J Infect Dis **2014**; 209:1628-3410.1093/infdis/jit671

[53] Duintjer Tebbens RJ, Pallansch MA, Cochi SL, Wassilak SG, Thompson KM. An economic analysis of poliovirus risk management policy options for 2013-2052. BMC Infect Dis **2015**; 15:38910.1186/s12879-015-1112-8; Duintjer Tebbens RJ, Thompson KM. Poliovirus vaccination during the endgame: insights from integrated modeling. Expert Rev Vaccines **2017**; 16:577-8610.1080/14760584.2017.1322514

[54] Okayasu H, Sein C, Hamidi A, Bakker WAM, Sutter RW. Development of inactivated poliovirus vaccine from Sabin strains: A progress report. Biologicals **2016**; 44:581-7; Sutter RW, Okayasu H, Kieny MP. Next Generation Inactivated Poliovirus Vaccine: The Future Has Arrived. Clin Infect Dis **2017**; 64:1326-710.1093/cid/cix116

Several programs have recently initiated clinical trials which will extend well into the post-certification period and new IPV vaccine supplies are projected to come to market between 2019 and 2024.

There are also discovery and translational phase IPV projects designed to further reduce the risks of an industrial or laboratory containment breach, including vaccines produced from genetically modified Sabin strains (NIBSC strains) or virus-like particles (VLPs), and vaccines that include novel adjuvants like oil-in-water emulsions, dmLT and toll-like receptor (TLR) agonists.[55] Because the timelines for vaccines incorporating any of these approaches will extend beyond 2024, and the development costs will be great, it is uncertain whether any will be available for global use either in standalone or combination vaccine formulations.

Enhanced IPV delivery technology — New vaccine delivery technologies have the potential to facilitate vaccine administration, reduce dose number, spare antigen, and lower cold chain requirements and storage costs, thereby facilitating both routine and campaign-based IPV immunization. Several disposable syringe jet injector devices that deliver vaccine either intramuscularly or intradermally have been evaluated clinically for IPV delivery.[56] Injection devices induce comparable immunogenicity and are preferred by health care workers compared with needle and syringe. However, their future utility is uncertain due to the added costs of the devices and health care worker training, and because SAGE does not recommend IPV for campaigns or for outbreak control, although this could change when the IPV supply is adequate.

Microarray patches (MAPs) that deliver vaccine directly into the dermis can be applied quickly and easily by minimally trained health care workers have the potential to reduce vaccine costs by dose sparing and to reduce shipping, storage, and cold chain costs. MAP availability could facilitate IPV delivery for both routine immunization and during campaigns for cessation or outbreak control. WHO and the BMGF currently support three MAP developers, but progress has been slow due to limited IPV bulk vaccine availability from manufacturing partners and to technical impediments. As of June 2017, MAPs suitable for clinical study have not been produced by any of the developers and future of MAP technology for polio immunization is uncertain.

[55] Norton EB, Bauer DL, Weldon WC, Oberste MS, Lawson LB, Clements JD. The novel adjuvant dmLT promotes dose sparing, mucosal immunity and longevity of antibody responses to the inactivated polio vaccine in a murine model. Vaccine **2015**; 33:1909-1510.1016/j.vaccine.2015.02.069; Hawken J, Troy SB. Adjuvants and inactivated polio vaccine: a systematic review. Vaccine **2012**; 30:6971-910.1016/j.vaccine.2012.09.059; Baldwin SL, Fox CB, Pallansch MA, Coler RN, Reed SG, Friede M. Increased potency of an inactivated trivalent polio vaccine with oil-in-water emulsions. Vaccine **2011**; 29:644-910.1016/j.vaccine.2010.11.043; Fox H, Knowlson S, Minor PD, Macadam AJ. Genetically Thermo-Stabilised, Immunogenic Poliovirus Empty Capsids; a Strategy for Non-replicating Vaccines. PLoS Pathog **2017**; 3:e100611710.1371/journal.ppat.1006117

[56] Resik S, Tejeda A, Mach O, et al. Immune responses after fractional doses of inactivated poliovirus vaccine using newly developed intradermal jet injectors: a randomized controlled trial in Cuba. Vaccine **2015**; 33:307-1310.1016/j.vaccine.2014.11.025; Clarke E, Saidu Y, Adetifa JU, et al. Safety and immunogenicity of inactivated poliovirus vaccine when given with measles-rubella combined vaccine and yellow fever vaccine and when given via different administration routes: a phase 4, randomised, non-inferiority trial in The Gambia. Lancet Glob Health **2016**; 4:e534-4710.1016/S2214-109X(16)30075-4; Anand A, Zaman K, Estivariz CF, et al. Early priming with inactivated poliovirus vaccine (IPV) and intradermal fractional dose IPV administered by a microneedle device: A randomized controlled trial. Vaccine **2015**; 33:6816-2210.1016/j.vaccine.2015.09.039

Work continues on delayed-release IPV formulations that are delivered by needle and syringe (Langer) or silk protein MAP (Vaxxes), designed to reduce the number of vaccine doses required for complete immunization. These projects remain translational and are not expected to lead to marketable IPV until 2023 or later.

Genetically stable new OPV — Monovalent Sabin OPV (mOPV) vaccines are the principal countermeasure for response to VDPV outbreaks occurring after bOPV cessation. However, mOPV use in the setting of declining humoral and mucosal immunity will carry an increasing risk of new VDPV generation and spread within and beyond the outbreak area. To mitigate this risk, BMGF has funded a consortium of virologists at NIBSC, CDC, FDA and UCSF who have developed a panel of Sabin-derivative OPV vaccine strains modified to increase genetic stability and reduce neurovirulence compared with the Sabin viruses. Under a grant to PATH, two new OPV type 2 (nOPV2) candidate strains have been manufactured for clinical study and human trials are now underway in Belgium. Proof of concept is anticipated by 2019 and, if successful, nOPV2 could be available as early as 2021. New OPV1 and OPV3 strains created in the nOPV2 backbone strains are in preclinical development and may be available for human testing in 2018. To date, planning for nOPV vaccine procurement and stockpiling has not begun.

Goal 3: Detect and Respond

Continued research and development will be required to support post-certification surveillance and outbreak response planning, including modeling, operational research, communications and GIS technology, specimen collection for environmental surveillance, and identification and characterization of polioviruses in the field and in the laboratory.

Modeling — As polio cases decline towards zero, the relative sensitivity of AFP surveillance and environmental surveillance will change. Ongoing modeling can assist in surveillance planning as the program adapts to changing risks over time and in different geographies and can contribute to improving site selection, sampling frequency, and other operational facets of environmental surveillance. Modeling will be needed to better understand the post-certification risks from cVDPV viruses of all 3 types and from iVDPV emergences, and how these risks will vary over time.

Operational research to improve outbreak response — Operational research on outbreak response planning, campaign monitoring, and assessment includes development and deployment of new tools such as GIS mapping to improve microplans and smart phone technology to capture and transmit data and messages to and from the field.

Environmental surveillance — In the absence of AFP cases, the world will rely on environmental surveillance (ES) to detect new outbreaks, monitor persistent transmission, and confirm the disappearance of Sabin poliovirus after the withdrawal of bOPV.[57] Improvements to environmental surveillance will require research on optimization of site selection through modeling, demography, and use of GIS technology; continued innovation of specimen collection such as the bag-mediated filtration system, point-of-collection screening for rapid poliovirus identification, and application of deep genomic

[57] Hovi T, Shulman LM, van der Avoort H, Deshpande J, Roivainen M, EM DEG. Role of environmental poliovirus surveillance in global polio eradication and beyond. Epidemiol Infect **2012**; 140:1-1310.1017/S095026881000316X

sequencing to distinguish and characterize poliovirus isolates from individual excretors in the sample population.

Antiviral drugs — Persons living with inherited B cell immunodeficiency syndrome in OPV using countries create risk to the program from persistent excretion of iVDPV viruses after OPV has stopped. In 2007, the U.S. National Academy of Sciences recommended development of at least two antiviral drugs to reduce the risk of outbreaks from immune deficient iVDPV excretors, and possibly to treat persons exposed to live polioviruses following a breach of containment at a manufacturing facility or laboratory. From a continuous discovery effort, only two compounds with promising activity and an acceptable safety profile have been identified.[58] Pocapavir, a capsid inhibitor, demonstrated potent activity in human volunteers during an OPV challenge study in Sweden, but induced excretion of resistant virus in approximately 40% of participants.[59] The 3C protease inhibitor V7404 also inhibits polioviruses in vitro, but has low oral bioavailability. The current focus of the program is formulation improvement to increase the V-7404 bioavailability and to conduct Phase I safety studies with V-7404 and with a combination of pocapavir and V-7404 (ViroD7000). Assuming successful completion of these trials, ViroD7000 may be available for distribution under named-patient protocol and further assessed for efficacy in a concurrent Phase II challenge study to begin in late 2018. However, antiviral drug development will inevitably extend into the post-certification era.

Identification of iVDPV excretors — Even with availability of effective antiviral drugs, the risk from iVDPV excretors will be reduced only with effective surveillance and treatment protocols. Recent prevalence surveys by WHO and by a consortium of Taskforce for Global Health, CDC, and Jeffrey Modell Foundation investigators each found a prevalence of 1% iVDPV excretion prevalence among patients with hereditary immunodeficiency syndromes in selected middle-income countries in Africa, the Middle East and Asia. The WHO team has studied the feasibility of extending surveillance beyond the centralized immunology clinics in Egypt with mixed success. The objectives, scope, strategies, and operational requirements for pre- and post-eradication iVDPV surveillance are now under review and discussion and a more detailed (although still incomplete) plan will be included in future drafts of this document.

Other Considerations

Polio-focused research and development not only requires substantial resource allocation, but because of its unique mission, needs a forum to identify knowledge gaps and research needs, and a mechanism for scientific review and translation of research data into public health and immunization policy. Future drafts of this document will reflect stakeholder discussions and decisions on the status of the PRC, research oversight and support after the closure of the GPEI at certification.

[58] McKinlay MA, Collett MS, Hincks JR, et al. Progress in the development of poliovirus antiviral agents and their essential role in reducing risks that threaten eradication. J Infect Dis **2014**; 210 Suppl 1:S447-5310.1093/infdis/jiu043

[59] Collett MS, Hincks JR, Oberste MS, van er Avoort HGM. Anti-poliovirus activity of pocapavir in a human mOPV1 challenge model. In: 53rd Interscience Conference on Antimicrobial Agents and Chemotherapy. (Denver). **2013**.

C. Monitoring Activities

To be added with the third draft

D. Future Financing Needs

1. Background and Context

Placeholder: Summary of projected GPEI spend 2013 – 2020 to achieve certification, tied to projected range of post-certification costs. This section will also describe investment trends by activity over time.

2. Objectives

The purpose of the PCS financial requirements model is to develop a robust estimate of the projected costs associated with polio essential activities. This estimate is an essential step to enable the mainstreaming of these activities in the post-certification period and communicate these requirements to agency partners, national and global health initiatives, ministries of health, funding agencies and donors. The model will also serve as a baseline to anchor stakeholders across various organizations and geographies on the key operational and programmatic assumptions underpinning the forecasted activities, and any sensitivities to those assumptions that may drive a change in the resourcing required.

3. Scope and Assumptions

The financial requirements reflected in this document cover the activities that are projected to occur in the 10-year period following certification. As such, this model will be closely linked to the financial resourcing requirements (FRR) to achieve WPV eradication developed in support of the PEESP. In contrast to the endgame strategy, however, the PCS model is anchored on the "trigger event" of reaching the certification milestone, not on a specific calendar date, and thus, the period addressed by this estimate of financial requirements will ultimately be determined based on when the certification milestone occurs.

It is also important to recognize that the financial requirements model addresses the essential activities required at a global level. While the PCS lays out a number of specific activities that need to occur at the national and regional levels to support the gains of the GPEI and protect a polio-free world, the global post-certification financial requirements model does not include the cost of those activities that will be undertaken by individual countries or regions, but rather includes only the cost of any global support or facilitation required to ensure successful execution.

The methodology and assumptions used to develop the financial requirements are for planning purposes only and are not intended to dictate nor constrain the actual operational implementation of work required to support each goal. This model has been developed in support of transition planning, to facilitate discussions around the financial resources needed to undertake the post-certification activities described, and is agnostic as to which implementing partners assume responsibilities for operationalizing and implementing PCS recommendations. This planning tool also assumes a level of operational continuity between the late stages of the pre-certification period and the immediate post-certification period. To support operational continuity, the projected activities and associated costs have been examined in the context of, and compared to, the final years of the existing GPEI budget through 2020 to prevent any planning gaps or errors that may result from a strategy shift as the certification milestone is achieved.

Standard definitions for each activity category are included within the financial requirements model to capture expectations of the required activities that are based on present knowledge and the GPEI's lessons learned to date. It will be important to periodically reexamine these definitions upon entering a later phase of post-certification planning to ensure that all working assumptions and protocols are in line with the demands of maintaining a polio-free world.

4. Budget Drivers and Cost Components

The PCS financial requirements estimate was developed using an activities-based approach to cost modeling where a directly correlated driver can be identified and reasonably estimated.

Placeholder: Describe major activities (in layman's terms) for each goal:

- Goal One: Facilitate and audit containment of polio-essential facilities
- Goal Two: SIA's, stockpiles
- Goal Three: Surveillance (environmental, AFP, lab support), outbreak preparedness
- Cross-cutting Enabling Activities: Research and core governance infrastructure

Sample summary table: Goal > Activity > Driver > Assumptions > Scenarios and sensitivities

Goal	Activity	Driver	Assumptions	Scenarios or Sensitivities

Placeholder: Discuss and quantify the top three components of the budget, assumptions, and sensitivities of each. Identify the key activities that are not included in the global estimate due to being owned at the national level. Flag any known gaps and TMG mitigation strategy. Call out regional components/global components.

5. Scenarios

The financial estimate of post-certification costs represents a continuum of potential resourcing requirements based on a range of low/intermediate/high scenarios for primary cost drivers (e.g. stockpiles, outbreak response, surveillance levels, IPV availability). These scenarios are anchored on a realistic mix of favorable outcomes of some drivers (e.g., IPV availability) and less favorable projections for other drivers (e.g., ramp-down of technical assistance in key regions) based on the best information and programme data available today. As such, the scenarios presented in this document reflect the consensus among a cross-cutting stakeholder base around the most-likely range of outcomes for the most significant programmatic and technical drivers.

- Low scenario placeholder
- Intermediate scenario placeholder
- High scenario placeholder

6. Recommendation

Placeholder: Tie into PACT work, RM strategy. Acknowledge the critical role of donors; protecting investments made to-date. Cite any major sensitivities that feel too broad/risky - timeframe for removing the uncertainty.

7. Risks, Risk Mitigation, Contingency Planning

Placeholder: Identify key risk factors, likelihood of occurrence, severity if realized, detection risk. Potentially call-out annual cost if key risks materialize. Note: This section will be drafted as we understand the initial outputs from the model and key sensitivities that emerge.

E. Advocacy and Resource Mobilization

The GPEI has successfully mobilized significant funds over the last twenty years through a resource mobilization and advocacy model which has driven commitment from donors. One of the key factors of this success has been joint advocacy and resource mobilization efforts across partners with a common communications narrative.

Under the current management group structure of the GPEI, the Polio Advocacy and Communications Team (PACT), which allows for coordination between GPEI core partners and advocacy partners, is responsible for the development and implementation of a cross-agency external relations strategy. The main objective of the external relations strategy is to ensure international financial and political commitment to, and public confidence in, the Polio Eradication & Endgame Strategic Plan. The ongoing external relation strategy's key focus is to make sure the financial needs of the Endgame Strategic Plan are met until certification. This will ensure all four objectives are properly funded until this period.

The two strategic priorities of the external relations strategy for the past two years have been: 1) to mobilize pledges against the additional US$ 1.5 billion requirement; and 2) to secure and monetize the pledges made by donors against the original US$ 5.5 billion budget.

As of July 2017, following a successful event in Atlanta on 12 June 2017, where US$ 1.2 billion was pledged and announced, the funding gap on the overall US$ 7.0 billion budget stood at US$ 300 million. The PACT therefore still needs to secure additional commitments of US$ 300 million from potential donors and existing donors that were not in a position to pledge in Atlanta. The PACT will also work with the generous donors who pledged in Atlanta to begin monetizing their pledges to make sure programmatic plans can be operationalized as soon as possible.

Given that resource mobilization in support of polio-essential functions will need to continue for the 10 years of the PCS period, albeit at a lower level, a critical part of this process will be planning for mainstreaming polio resource mobilization and advocacy into implementing partner agencies and national governments, particularly as countries will be responsible for mobilizing resources to support their own post-certification activities in line with the PCS recommendations. This will include ensuring that the polio-essential functions defined by the PCS are budgeted; that the PCS is referenced in agency operational planning; and that best practices and lessons learned from GPEI resource mobilization, advocacy and communications are also mainstreamed.

As previously highlighted, it will be critical to not only maintain essential functions such as containment and surveillance, but also make sure there is a continuum after certification so that functions do not suddenly stop. There will be a need to ensure that, for instance, the necessary stockpiles of mOPV and IPV are in place leading up to the bOPV cessation period and that surveillance activities continue without interruption.

The GPEI, through the PACT, will therefore need to work to mobilize resources for some activities of the pre-cessation period to ensure this continuum. As a lead time of between six and 18 months is often needed to mobilize resources and for some activities, notably vaccines, might take a longer time, advocacy work toward securing pledges and commitments for pre-cessation activities will need to start at least 18 months prior to certification.

To do this, the PACT will be developing a **Post-Certification External Relations Strategy** (PCERS) to support Post-GPEI PCS polio essential-functions funding and start mobilizing resources for the pre-cessation period.

As soon as the financial model and scenarios of the Post-Certification Strategy have taken shape and indicative financial needs have been identified for the pre-cessation functions, the PACT will be able to start the process of the development of the PCERS and work toward securing pledges and commitments for the pre-cessation period. The planning for the development of this strategy should start no later than in Quarter 4 of 2017, as soon as the PACT has revised its current strategy and plan of action in Quarter 3 to finalize the mobilization and monetization of the US$ 1.5 billion.

It will be critical for the success of GPEI and the future of the polio-essential functions that the PACT develop clear messages and a proactive communications plan both to ensure donors and stakeholders fully understand the financial requirements and their corresponding timelines, and to clearly delineate between the GPEI Endgame Strategic Plan Financial Resource Requirements (GPEI FRRs) and the **non-GPEI** post-certification financial requirements.

In terms of sequencing, the PACT will therefore:

- Ensure sufficient donor commitments are available through to certification. whilst developing a PCERS for the PCS period
- Develop a plan to communicate and advocate clear messages on what will be needed to sustain a polio-free world (with a focus on key markets)
- Work to obtain donor commitments for continued support and present financial needs
- Implement the PCERS in order to ensure funds are available for the pre-cessation period, and
- Hand-over the PCERS to implementing agencies for the post-cessation period.

Annex A: PCS Engagement List

To be added with the final draft

Annex B: PCS Prerequisites and Assumptions

As a strategic plan that fulfills the fourth and final goal of the Polio Eradication Endgame Strategic Plan (PEESP) and the first goal of the GPEI Transition Management Group (TMG), the PCS provides a necessary bridge from WPV eradication, through transition planning for the closure of the GPEI, and on into the future mainstreaming of polio-essential functions in the post-certification period. As such, the PCS dovetails the work that is needed to complete the job of eradication with the activities, initiatives, research, and developments that need to be in place by certification, when the PCS will launch.

The purpose of this annex is to detail both prerequisites and assumptions that should be closely monitored and confirmed in the time leading up to certification so the future managers of global health are prepared to implement the PCS.

In this context –

- **Prerequisites** denote those conditions that are determinants for launching the PCS. It is only after these conditions are met that the full scope of the PCS can begin.
- **Assumptions** address a range of expectations on what will be happening or will have occurred at the time the PCS starts.
  - Some assumptions are based on established and evolving workplans related to both the endgame strategic plan and GPEI-wide transition planning, including agency partner and country-level planning. These actively inform PCS goals, objectives, and activities.
  - Other assumptions are based on initiatives and developments across other global health partnerships—such as transitions in country financing for vaccines, from co-financing with support by the Gavi Alliance to full self-financing.
  - The PCS also makes assumptions based on the current epidemiology of the virus. Where appropriate, these are highlighted so deviations from this expected landscape can be accommodated to future realities.

For current partners and stakeholders of the global polio eradication effort, the following prerequisites and assumptions are offered to provide clarity on what activities and outcomes belong to this future-oriented strategic plan and what activities and outcomes must be achieved before the PCS takes effect.

For future managers of public health, they are offered to support the review, revision, and adjustment of PCS guidelines as the world nears global certification. This review period is addressed in [placeholder for Enabling and Cross-Cutting Areas sub-activity TBD]. It should be noted that, as assumptions about the maturity of pre-certification activities inform the PCS financial model, if these activities do not keep pace with PCS assumptions, it will impact the plan's future financial requirements.

Overall Prerequisites and Assumptions

Prerequisites

- The PCS is based on the fundamental prerequisite of global wild poliovirus eradication. WPV eradication must be achieved before the timeline to certification and post-certification can begin.
- Placeholder: "Certification is based on …" Once GCC requirements for WPV certification are finalized, they will be brought forward here with a reference (and link) to GCC documentation.

Assumptions

- The PCS assumes that agency partners and countries will have implemented transition plans, so they have the capacity to begin coordination and oversight of global and regional guidelines.
- Placeholder: Some assumptions from enabling and cross-cutting areas to appear here.

Goal One: Contain Poliovirus Sources

Prerequisites

Because of the lack of a mandate from WHO or GCC to enforce adherence to GAPIII requirements by countries or facilities holding polioviruses, global implementation of GAP III Phases I, II and IIIa, may be uneven by the time of global WPV certification, with some countries having completed all phases, whereas others are still pending completion of some requirements.

Containment prerequisites are in the process of being defined through stakeholder input with GCC, CMG, and others. The major pending questions are:

- Will containment be a prerequisite for global certification?
- What elements of containment will be considered essential at the global level or at the regional/country level? For example,
    - Will all countries be required to have containment in place before global certification or delays in a few countries will be accepted?
    - Will it be acceptable for PEFs to have started the process of certification and have interim certificates of containment?
    - What is the degree of implementation of secondary and tertiary safeguards expected for countries with PEFs holding WPV?

Assumptions

- The containment activities described in the PCS are based upon the strategies described in GAPIII, which will be revised during the endgame phase. However, it is expected that the revisions will address specific questions and challenges to implementation processes or procedures, whereas the general strategies and guidelines, which form the basis of the PCS, will be upheld.
- The PCS assumes that through the current effort of the CMG and other GPEI groups, Phases I and II will have been completed globally before the certification of WPV eradication.
- Although the decision on specific containment pre-requisites is still pending, the PCS assumes that containment of all WPV (i.e. Phase IIIa) will be in place around, or shortly after, certification of WPV eradication. Thus, preparatory activities for Phase IIIa, such as update of inventories to include facilities with any WPV materials (not only type 2), and validation of destruction or transfer of all WPV materials in facilities not designated as PEFs, are expected to be carried out before certification, and are not part of PCS.

Goal Two: Protect Populations

Prerequisites

- Objective 2.1: The country-level withdrawal of bOPV can only be initiated after global certification is attained and the pre-cessation readiness factors have satisfactorily been achieved.
- Objective 2.2: Access to safe, effective IPV requires a sufficient global supply to enable all countries to provide two doses (full or fractional) of IPV as part of their routine EPI schedule as recommended by SAGE. Not all countries may choose to implement this recommendation, but a minimum requirement to meet this objective would be adequate quantities of vaccine to enable this option.

Assumptions

Objective 2.1

- By April 2018, SAGE recommends and GPEI endorses a set of readiness factors for bOPV cessation along with specific parameters expected for their satisfactory achievement.
- By two years prior to certification, the GPEI establishes a recommended strategy and calendar for pre-cessation SIAs. Sufficient bOPV vaccine and other resources will be available to fully implement this calendar
- Countries have sufficient commitment, resources, and technical support to effectively implement bOPV withdrawal. The withdrawal and destruction of bOPV from all levels of national EPI systems will be sufficiently thorough to minimize risk of subsequent inadvertent use of the vaccine.
- The status of IPV supply, containment, response capacity, and poliovirus surveillance are all adequate to meet parameters established for the relevant readiness factor.
- The epidemiologic status of PV remains conducive to bOPV withdrawal (e.g., no further identification of WPV, lack of persistent cVDPV)

Objective 2.2

- Manufacturing capacity expands sufficiently to meet required demand for IPV.
- GAVI agrees to include IPV in its Vaccine Investment Strategy and receives adequate funds to support eligible countries to meet the vaccine requirements recommended by SAGE.
- Middle-income countries have affordable options (e.g., adjuvanted vaccine, hexavalent) for IPV.
- Costs and efficiencies of ID devices are within parameters that encourage use of fractional dosing.
- Routine immunization systems in all countries, especially those at high risk for poliovirus emergence, to effectively deliver IPV in order to meet SAGE and GAPIII recommendations.

Goal Three: Detect and Respond

Prerequisites

Objective 3.1: Countries should maintain at least the minimum capacities for surveillance and response required by IHR. Countries are willing to conduct a national risk assessment and strive to fulfill the appropriate recommended strategies.

Objective 3.2: A comprehensive response capacity requires that adequate supplies of effective, affordable antivirals and stockpiles of IPV and all three mOPV types are available at the time of certification.

Assumptions

Objective 3.1

- All types and categories of polioviruses (WPV, VDPV, and Sabin) are considered threats to global security and reportable under IHR. Countries are willing to promptly notify WHO of any detected PV.
- The risk of VDPV2 is extremely low by the time of certification and will not be a primary risk for PV emergence.
- Adequate laboratory reagents, supplies, and staff are available to effectively provide testing of isolated. Satisfactory transport mechanisms are in place to meet any containment requirements.
- Surveillance staff have adequate transport and support to regularly conduct active AFP surveillance and implement environmental surveillance where appropriate.

Objective 3.2

- Stockpiled supplies of antivirals, IPV, and mOPV are adequate to respond effectively to any PV detection.
- By end 2018 a comprehensive review will be conducted of the global and regional staffing requirements in the post-certification era.

Annex C: Country Risk Classification

General

The main goal of polio surveillance in the post-certification era is to ensure rapid detection of any poliovirus. Although WPV will have been eradicated, the risk for WPV re-introduction from containment breaches will persist as long as it is used for manufacturing vaccines and WPV-containing samples are stored. Likewise, cVDPV risks will exist due to containment breaches, re-emergence of previously identified cVDPV strains, or emergence of new cVDPV strains. Lastly, there is the potential of an individual with primary immunodeficiency (PID) to shed iVDPV and seed an outbreak. These risks and potential consequences are important considerations for selecting appropriate strategies for poliovirus surveillance in the post-certification era.

The risks for polio will vary over time (between and within identified time periods, *refer to Table 6*). Therefore, countries should consider adapting long-term strategies that will efficiently address the varying risks to avoid the complexities associated with changing strategies over a limited, short period of time (e.g., 10 years). Furthermore, the risks for WPV and cVDPV differ from iVDPV, therefore criteria for classifying WPV and cVDPV (Table X) are presented separately from iVDPV (Table Y). In addition, the recommended surveillance strategies for WPV and cVDPV may also differ from those used to detect iVDPV excretors therefore classification of "high risk" for iVDPV does not mean "high risk" for WPV and cVDPV. Note that aVDPVs are treated as cVDPVs.

Final determination and classification of country risk categorization will be done in collaboration with regional offices to ensure continuity of surveillance across areas. Although not indicated in the tables, countries will need to take into considerations the risks of their neighboring countries.

The country risk classifications will change over time so countries may move from high to low, or low to high risk. The Post-Certification Strategic (PCS) plan will be updated as certification approaches and periodically thereafter. This presents opportunities to update the criteria used to categorize risk as well as country risk classifications. Countries may also move risk categories in between updates to the PCS plan. For example, a low-risk country that experiences a polio outbreak will become a high-risk country, requiring changes to its long-term surveillance activities. This will also necessitate Regional Office collaboration on final determination of neighboring countries. Of note, a number of the criteria used for country risk classification are based on time since an important milestone. For example, the current classifications are based on time since certification. With subsequent updates of the PCS plan, other milestones will be used such as bOPV cessation.

Country risk classification for WPV and cVDPV

Each of the considerations listed in Table 9 poses a risk for the occurrence of polio. If a country meets the criteria of "high risk" for any of the listed considerations, it is a "high risk" country. Likewise, if a country meets the criteria of "medium risk" for any of the listed considerations, it is a "medium risk" country. However, final classification will be determined in collaboration with Regional Offices.

Table 9. Summary of country risks for WPV and cVDPV/aVDPV

Poliovirus Classification	Considerations	Country prioritization		
		High risk	**Medium risk**	**Low risk**
WPV	Containment breach	• Polio vaccine manufacturing facility located in a low-income country	• Polio vaccine manufacturing facility located in a middle-income country and most recent national IPVfinal^ coverage <90% OR • Laboratory PEF located in a low-income country	• Polio vaccine manufacturing facility located in a a. High income country b. Middle income country and most recent national IPVfinal^ coverage ≥90% OR • Laboratory PEF located in the country with strong or moderate health infrastructure •
cVDPV/aVDPV	Undetected cVDPV transmission	• Time since cVDPV last detected in the country was in the 5 years prior to certification	• Time since cVDPV last detected in the country was in the 6-8 years prior to certification	• Time since cVDPV last detected in the country was ≥9 years prior to certification
	Emergence of cVDPV1 or 3 /aVDPV1 or 3: bOPV use in RI	• Predominant use of bOPV or mixed bOPV/IPV in the 5 years prior to certification and OPV3 coverage <80%	• Predominant use of bOPV or mixed bOPV/IPV in the 5 years prior to certification and OPV3 coverage ≥80%	• Only IPV used in RI in the 5 years prior to certification
	Emergence of cVDPV2/aVDPV2: mOPV2 use for OBR	• Used mOPV2 in the 5 years prior to certification and IPVfinal^ coverage <90%	• Used mOPV2 in the 5 years prior to certification and IPVfinal^ coverage ≥90%	• Did not use any mOPV2 prior to certification
	Containment breach		• Laboratory PEF located in a low-income country	• Laboratory PEF located in a high or middle-income country

*Country income according to World Bank classification of high-, middle- and low-income countries.
^IPVfinal = last recommended IPV dose as part of the EPI routine immunization schedule. As of 2017 this is one dose but may include a second dose in the future.

Country risk classification for iVDPV

The risk of a country experiencing an iVDPV outbreak is dependent on a number of factors including the prevalence of PID, country income (used as a proxy for health and sanitation infrastructure), exposure to OPV, and population immunity to polio. These factors must be considered together to assess country risk and is reflected in Table 10 with the use of "AND". Once again, final classification will be determined in collaboration with Regional Offices.

Note that PID surveillance to detect iVDPV excretors is still under development and the criteria for country risk classification may change.

Table 10. Summary of country classification for iVDPVs

Poliovirus classification	Considerations	Country prioritization	
		High risk	**Not a high risk**
iVDPV	1. Primary immunodeficiency (PID) prevalence AND 2. Country income AND 3. OPV exposure AND 4. Population immunity to polio	1. Prevalence of PID >X% AND 2. Middle or high-income country AND 3. Any OPV use in the 5 years prior to certification AND 4. OPV3 coverage <80%	1. Prevalence of PID ≤X% AND 2. Middle or high-income country AND 3. Any OPV use in the 5 years prior to certification AND 4. OPV3 coverage ≥80% OR 1. Prevalence of PID ≤X% AND 2. Low income country AND 3. Any OPV use in the 5 years prior to certification OR 1. OPV not used in the 5 years prior to certification

*Country income according to World Bank classification of high-, middle- and low-income countries.

Annex D: Other Relevant Surveillance Systems

Most countries have established comprehensive routine public health surveillance to measure disease burden, including monitoring morbidity and mortality trends, primarily through regular passive reporting from health facilities. Such indicator-based surveillance (IBS) is often a combination of clinical/syndromic or laboratory- based diagnosis. (AFP surveillance is an example.) Although standardized IBS approaches for both global[60] and regional levels (e.g., Integrated Disease Surveillance and Response in Africa[61]) have been proposed, case definitions and implementation can vary widely. Reporting is usually aggregated at local levels and forwarded to national levels weekly or monthly. Routine surveillance systems also usually mandate immediate notification of certain diseases or syndromes (including AFP), however these systems are usually deemed inadequate for use in an eradication program due to the high variability in completeness, timeliness, validity, and reliability of data. Many countries have supplemented the passive health information systems with parallel active AFP surveillance networks through assistance from GPEI (see above).

There are several other 'vertical' surveillance systems that have either direct or indirect relevance to PV.

Vaccine-Preventable Diseases (VPDs). In addition to AFP surveillance for polio, there are other global/national systems to track VPDs which are outbreak-prone and/or have specific control/elimination targets (e.g., measles/rubella, Japanese encephalitis, maternal-neonatal tetanus, yellow fever). These other systems also utilize IBS with a combination of clinical and syndromic or laboratory-based diagnoses; however, none have yet fully implemented the same extensive active, case-based surveillance system central to AFP surveillance. Measles/rubella surveillance is moving towards a case-based approach for all countries that relies on a comprehensive global diagnostic laboratory network similar to the GPLN. However, several areas that still have a high incidence of measles (e.g., India, parts of Africa, etc.) continue to rely on clinical diagnosis or epidemiologically linked cases to identify clusters of measles/rubella cases. Other common VPDs such as invasive bacterial diseases (e.g., meningitis), rotavirus, and influenza, depend heavily upon sentinel site surveillance to track disease trends or monitor program impact. Polio eradication efforts are unique among programs aimed at VPDs in their extensive use of ES.

High-threat pathogens. Surveillance for "high-threat pathogens" (i.e., highly infectious agents that produce severe disease such as viral hemorrhagic fevers, meningitis, cholera, Zika, etc.) utilizes a mix of surveillance strategies based on risk level in order to achieve program objectives to control or eliminate epidemics. Case-based surveillance reporting from health facilities is generally used in high-risk countries, a sentinel surveillance approach in moderate-risk countries, and a routine population-based surveillance system with aggregate reporting in low risks countries. Surveillance is usually syndromic with highly variable capacities for laboratory diagnosis. The primary objective of surveillance for relatively rare diseases with high mortality and/or high potential risk for outbreaks (e.g., Ebola) is to provide immediate detection and reporting of even suspected cases. However, even for these diseases,

[60] WHO Recommended Surveillance Standard, 2nd ed. Geneva, WHO; 1999.
[61] Technical Guidelines for Integrated Disease Surveillance response in the African Region, 2nd ed. Brazzaville, Atlanta: Who Regional Office for Africa, CDC; (2010)

the focus is on passive reporting from district or tertiary health care facilities except during outbreaks when more active approaches are implemented.

Enteroviruses. Enterovirus surveillance has been used as a supplementary or alternative surveillance system to AFP, especially in countries which either never developed more targeted PV surveillance or found it difficult to sustain the expected AFP quality indicators over time. Enterovirus surveillance is commonly utilized in Europe to detect outbreaks, establish disease burden, or conduct virological research for a wide variety of syndromes, including paralysis, febrile-rash, respiratory infections, aseptic meningitis, gastroenteritis, etc.[62] A similar and slightly more focused system targeting identification of clusters of acute flaccid myelitis is being used in the United States. However, enterovirus surveillance has very low specificity for detecting polio transmission. Any poliovirus detected through this system must be referred to a GPLN laboratory for confirmation, intratypic differentiation, and sequencing if necessary.

Community-based surveillance (CBS) can be a useful source of Event Based Surveillance (EBS) to track disease trends or identify unusual health events at the local level; however, the scope, reliability, and sustainability of these systems vary widely. In Indonesia, for example, CBS has been used for many years to regularly provide supplemental inputs to the national health information system. A less structured approach relies on "community informants" in each village to periodically text health events to district health workers, but this system has often been difficult to sustain. A more time-limited form of CBS has been used in several countries that are in the midst of disease outbreaks, recovering from recent natural disasters, or are undergoing complex disruptions of their security. In several recent disasters, the International Federation of the Red Cross (IFRC) has established an organized system of trained local health "volunteers" who are usually paid a small stipend to monitor trends and detect clusters of various syndromes, including paralysis, in their districts through regular interviews of village leaders.[63] While inputs from CBS may not be very specific, they can enhance the sensitivity of communicable disease surveillance and provide more community ownership of their health system.

[62] CDC and WHO Regional Office for Europe. Enterovirus surveillance guidelines: guidelines for enterovirus surveillance in support of the Polio Eradication Initiative. Copenhagen. 2015.
[63] IFRC. Community based surveillance: guiding principles. Geneva, March 2017.

List of Tables and Figures

Tables

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