

Dear SAGE members,

Below, please find the final version of the Polio Post-certification Strategy (PCS) as approved by the POB on 29 January 2018 and incorporating inputs from the SAGE Polio WG at their meeting on 21 February 2018. We would welcome your comments on the PCS either via email (general comments or notations on this document) prior the SAGE meeting or during Michel's presentation to you on 17 April.

This document includes annotated comments and/or highlights of the significant changes incorporated into the final version compared to v3.0 which was previously sent for your review on 17 November 2017 by Michel. (There have been some additional minor edits for clarity or brevity which have not been highlighted.)

Note that the core goals, strategies, and activities have not changed. Briefly, the final version contains the following primary additions/alterations from the prior version:

Content:

- Addition of a *Forward*
- Additional changes in the *Executive Summary* and *Introduction* to highlight the role of future owners and clarify the scope of the PCS.
- Some further details added in Goal 3 on AFP surveillance and PID surveillance as requested by the SAGE Polio WG

Format:

- Moved all tables from Goal 3 to a separate annex. Note that the final version will have further graphic edits and some of the pictures may be changed.

Following your approval, the PCS will be presented to the WHA.

Most sincerely,

PCS Development Team

Polio Post-Certification Strategy

A risk mitigation strategy
for a polio-free world

Commented [BB1]: Title changed from "strategic plan" to "strategy" to highlight that this document focuses on providing technical/polio guidance and not implementation.

Commented [BB2]: SC has recommended to remove prominent GPEI branding and partner logos. GPEI authorship is acknowledged on next page.



Published by the World Health Organization (WHO) on behalf of the Global Polio Eradication Initiative (GPEI). This report reflects contributions from an extensive consultation process led by the agency partners of the GPEI: Rotary International, WHO, the U.S. Centers for Disease Control and Prevention (CDC), the United Nations International Children's Emergency Fund (UNICEF), and the Bill & Melinda Gates Foundation.

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Polio Post-Certification Strategy

A risk mitigation strategy
for a polio-free world

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Foreword

Commented [BB3]: Added Foreword to provide background and purpose of the PCS as well as issue a call to action to sustain a polio-free world. Signatures pending.

For

The Post-Certification Strategy (PCS) was initiated by the Global Polio Eradication Initiative (GPEI) in early 2017 to define technical standards for the functions required to sustain a polio-free world. It is a risk mitigation strategy anchored to three goals for the post-certification period: containing polioviruses, protecting populations, and detecting and responding to a polio event.

While the PCS will not begin until the global interruption of wild poliovirus (WPV) is certified, the strategy should be reviewed prior to certification, as decisions and criteria for certification and withdrawal of the bivalent oral poliovirus vaccine (bOPV) will be further clarified by the Strategic Advisory Group of Experts on Immunization (SAGE) and the Global Commission for the Certification of Poliomyelitis Eradication (GCC). The PCS will be an evolving strategy, requiring careful evaluation of ongoing risks, and deliberate periods of revision and adjustment should be determined over the course of the 10-year time frame of the strategy.

The process for developing the strategy was conducted in a broad consultative manner with various polio stakeholders, including: technical experts, regional and country focal points, funders, advisors, and modelers, among others. (See **Annex A** for a full stakeholder list.) The strength of the strategy is largely attributed to the insights and questions voiced through workshops, meetings, emails, surveys, and many direct edits to the strategy's formulation. These consultations brought into focus the many implementation challenges in making the shift required from the current GPEI partnership model to a post-GPEI period model that is yet to be determined.

It should be noted, the PCS is a strategy, not an implementation plan—and consequently, it does not address governance, management, coordination, and cost elements. It is important for the stakeholders that will continue to implement polio functions post-certification to start defining these implementation elements to ensure a smooth transition from the GPEI partnership.

The PCS is thus shared as a call for leadership and action in navigating a polio-free world which generations have worked hard to secure. Many stakeholders will be involved. Primary ownership will stay with country governments and will require continued support from some of the current polio partners and increasing support from immunization groups. Together with new partners and groups, the “future owners” of these functions will include national governments (Ministries of Health and Finance), nongovernmental organizations, technical advisory groups (GCC, SAGE), and global immunization and other public health development partnerships (Gavi, Measles and Rubella Initiative), as well as donors and the current GPEI implementing partners. With the dissolution of the GPEI partnership, new global governance and coordinating mechanisms will need to be put in place with even greater global accountability to fall to WHO and the Member States.

In January 2018, the WHO Executive Board “*decided to take note of the draft Global Polio Eradication Initiative post-certification strategy, urging all Member States to take appropriate measures to ensure that their short- and long-term health sector plans reflect the need to sustain the polio-essential functions necessary to ensure a polio-free world.*” The Polio Oversight Board endorsed the strategy and it will be presented at the World Health Assembly in May 2018.

POLIO POST-CERTIFICATION STRATEGY
Draft 4.5

Over the past three decades in the pursuit of polio eradication, 20 million volunteers have vaccinated more than 2.5 billion children worldwide against polio—saving 16 million people from paralysis. We need to ensure that these efforts do not go to waste by sustaining a polio-free world through the successful implementation of the functions and activities outlined in this strategy. Eradication will truly be a collective, global achievement—and preserving it will require all countries to take action to stay vigilant and engaged.

DRAFT

Acronyms

A		MoH Ministry of Health	
AFP	Acute flaccid paralysis	mOPV	Monovalent oral poliovirus vaccine
aVDPV	Ambiguous vaccine-derived poliovirus	N	
B		NAC	National authority for containment
bOPV	Bivalent oral poliovirus vaccine	NCC	National Certification Commission
BMGF	Bill and Melinda Gates Foundation	nOPV	New oral poliovirus vaccine
C		NPAFP	Non-polio acute flaccid paralysis
CAG	Containment Advisory Group	NPCC	National polio containment coordinator
CBS	Community-based surveillance	O	
CDC	U.S. Centers for Disease Control and Prevention	OPV	Oral poliovirus vaccine
cVPDV	Circulating vaccine-derived poliovirus	P	
CWG	Containment Working Group	PAVDs	Polio antiviral drugs
E		PCS	Post-Certification Strategy
EBS	Event-based surveillance	PEESP	Polio Eradication and Endgame Strategic Plan
EIA	Enzyme immunoassay	PEF	Poliovirus-essential facility
EOC	Emergency Operations Center	PHEIC	Public Health Emergency of International Concern
EPI	Expanded Programme on Immunization	PID	Primary immunodeficiency disease
ES	Environmental surveillance	POB	Polio Oversight Board
EVS	Enterovirus surveillance	POC	Point of care
EWAR	Early warning and response	POLIS	Polio information system
F		POSE	Polio outbreak simulation exercise
fIPV	Fractional inactivated poliovirus vaccine	PRC	Polio Research Committee
G		Q	
GAPIII	Global Action Plan to minimize poliovirus facility-associated risk (3rd edition)	QA/QC	Quality assurance/quality control
GCC	Global Commission for the Certification of Poliomyelitis Eradication	R	
GHSA	Global Health Security Agenda	RCC	Regional Certification Commission
GIS	Geographic information system	RI	Routine immunization
GOARN	Global Outbreak Alert and Response Network	S	
GPEI	Global Polio Eradication Initiative	SAGE	Strategic Advisory Group of Experts on Immunization
GPLN	Global Polio Laboratory Network	SIA	Supplementary immunization activity
GPSAP	Global Polio Surveillance Action Plan	sIPV	Sabin strain inactivated poliovirus vaccine
GVAP	Global Vaccine Action Plan	T	
I		TA	Technical assistance
IBS	Indicator-based surveillance	TAG	Technical advisory group
ID	Intradermal	tOPV	Trivalent oral poliovirus vaccine
IDSR	Integrated disease surveillance and response	U	
IHR	International Health Regulations	UNICEF	United Nations International Children's Emergency Fund
IM	Intramuscular	V	
IMS	Incident Management System	VAPP	Vaccine-associated paralytic poliomyelitis
IPV	Inactivated poliovirus vaccine	VDPV	Vaccine-derived poliovirus
ITD	Intratyptic differentiation	VI	Virus isolation
iVDPV	Immunodeficiency-associated vaccine-derived poliovirus	VLPs	Virus-like particles
J		VPD	Vaccine-preventable disease
JEE	Joint External Evaluations	W	
M		WHO	World Health Organization
MAPs	Microarray patches	WPV	Wild poliovirus



The Global Polio Eradication Initiative has started to define the technical standards required to sustain a polio-free world—the core of which is found in this *Post-Certification Strategy*.

Executive Summary

The world is making tremendous progress toward eradicating the second human disease in history. The fewest number of wild poliovirus (WPV) cases have been recorded in 2017, and only three countries are defined as endemic where the virus may continue to circulate in these populations. Country Ministries of Health (MoH) and government leadership are critical to interruption of WPV, the goal of eradication.

Founded in response to the 1988 resolution of the World Health Assembly that declared a commitment to the eradication of polio, the Global Polio Eradication Initiative (GPEI) coordinates global, regional, and country efforts through technical assistance, resource mobilization, vaccine procurement, and other key activities. The partnership is spearheaded by the World Health Organization (WHO), Rotary International, the U.S. Centers for Disease Control and Prevention (CDC), the United Nations International Children's Emergency Fund (UNICEF), and the Bill and Melinda Gates Foundation (BMGF), working closely with countries, donors, foundations, and nongovernmental organizations. The GPEI will accomplish their goal when the Global Commission for the Certification of Poliomyelitis Eradication (GCC) certifies all WPV types (1, 2 and 3) have been eradicated. The *Polio Eradication & Endgame Strategic Plan 2013-2018* (PEESP) defines the objectives and activities required to achieve eradication—and, as this milestone nears, the GPEI has started to identify what will be needed to sustain this progress on a global scale.

Protecting a Polio-Free World

In 1995, the Health Assembly charged the GCC with the following tasks: (1) defining the parameters and processes by which polio eradication will be certified, guiding regions and countries in establishing their data collection processes; (2) receiving and reviewing the final reports of Regional Certification Commissions (RCCs) of polio eradication; and (3) issuing, if and when appropriate, a final report to the Director-General of WHO, certifying that global polio eradication has been achieved. As stated in a January 2004 WHO bulletin, the main criteria set by the GCC for global polio-free certification was to show the absence of WPV from cases of acute flaccid paralysis (AFP, suspect for polio), healthy individuals, or environmental samples in all WHO regions for a period of at least three years in the presence of high-quality, certification-standard surveillance.¹ A separate process will be undertaken by the GCC and the Strategic Advisory Group of Experts on Immunization (SAGE) to determine the criteria and method to validate the absence of vaccine-derived poliovirus (VDPV) after global withdrawal of the bivalent oral poliovirus vaccine (bOPV).

As the GPEI partnership works towards eradication, it has also engaged a broad set of stakeholders from polio and immunization teams, partners, regional colleagues, donors, and other health initiatives to gather input and define the technical standards to sustain a polio-free world—

¹ For the definition of eradication as the interruption of WPV transmission, see World Health Organization. Smith J, Leke R, Adams A, and Tangermann RH. Certification of polio eradication: process and lessons learned. *Bulletin of the World Health Organization*. January 2004;82:24-30.

the core of which is found in this *Post-Certification Strategy* (PCS). (See **Annex A** for a detailed engagement list.)

The focus of this document is to provide the future guardians of a polio-free world with a starting point by documenting the functions and activities required to sustain eradication until future risks are deemed no longer relevant. The threats of re-emergence of the virus after global certification addressed in this strategy fall into three categories: (1) continued use of oral poliovirus vaccine (OPV), (2) unsafe handling of any polioviruses, and (3) undetected transmission. The PCS outlines how to address, reduce, and (where possible) eliminate these risks.

The risks to sustaining WPV eradication are higher in some of the world's poorest countries. Polio transition, particularly for countries with weak health systems, could impact routine immunization and general disease surveillance quality, which may be put at risk by the withdrawal of polio resources. Managing the process will require leadership from groups both inside and outside of the GPEI partnership.

Commented [BB4]: Added para to highlight differential impact of transition

As per the decision taken by the Polio Oversight Board (POB) in October 2017, the GPEI partnership will support post-GPEI programmes with implementation planning.² Anticipating the transfer of skills, knowledge, and resources of a programme that is over 30 years old, it will be important to start implementation planning now as the GPEI partnership will dissolve at certification. Following the review and endorsement of the PCS by the POB, the GPEI and prospective future owners of the PCS will come together to ensure the success of the strategy and to safeguard this extraordinary achievement. Throughout this document, mention of the future owners of the PCS will refer to a wide range of stakeholders who share an interest in sustaining and building upon the success of global WPV eradication. These groups include: national governments (Ministries of Health and Finance), nongovernmental organizations, technical advisory groups (GCC, SAGE), and global immunization and other public health development partnerships (Gavi, Measles and Rubella Initiative), as well as donors and the current GPEI implementing partners. Polio functions, as coordinated by the future owners, will continue to be implemented under the framework of the International Health Regulations (IHR), the Global Health Security Agenda (GHSa), and the Global Vaccine Action Plan (GVAP).

Commented [BB5]: Added para on future owners

Over the course of the polio eradication effort, the resources supporting polio activities at the global, regional, and country level have also supported broader health initiatives such as measles accelerated control or elimination activities, surveillance for vaccine-preventable diseases such as yellow fever, outbreak response ranging from Ebola to the plague, and delivery of anti-malarial bednets, Vitamin A supplements, and humanitarian aid.³ A significant portion of polio staff time is spent supporting activities related to broader immunization and healthcare goals.⁴ Current polio resources, funding, and systems will need to be transitioned to either (1) groups that will support maintaining a polio-free world, or (2) groups that have relied on polio resources to accomplish their health goals.

² See minutes from the October 2017 meeting of the Polio Oversight Board, available at:

<http://polioeradication.org/wp-content/uploads/2016/07/pob-meeting-minutes-02102017.pdf>.

³ Global Polio Eradication Initiative, World Health Organization. *Polio Eradication & Endgame Strategy* 2013-2018. February 2013.9. http://polioeradication.org/wp-content/uploads/2016/07/PEESP_EN_A4.pdf.

⁴ For examples of activities and time spent toward broader immunization and healthcare goals, see Van den Ent MM, Swift RD, Anaokar S, Hegg LA, Eggers R, Cochi SL. Contribution of Global Polio Eradication Initiative-funded personnel to the strengthening of routine immunization programs in the 10 focus countries of the Polio Eradication and Endgame Strategic Plan. *JID* 2017;216(S1):S244–9. <https://doi.org/10.1093/infdis/jiw567>.

The PCS: A Risk Mitigation Strategy

Commented [BB6]: Added summary of goals and activities

The following three goals have been identified to mitigate the current and future risks to maintain a polio-free world: (1) contain polioviruses, (2) protect populations, and (3) detect and respond to a polio event.

Goal One: Contain Polioviruses	
Objective 1.1 To achieve and sustain containment of polioviruses in laboratories, vaccine manufacturing and other facilities	Activity 1.1.1 Support reduction of the global number of facilities storing and handling poliovirus Activity 1.1.2 Implement and monitor long-term containment of poliovirus in facilities with appropriate safeguards
Goal Two: Protect Populations	
Objective 2.1 To protect populations from VDPV and VAPP 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 all use
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 availability of affordable IPV and its effective, efficient delivery to facilitate high immunization coverage
Goal Three: Detect and Respond to a Polio Event	
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
Objective 3.2 To develop and maintain adequate global and regional capacity and resources to support national efforts to rapidly and effectively contain any detected poliovirus and stop any poliovirus transmission	Activity 3.2.1 Identify future outbreak risks, develop and implement preparedness plans, and prepare response strategies Activity 3.2.2 Sustain trained human capacity and create, maintain, and manage adequate stockpiles of polio vaccine and antivirals to appropriately respond

bOPV= bivalent oral poliovirus vaccine; IPV= inactivated poliovirus vaccine; SIAs= supplementary immunization activities; VAPP= vaccine-associated paralytic poliomyelitis; VDPV= vaccine-derived poliovirus

Cross-cutting research on new diagnostic tests, oral poliovirus vaccine (OPV) and inactivated poliovirus vaccine (IPV) formulations, and antivirals, as well as surveillance and vaccine delivery enhancements, will contribute to each of the post-certification goals and inform the development of relevant public health policies.

Commented [BB7]: Added para to note contribution of research

This document does not address governance, management, financial estimates, or monitoring elements which will be critical to implementation, as it is the future owners who will determine the organization and management of the PCS goals. Implementation planning requires: (1) the planning efforts of country Ministries of Health and Finance who will need to financially and programmatically adhere to these three goals; (2) the internal planning efforts of the organizations that will continue to support these functions and activities (GPEI and non-GPEI organizations); and (3) planning by new partners and health initiatives beyond the GPEI to fund integration of polio activities and strengthen immunization and surveillance systems.

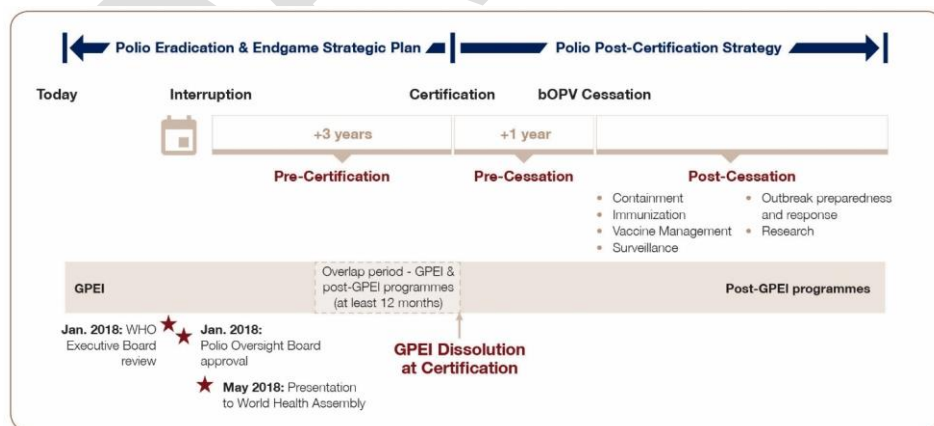
Commented [BB8]: Added para to clarify the scope of the PCS

It is critical to identify the future owners and initiate the planning process by the 2018 World Health Assembly so both knowledge transfer and an assessment can be made regarding the capacity, capability, and change effort required for the future owners to be successful.

The transition or hand-off of the functions described in these three goals must begin well before the dissolution of the GPEI partnership through an overlap period of coordination.⁵ (See **Figure 1**.) Since funding will need to be raised pre-certification, the GPEI will develop cost estimates and an investment case for the funds required to ensure the successful global withdrawal of bOPV. Additionally, a separate financial model with high-level costs for the longer term period after bOPV withdrawal—with assumptions for key decisions that are unknown today—will be developed with the future owners of the PCS. Lastly, national transition plans will also include costs as estimated for activities performed at the country level.

Commented [BB9]: Modified this para and Figure 1 below to emphasize the linkages and transition from the PEESP to the PCS.

Figure 1: Timeline for the pre- and post-certification periods



⁵ For more on the decision to dissolve the partnership at certification, see minutes from the April 2017 meeting of the Polio Oversight Board. http://polioeradication.org/wp-content/uploads/2017/06/POB_Minutes_Mtg20170422.pdf.

On the Verge of Success

The world will need to work together to protect the success of eradication by planning well in advance for the transition of moving from the eradication effort of the PEESP to the sustained effort of the PCS. Key factors to effectively implement this PCS will require even greater ownership and self-funding from country governments, continued donor support for fragile countries, and a shift in technical assistance from polio-dedicated groups to broader immunization, vaccine-preventable disease surveillance, and health emergencies groups within partner organizations.

DRAFT

The *Post-Certification Strategy* presents global and regional requirements that country programmes can expect to address after the closure of the Global Polio Eradication Initiative.



Introduction

Purpose

While the global eradication of wild poliovirus (WPV) merits recognition for the scale and scope of work required, the activities and functions essential for “getting the job done” must now be reimagined for the post-certification era to safeguard against the re-emergence of poliovirus.⁶

The Post-Certification Strategy (PCS) provides recommendations for mainstreaming the functions required for maintaining a polio-free world after global WPV certification. It covers the period starting from certification and extending for 10 years.

As the interruption of WPV worldwide will hold significance for global public health, it will be important to situate the PCS within broader public health regulations and frameworks, specifically the International Health Regulations (IHR), the Global Health Security Agenda (GHSa), and the Global Vaccine Action Plan (GVAP).⁷

The IHR provides the foundation 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, report, assess, and respond to public health events. In addition to this focus on protection, detection, and response, the IHR calls for multilateral, multisectoral, and international coordination to strengthen country, regional, and global capacity for public health concerns and

PCS Engagement & Audience

The PCS was developed through an iterative consultative process with experts within and beyond the GPEI. This extensive engagement aimed to provide opportunities for stakeholders at the global, regional, and national levels to offer input on the approach and elements of the strategy.

The PCS is intended for use by GPEI technical advisory groups, private and public-sector partners, and the future managers of the PCS more broadly, including some current agencies and donors as well as those outside of the GPEI.

The PCS also provides broad strategic recommendations to national level stakeholders, such as Ministries of Health (MoHs), which will be expected to sustain a polio-free world.

See **Annex A** – PCS Engagement List

⁶ While there is an epidemiological difference between “emergence” (in the case of a new VDPV), “re-emergence” (from previously identified cVDPVs), and “re-introduction” (of WPV, VDPV, or Sabin from release), for the purposes of this strategy and a more general readership beyond the GPEI, re-emergence is used to signal the return of polioviruses (WPV, VDPV, and Sabin) into a polio-free world after certification.

⁷ World Health Organization. International Health Regulations, third edition. 2016. <http://www.who.int/ihr/publications/9789241580496/en/>.

Global Health Security Agenda - <https://www.ghsagenda.org/about>.

Global Vaccine Action Plan 2011-2020. May 2012. http://www.who.int/immunization/global_vaccine_action_plan/.

health security risks. The GHSA, as an initiative for implementing the IHR, supports global health security through reviews aimed at identifying gaps and strengths in country capacity. GVAP offers a framework for global equity by focusing on risks that impede universal access to public health programmes, as it endeavors to strengthen routine immunization programmes to meet vaccination coverage targets, accelerate control of vaccine-preventable diseases (VPDs), and introduce new and improved vaccines. For the successful implementation of the PCS, it will be important to integrate post-certification goals within the “GVAP 2.0” under development to cover the period 2021-2030.

These regulations and frameworks are critical to the post-certification era as they provide global mechanisms and structures to ensure a polio-free world. The PCS has drawn upon them in outlining the activities, initiatives, research, and developments that will need to be in place by certification, when the PCS will begin.

The PCS contributes to bridging from the eradication effort to a polio-free world. Once this milestone is achieved, ownership and accountability will need to transfer from the global GPEI partnership with its centralized controls to existing IHR and Health Assembly mechanisms and national governments with decentralized controls. The future owners, many of whom are already involved with the polio programme, will include national governments (Ministries of Health and Finance), nongovernmental organizations, technical advisory groups (GCC, SAGE), global immunization and other public health development partnerships (Gavi, Measles and Rubella Initiative), donors, and the current GPEI implementing partners.

Commented [BB10]: Added para on future owners

Scope

The PCS is one part of a broader GPEI transition planning effort that addresses the changes associated with global certification of WPV eradication and the closure of the GPEI. A Transition Planning Framework has been developed with distinct goals (see *right panel*).⁸

The PCS outlines functions required to sustain polio eradication.

The GPEI has identified functions that must continue in the post-certification period to sustain eradication. These ongoing functions will include containment, immunization with appropriate polio vaccines, poliovirus surveillance, and outbreak response. Other activities that GPEI staff have performed to help strengthen and support broader health systems will be addressed through transition planning at the country and agency level.

GPEI Transition Planning

Transition planning has three distinct goals:

- Maintain and mainstream functions required to sustain eradication after certification, to protect a polio-free world
- Where feasible, desirable and appropriate, transition the capacities, processes, and assets that the GPEI has created to support other health priorities
- Capture and disseminate the lessons of polio eradication

The PCS supports the first goal of transition planning by providing global standards and guidance for polio-specific needs. Transition planning is underway at the agency level for each of the GPEI partners and at the country level, with special focus on 16 priority countries that represent the largest footprint for GPEI support.

⁸ Global Polio Eradication Initiative. *Polio Transition Planning Framework*. March 2017.

The PCS is a global strategy.

The PCS presents strategies, activities, functions, and mechanisms required to maintain a polio-free world. Its focus is on global and regional requirements that country programmes can expect to address after the closure of the GPEI. Because not all countries share the same risks, the PCS does not provide detailed guidance for how these functions should be incorporated within national health systems.

Country transition plans should propose how to mainstream implementation of the required functions both by building long-term capacity and by assuming a progressively greater percentage of costs within their national health budget. They should ensure that the national management of polio functions within integrated surveillance, immunization systems, and outbreak response systems is strong enough to adopt and implement the high-level guidance provided in the PCS.

The GPEI recognizes that a number of countries—particularly those with poor infrastructure and fragile health systems or those undergoing sustained emergencies and conflict—may not have the capacity to fully plan for the mainstreaming of polio functions in the absence of donor and partner agency support. For these countries, the GPEI has provided dedicated support to help build their transition plans.

PCS recommendations are provided independent of future ownership.

The intent of the PCS is to provide the information needed for future owners to step forward and take ownership of the functions required to sustain WPV eradication and maintain a polio-free world. Once the future owners are identified, a coordinated effort to implement the strategy is critical. The planning process should start well before certification, and the transition of ownership responsibly shifted from the GPEI partnership to the future owners.

Assumptions

To define the activities, operations, and structures needed in the post-certification period, the PCS is built upon certain assumptions.

1. Global eradication of all WPVs will be certified and all regions will have met the expected certification criteria for surveillance and immunity.
2. The likelihood of poliovirus re-emergence will decrease with time, but the severity of the consequences will increase with time. The re-emergence of sources of types 1 or 3 may be more prevalent than type 2 due to more recent transmission and possible inadequate use of bOPV at the time of certification.⁹ For the purposes of future risk management, both WPVs and vaccine-derived polioviruses (VDPVs) are treated as an equal risk for community transmission.
3. Under the IHR, detection of any poliovirus (WPV, VDPV, or Sabin virus more than 4 months after last use of monovalent OPV [mOPV] or post-bOPV cessation) must be notified to WHO. Depending on the risk of international spread and other factors, the detection could constitute

⁹ WPV2 eradication has been certified since September 2015. Use of mOPV2 is expected to have stopped well before certification, unless current cVDPV2 outbreaks have spread further or have not been stopped at that time. Chronic excretion of an iVDPV2 is possible (though a low risk) with countries that used mOPV2 <5 years prior to certification.

a Public Health Emergency of International Concern (PHEIC) requiring a prompt, globally coordinated response.

4. Implementation planning will begin well before certification to define the future governance, management, and coordinating structures and processes with clear ownership identified for the PCS functions.

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Risks

Global consensus on precise strategies, activities, and policies is needed to anticipate and respond to the possible re-emergence of poliovirus in the post-certification era. The PCS focuses on three risk categories: continued OPV use, unsafe handling, and undetected transmission.¹⁰

Risk Category #1: Continued OPV use

While OPV is an extremely safe and effective tool for producing mucosal and humoral immunity against the virus, continued OPV use creates a risk of vaccine-associated paralytic poliomyelitis (VAPP) or re-emergence of VDPVs—which will gradually decline with time after the last use of OPV.

- VDPVs: In populations with low immunization coverage, Sabin viruses from OPV may both revert to a neurovirulent form capable of causing paralysis (vaccine-derived poliovirus, or VDPV) and regain the capacity for sustained circulation (circulating VDPVs or cVDPVs). Additionally, immunodeficiency-associated VDPVs (iVDPVs) can result when individuals with primary immunodeficiency diseases (PID) exposed to OPV excrete the virus for prolonged periods. Lastly, isolated mutated vaccine viruses detected in humans or the environment with no evidence of circulation (ambiguous VDPVs or aVDPVs) may spontaneously die out or become cVDPVs.
- VAPP: After receiving OPV, an individual will usually shed Sabin vaccine viruses for a limited period of time. Very sporadically, the vaccine virus can cause VAPP either in a vaccine recipient or a close unvaccinated or nonimmune contact of the recipient.

Risk Category #2: Unsafe handling of any polioviruses

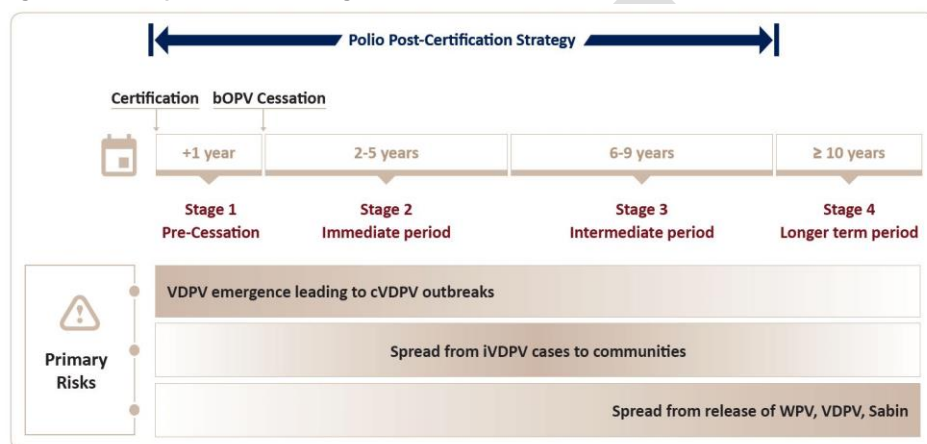
Unsafe storing and handling of materials that contain poliovirus may result in unintentional or accidental release of the virus into the environment from a vaccine manufacturer or a research or diagnostic laboratory working with poliovirus materials. There may also be facilities with forgotten stores of poliovirus materials, such as unaccounted-for vaccine vials or test specimens that also may result in the release of polioviruses. The intentional release of poliovirus is also possible, though the epidemiological impact and associated response strategies are the same as with accidental release. The potential consequences of accidental or intentional releases will increase with time as population immunity declines after bOPV withdrawal.

¹⁰ Aylward RB, Cochi SL. Framework for evaluating the risks of paralytic poliomyelitis after global interruption of wild poliovirus transmission. *Bulletin of the World Health Organization*. 2004;82(1):40-6.

Risk Category #3: Undetected transmission

There also remains a risk of undetected transmission since poliovirus can circulate in communities at low levels without resulting in cases of paralysis. With sensitive global surveillance at the time of certification, there will be high confidence that WPV transmission will have been interrupted. The risk of undetected or more likely delayed detection of a cVDPV transmission will be low but persists, depending on the time that has passed since cVDPV was last detected. Sustaining sensitive global surveillance for poliovirus will be required as long as there is risk of any poliovirus re-emergence.

Figure 2. Risk of poliovirus re-emergence over time



Assessing Risk over Time

The primary risk and source of re-emergence is expected to vary over time after bOPV cessation. While **Figure 2** (above) 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. The consequences for each risk also may vary considerably depending on when and where the re-emergence occurs. An analysis of the projected magnitude and frequency of each risk is presented in each goal and in **Annex B**.

Evolution of Risk across Post-Certification Stages

- Pre-cessation to immediate post-cessation period

Although still projected to be relatively rare occurrences, VDPVs will be the primary risk of a poliovirus re-emergence in the pre-cessation (0-1 year post-certification) and immediate post-cessation periods (2-5 years post-certification) due to the prior use of OPV. While the precise risk of a VDPV (either aVDPV or cVDPV) being detected and resulting in further community

transmission will depend on multiple local circumstances, the risk of a cVDPV 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 in areas of poor sanitation will steadily accelerate as population immunity declines due to waning mucosal immunity and the growing number of OPV-naïve birth cohorts.¹¹

- Intermediate post-cessation period

As the risk of cVDPV wanes, the primary risk for poliovirus re-emergence in the intermediate post-cessation period (6-9 years post-certification) will come from an iVDPV spreading within a community. No poliomyelitis outbreaks to date have been attributed to iVDPV; nevertheless, this is a possibility that needs to be considered. While spread from PID patients is a rare occurrence, the potential risk for iVDPV transmission in a community will rise as population mucosal immunity declines post bOPV cessation. The highest risk for this scenario is among underimmunized populations in a few middle-income countries with a history of OPV use and a relatively high prevalence of PID patients.

- Longer term post-cessation period

A release of any category of poliovirus (WPV, VDPV, or Sabin) from a laboratory, manufacturing or research facility is unlikely. However, such events have occurred, and the possibility of a new one will persist as long as facilities are storing and handling polioviruses.¹² Intentional or unintentional release becomes a primary risk in the longer term post-cessation when the risks of VDPV emergence have been reduced.

Securing the world from the re-emergence of the virus is dependent on recognizing and addressing these risks. In general, a country's risk profile and most likely source of poliovirus re-emergence will be determined by its prior history of OPV use and cVDPV outbreaks, health and sanitation infrastructure capacity, and immunization coverage. (See **Annex C** for more on country risk.)

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.

Goals

The mitigation strategies of the PCS address the recognized source of risk through three goals:

1. **Contain polioviruses.** The objective of goal one is to achieve and sustain restricted safe handling of polioviruses in laboratories, vaccine manufacturers, and other facilities (such as research institutions) to prevent their re-introduction in a polio-free world. The key areas of focus will be to reduce the number of facilities storing and handling poliovirus globally,

¹¹ 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. *BMC Infect Dis* 2015; 15:389. doi: 10.1186/s12879-015-1112-8.

¹² Duizer E, Ruijs WL, van der Weijden CP, Timen A. Response to a wild poliovirus type 2 (WPV2)-shedding event following accidental exposure to WPV2, the Netherlands, April 2017. *Eurosurveillance* 2017; 22(21).

and to implement and monitor long-term appropriate safeguards in those facilities that retain poliovirus.

2. **Protect populations.** The second goal is to protect populations from (1) vaccine-derived polioviruses (VDPV) and vaccine-associated paralytic poliomyelitis (VAPP) by preparing and coordinating the global withdrawal of bOPV, and (2) any poliovirus re-emergence by providing access to safe, effective vaccines.
3. **Detect and respond to a polio event.** The focus of the third goal is to promptly detect any poliovirus in a human or in the environment through a sensitive surveillance system and to maintain adequate capacity and resources to effectively contain or respond to a polio event.

Timeline and Strategic Transition

The technical standards and recommendations included in the PCS are offered as the last strategic phase of the eradication effort, and thus the PCS builds upon the PEESP. Many of the functions and activities identified in the PCS are already in place as part of the endgame strategy, and they will remain critical for the post-certification period.

The PCS will start at certification, three years after the global interruption of WPV transmission, and extend for 10 years after certification.¹³ Planning and implementation of the PCS, however, will need to start before certification to ensure the necessary resources are in place with the level of quality required to maintain a polio-free world.

Depending on the epidemiology of poliovirus transmission after 2017, the GPEI, donors, and country governments will identify the need for adjustments to the strategy and timeline. The PCS will require updates as risks to environmental, organizational, and programmatic factors change over time. While the PCS anticipates revisions—likely to include a year prior to certification, after bOPV cessation, and at the midterm of the PCS's 10-year duration—it is the future owners of the PCS who will re-evaluate the strategy, as and when appropriate.

Next Steps

This document is one step toward identifying future owners of the PCS after the closure of the GPEI. It is put forward as a call for leadership from groups within and beyond the GPEI partnership who are committed to preserving the gains of the polio eradication effort.

After extensive consultation with stakeholders from polio and immunization teams, donors, partners, regional colleagues, and other health initiatives, as well as the WHO Executive Board and the Polio Oversight Board (POB), the strategy will be presented to the World Health Assembly in May 2018.

Financial modeling has been underway to prepare high-level financial estimates for both the period immediately after certification until bOPV cessation and the longer period after cessation.

¹³ To illustrate the time to certification and the duration of the strategy: if WPV circulation is interrupted in 2018, global certification could be declared in 2021, and the Post-Certification Strategy would begin in 2021 and continue until 2030.

Commented [BB12]: Removed specific expected dates of eradication from main text and added illustrative example as a footnote

In 2018, these estimates will be used to produce an investment case for the funds required to ensure the successful global withdrawal of bOPV. Taken together with agency transition plans and country transition plans, these supports for the post-certification era will be shared as the GPEI, national governments, advisory groups, global partners, and donors work together to plan, coordinate, and eventually mainstream or integrate the functions outlined in this document for sustaining a polio-free world.

DRAFT



Achieving containment of all polioviruses and monitoring compliance of laboratories and biomedical facilities with all containment requirements will be critical functions post-eradication.

Contain Polioviruses

Main Objectives	Major Activities
Objective 1.1	Activity 1.1.1
To achieve and sustain containment of polioviruses in laboratories, vaccine manufacturing and other facilities	Support reduction of the global number of facilities storing and handling poliovirus
	Activity 1.1.2
	Implement and monitor long-term containment of poliovirus in facilities with appropriate safeguards

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Introduction

After the global interruption of WPV transmission and cessation of bOPV use, certain laboratories and manufacturing facilities will need to continue handling polioviruses for vaccine production, quality control, diagnostics, and research. Accidental or intentional release of poliovirus from facilities may re-establish poliovirus circulation in the population.

To minimize the risks posed by facilities handling poliovirus, containment was included as a goal for the endgame strategic plan. The global strategies and mechanisms to achieve effective poliovirus containment were outlined in the third edition of the Global Action Plan (GAP III) to minimize poliovirus facility-associated risk, endorsed by the World Health Assembly in May 2015.¹⁴

Achieving containment of all polioviruses (wild and Sabin) and monitoring compliance with containment requirements will be critical functions post-eradication.

Description of the Goal

Goal One aims to achieve and sustain effective poliovirus containment measures to mitigate the likelihood and consequences of re-introducing poliovirus from laboratories or vaccine manufacturing facilities into a polio-free world. The major principles of poliovirus containment are: (1) minimal number of facilities storing and handling poliovirus infectious and potentially infectious materials; (2) minimal risk of exposure for the worker or community as a result of operations; (3) minimal susceptibility of workers to poliovirus infection; and (4) minimal consequences of release in the community.

¹⁴ World Health Organization. GAP III: WHO global action plan to minimize poliovirus facility-associated risk. Geneva, Switzerland. http://polioeradication.org/wp-content/uploads/2016/12/GAPIII_2014.

Objective 1.1: Achieve and sustain containment

A. Risks

The likelihood of an accidental poliovirus release will depend on the number of facilities handling polioviruses and on the adherence to biorisk management standards applied during storage and manipulation of poliovirus-harboring materials. Two recent spills from vaccine production facilities have highlighted the possibility of this event.^{15,16} Deliberate release of wild, vaccine- or genetically-engineered polioviruses is also possible.^{17,18}

The potential for polioviruses released from facilities to reinitiate transmission in surrounding communities will depend on several factors.^{19,20} First, the category of poliovirus-containing material released, as WPV and VDPVs are considered to have higher infectivity and transmissibility than OPV/Sabin strains. Cell cultures or concentrates used for vaccine production or certain tests have >10 000-fold higher concentration than stools or respiratory samples. Second, population immunity to poliovirus will decline with time, especially in countries with low routine vaccination coverage. Although provision of IPV through routine immunization will protect against paralysis and transmission of re-introduced polioviruses through the oropharyngeal route, it will confer very limited protection against intestinal infection and transmission through the fecal-oral route. Because of the phased cessation of OPV, low population immunity levels will occur earlier for type 2 than for types 1 and 3. Third, population density and migration, sanitation infrastructure and climate, as well as local surveillance and response capabilities may enhance or minimize spread.

Considering these factors, modeling analysis found that a poliovirus release from vaccine production sites into countries with high transmission risk several years after bOPV cessation could result in uncontrollable transmission.²¹ Currently, most laboratories and vaccine production facilities are in Europe and North America, where community vaccination with IPV could prevent transmission following a poliovirus release; however,

The potential for polioviruses released from facilities to reinitiate transmission will depend on:

1. The category of poliovirus
2. Population immunity at the time of release
3. Factors such as population density and migration, sanitation infrastructure and climate, as well as surveillance and response capabilities

¹⁵ Duizer E, Ruijs WL, van der Weijden CP, Timen A. Response to a wild poliovirus type 2 (WPV2)-shedding event following accidental exposure to WPV2, the Netherlands, April 2017. *Eurosurveillance* 2017; 22(21).

¹⁶ Duizer E, Rutjes S, Husman AMR, Schijven J. Risk assessment, risk management and risk-based monitoring following a reported accidental release of poliovirus in Belgium, September to November 2014. *Eurosurveillance* 2016; 21(11): pii=30169.

¹⁷ Cello J, Paul AV, Wimmer E. Chemical synthesis of poliovirus cDNA: generation of infectious virus in the absence of natural template. *Science* 2002; 297(5583): 1016-8.

¹⁸ Aylward RB, Cochi SL. Framework for evaluating the risks of paralytic poliomyelitis after global interruption of wild poliovirus transmission. *Bull World Health Organ* 2004; 82(1): 40-6.

¹⁹ 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(6): 1449-69.

²⁰ Fine PE, Ritchie S, Fine PEM, Ritchie S. Perspective: determinants of the severity of poliovirus outbreaks in the post eradication era. *Risk Anal* 2006; 26(6): 1533-40.

²¹ 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: 389.

Sabin-IPV production may expand to middle- or low-income countries that are more likely to have conditions that facilitate community spread.

B. Context

GAPIII: Minimizing the risk of release from facilities

The risk of accidental or intentional release of poliovirus only could be eliminated if all polioviruses were destroyed and never re-synthesized. Unfortunately, this is not achievable because polioviruses are still necessary for vaccine production and other functions. However, effective containment can decrease the risk to acceptable levels. GAPIII proposes two major strategies to achieve effective containment: 1) reduce the number of facilities that store or manipulate poliovirus, and 2) implement stringent containment safeguards in facilities that continue to handle poliovirus, as well as in their hosting countries.

To reduce the number of facilities harboring poliovirus, all countries need to conduct surveys and inventories of all laboratories and biomedical facilities, public and private, which may be storing polioviruses. Those facilities for which storing and handling poliovirus are not critical will need to destroy (or transfer) any infectious materials. Potentially infectious materials such as clinical specimens can be destroyed, transferred, inactivated, or handled under certain restrictions, depending on their likelihood of harboring polioviruses and on the consequences of their unsafe storage or handling.²² Laboratories will also have to implement safe and secure working practices for handling new specimens potentially harboring poliovirus (i.e., from areas with a new outbreak), and destroy, transfer, or contain those specimens if presence of the virus is confirmed.

GAPIII Strategies for Containment

1. Reduce the number of facilities that store or manipulate poliovirus
2. Implement stringent containment safeguards in facilities that continue to handle poliovirus

Facilities that need to store and handle polioviruses to perform critical functions (poliovirus-essential facilities, or PEFs), and their host countries, should implement and comply with several containment safeguards. Safeguards will be more stringent for WPV/VPV than for OPV/Sabin poliovirus.

- **Primary safeguards** reduce the risk of accidental or intentional release of poliovirus from a facility. Key elements include modifications in facility infrastructure and management; use of biosafety and biosecurity procedures during manipulation, storage, and transport of potentially contaminated material; immunization of personnel; substitution of WPV with Sabin strains or further attenuated strains where possible; and contingency plans to respond to a poliovirus release or exposure.
- **Secondary safeguards** define vaccine-induced immunity requirements in the community to minimize the consequences of a poliovirus release.

²² World Health Organization. *Guidance for non-poliovirus facilities to minimize risk of sample collections potentially infectious for polioviruses. (In preparation).*

- **Tertiary safeguards**, required only for facilities handling and storing WPV/VPV, minimize the consequences of releases by locating facilities in areas with sewage infrastructure that reduces poliovirus transmission potential.

Current mechanisms to monitor containment activities

Several mechanisms have been created to provide oversight of the implementation of containment measures at the national and global level (see **Figure 3**).²³

To monitor progress in the global reduction of facilities with poliovirus, national polio containment coordinators (NPCCs) and National Certification Commissions (NCCs) prepare annual reports for the Regional Certification Commissions (RCCs) outlining how many facilities hold poliovirus materials and how many facilities plan to become PEFs, as well as progress in removing poliovirus materials from facilities not designated as PEFs.

Figure 3. Current oversight structure of containment activities



Facilities selected by national authorities to retain poliovirus and become PEFs are responsible for implementing primary safeguards. Countries hosting PEFs need to designate a national authority for containment (NAC) to certify that the PEFs and the country meet primary, secondary, and tertiary safeguards. The NAC will share the appropriate documentation with WHO and the Containment Working Group of the Global Certification Commission (GCC-CWG) for verification and endorsement of the certification process.

Two independent bodies support containment activities at the global level, providing reports and recommendations to the WHO Director General. The Global Commission for the Certification of

²³ World Health Organization. Containment Certification Scheme to support the WHO Global Action Plan for poliovirus containment. http://polioeradication.org/wp-content/uploads/2017/02/CCS_2016EN.pdf.

Poliomyelitis Eradication (GCC) acts as the oversight body to confirm the achievement of global containment of polioviruses. The Containment Advisory Group (CAG) advises on technical issues related to GAPIII (see **Figure 3**).

Current status of containment activities

GAPIII implementation was arranged in three phases aligned with phased-OPV cessation.²⁴ Phase I includes an inventory and reduction of facilities holding type 2 poliovirus materials; Phase II refers to containment of type 2 poliovirus; and Phase III refers to containment of all polioviruses. Phases I and II were to be implemented around the certification of WPV2 eradication in 2015 and after tOPV withdrawal in May 2016, respectively. Phase III implementation is expected to begin by the time all six WHO regions are certified as polio-free.

Global implementation of containment is moving ahead, but the schedule was delayed and Phases I and II are now progressing in parallel. To advance implementation during the endgame, the GPEI has increased technical support and funding for communications, advocacy, and training of stakeholders, including NACs and PEFs. The CAG recommendations and a new guidance for identifying and handling potentially infectious materials will address technical concerns from the biomedical community and will help countries meet containment requirements.²⁵

C. What Will Be Done

Strategic Priorities and Assumptions

The central strategies to achieve and sustain poliovirus containment in the post-certification period are: 1) continue the process of reducing the number of facilities retaining polioviruses; and 2) oversee implementation of safeguards and continuously monitor compliance with containment requirements in facilities retaining poliovirus and their host countries.

To inform post-certification containment activities, the following assumptions were used:

- Although GAPIII is expected to be revised during the endgame phase before certification, the revisions will likely address specific questions and challenges to implementation procedures, but the general strategies and guidelines will be upheld.
- By certification the number of facilities retaining poliovirus-containing materials will have decreased, but all the specific containment requirements established in GAPIII may not have been achieved. The GCC is expected to outline revised containment conditions that will need to be in place for the certification of WPV eradication and bOPV withdrawal.
- By certification, some containment-specific functions may have transitioned out of the current GPEI management structure, but oversight will likely be conducted through a similar

²⁴ World Health Organization. GAPIII: WHO global action plan to minimize poliovirus facility-associated risk. Geneva, Switzerland. http://polioeradication.org/wp-content/uploads/2016/12/GAPIII_2014.

²⁵ World Health Organization. Guidance for non-poliovirus facilities to minimize risk of sample collections potentially infectious for polioviruses. (In preparation).

governance structure in the early post-certification stages (up to two years after bOPV cessation).

Activity 1.1.1 – Support the global reduction of facilities retaining poliovirus

In preparation for bOPV withdrawal, countries will need to identify all facilities retaining any infectious or potentially infectious OPV/Sabin types 1 and 3 materials by updating the facility surveys conducted for type 2 poliovirus, which may also help in finding any remaining WPV or VDPV materials. Any facility not designated as a PEF will need to remove any poliovirus materials according to updated GAPIII and WHO guidelines.²⁵ These activities should be coordinated with the withdrawal and the destruction of bOPV stocks as explained in Goal 2.

To monitor this process, countries will share progress reports periodically with the GCC (through the RCCs or an alternative). To encourage global implementation, a status report could also be presented annually to the World Health Assembly.

The GCC will also use a summary of country reports to certify containment of all polioviruses after bOPV withdrawal. Once this milestone is reached, facilities that do not have a containment certificate should no longer handle or store any poliovirus materials. **National authorities will have the responsibility of ensuring compliance through regulatory or other type of mandate. Implementation of containment for all polioviruses (WPV, VDPV, and Sabin) may affect polio surveillance, vaccine production, outbreak response, and research activities.** (See **Table 1**).

Commented [BB14]: Added to clarify national responsibilities

Any country that experiences a poliovirus outbreak will have to update their facility survey to include laboratories that may have collected specimens harboring polioviruses and facilities that may have vaccine stocks—and destroy or contain those materials. An international oversight body will monitor these activities to certify containment of polioviruses in the country after the outbreak.

To support the global reduction in the number of facilities retaining poliovirus, dedicated staff at the global and regional level will conduct the following activities:

- Develop guidelines and training for surveys and containment reports and share with countries
- Update communication and advocacy strategies to ensure cooperation from the biomedical community
- Provide assistance to countries on regulatory and technical issues related to the implementation of facility surveys and compliance with poliovirus containment requirements
- Coordinate submission of country reports to the RCC and GCC (or other oversight bodies)
- Provide technical assistance on containment to countries facing outbreaks after certification
- Coordinate meetings of countries and regions with oversight bodies to monitor progress in activities

A high level of effort is expected for these activities during the first two to three years after certification, until the GCC certifies global implementation of containment of all polioviruses following bOPV withdrawal. New research developments may also help reduce the number of required PEFs, such as the replacement of virus cultures with other assays for the diagnosis of poliovirus infection or the production of vaccines using genetically modified poliovirus strains or virus-like particles that do not require containment. (See **Research Activities** section).

Activity 1.1.2 – Implement and monitor long-term poliovirus containment in facilities with appropriate safeguards

The risk of poliovirus re-introduction after a containment breach will decrease with time after certification as the number of facilities retaining polioviruses declines and those facilities handling poliovirus implement safeguards appropriately. However, the potential consequences of a breach will rise as population immunity decreases with time.²⁶ To mitigate these risks, it will be critical to maintain long-term national and international mechanisms that monitor facility adherence to containment requirements and retain technical and functional capacity for addressing new containment questions and responding efficiently to potential spills or community exposure.

At the national level, PEFs will need to meet and maintain the safeguards required by GAP III and allow periodic assessment by auditors and NACs. NACs will renew, modify, or withdraw the certificates of containment, in coordination with WHO and GCC-CWG (or other oversight body).

At the global and regional level, staff with expertise in poliovirus containment will support PEFs, countries, and oversight groups through the following activities:

- Develop and regularly update guidelines and technical materials related to poliovirus containment for laboratory or research communities, governments, and regulatory agencies
- Provide technical assistance and expert containment advice on certification processes and questions related to poliovirus containment (see **Table 1** for links with other polio functions)
- Maintain and regularly update a global inventory of PEFs
- Provide regular training on containment certification processes
- Support GCC-CWG activities, including the training of members, organization of meetings, and preparation of documentation necessary for review of containment certificates requests
- Provide secretariat functions to expert committees and oversight bodies (such as CAG, GCC)
- Provide technical assistance in investigating and responding to containment breaches in coordination with PEFs and outbreak response groups (national and international)

The GCC-CWG will continue verification of containment certificates for new or existing PEFs until containment of all poliovirus following bOPV cessation is certified. After reaching that milestone, the assignment of this function and oversight role may be reassessed.

The CAG or an equivalent expert advisory committee is likely to be required for several years after certification to answer new technical questions elicited by vaccine manufacturers, researchers, or others. In the long term, the CAG may merge with another expert body that reviews research on poliovirus, as was done with smallpox.

²⁶ 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: 389.

Table 1. The impact of containment on other post-certification activities

Effects of containment implementation	Actions to address these effects
Vaccine manufacture and stockpile	
<ul style="list-style-type: none"> Production of IPV and mOPV will require strict containment safeguards, which may increase vaccine cost and limit manufacturer availability mOPV stockpiles will need to be maintained in facilities with containment safeguards 	<ul style="list-style-type: none"> Consider containment requirements for manufacture during estimation of polio vaccine supplies Consider during planning of location of national and international mOPV stockpiles
Surveillance	
<ul style="list-style-type: none"> Regulations for international shipment of samples that contain or may contain poliovirus will be more stringent and will increase cost and complexity 	<ul style="list-style-type: none"> Ship poliovirus RNA (considered at lower infectious risk) instead of poliovirus isolates or stools to reference labs Update laboratory and field guidelines to include procedures for shipment of samples Account for extra cost/delays of sample shipments when planning surveillance activities
<ul style="list-style-type: none"> Tests that require handling live poliovirus, including serology, will be possible only in laboratories certified as PEFs Most polio laboratories will work on samples until poliovirus is detected; at which time the sample must be deactivated or transferred to a PEF laboratory 	<ul style="list-style-type: none"> Update protocols to test for poliovirus, either under containment (Annex 2 or 3 of GAPIII) or without containment (Annex 6 of GAPIII) Use serosurveys to measure population immunity judiciously to account for limited number of laboratories with testing capacity Replace WPV/Sabin strains with highly attenuated strains for serological testing when assays are available
Outbreak response	
<ul style="list-style-type: none"> Shipment of mOPV to respond to outbreaks may have stricter restrictions and require longer time 	<ul style="list-style-type: none"> Maintain global capacity to support country authorities with import permits and shipments
<ul style="list-style-type: none"> A new WPV/VDPV outbreak and the use of OPV to interrupt transmission will reintroduce polioviruses in facilities without appropriate containment safeguards 	<ul style="list-style-type: none"> Update outbreak guidelines to ensure that samples potentially harboring poliovirus and vaccine stocks are destroyed or contained after closing the outbreak
Research	
<ul style="list-style-type: none"> Laboratories conducting experimental research or supporting testing for vaccine clinical trials will need to be certified as PEFs 	<ul style="list-style-type: none"> Ensure adequate test capacity when planning poliovirus-related research
<ul style="list-style-type: none"> Use of live vaccines in clinical trials will not be available or will be very restricted for: <ul style="list-style-type: none"> Administration to individuals in study arms Challenge with OPV to assess mucosal immunity Determination of antibody levels by microneutralization to assess efficacy 	<ul style="list-style-type: none"> Adjust resources, time, and designs for clinical trials of new vaccines Support development of new diagnostic tools to facilitate research on new polio vaccines



In the post-certification era, attaining and sustaining high immunization coverage will require extensive coordination across global, national, and community levels.

Protect Populations

Main Objectives	Major Activities
Objective 2.1 –	Activity 2.1.1 –
To protect populations from VDPV and VAPP by effectively preparing and implementing the globally synchronized withdrawal of bOPV	Develop and implement plans (including pre-cessation SIAs) to withdraw bOPV from all use
Objective 2.2 –	Activity 2.2.1 –
To provide access to safe, effective vaccines for long-term protection from poliovirus for global populations	Implement future immunization policy to protect population against poliovirus
	Activity 2.2.2 –
	Support the availability of affordable IPV and its effective, efficient delivery to facilitate high immunization coverage

Commented [BB15]: Through out the PCS , prominece is given to VDPV over VAPP to reflect higher priority in terms of global implications.

Introduction

Oral poliovirus vaccine (OPV) is used in many countries because it is low-cost, easy to administer, and efficacious. However, because of the risks of population-wide spread of vaccine-derived polioviruses (VDPVs) and individual acquisition of vaccine-associated paralytic poliomyelitis (VAPP), OPV should be removed from use. Many countries have already discontinued the use of OPV and switched to inactivated poliovirus vaccine (IPV). Although IPV is highly effective in providing individual protection against paralysis, the vaccine's impact to limit transmission in settings with poor sanitation is less clear, albeit lower than that of OPV. Further challenges to the widespread introduction of IPV have been its cost and constrained global supply. These immediate challenges highlight the need for new immunization policies and strategies to ensure that long-term protection from any poliovirus re-emergence can be sustained throughout the post-certification period.

Description of the Goal

The goal of eliminating all paralytic polio disease and sustaining WPV eradication ultimately requires stopping all use of bivalent OPV (bOPV) globally and continuing to immunize with other safe, effective polio vaccines. These dual efforts—withdrawing bOPV and extending widespread IPV use in routine immunization to reach 90% seroconversion for each fully-vaccinated child—will mitigate the risks from VDPVs and VAPP and protect against the possible re-emergence of WPV.

Objective 2.1: Protect populations from VDPVs and VAPP

A. Context

Following the declaration of WPV type 2 global eradication in September 2015, the GPEI initiated sequential steps to withdraw OPV. The first of these was the global withdrawal of the type 2-containing vaccine, trivalent OPV (tOPV), and the switch to bivalent OPV (bOPV) with only types 1 and 3, an event that was synchronized worldwide in April-May 2016 by 126 OPV-using countries.

B. Risks

Table 2 summarizes the risks associated with VDPVs and VAPP, proposed measures to mitigate these risks, and relevant technical points which impact how these measures will be implemented. Further details are provided in Section C below.

Table 2. VDPV and VAPP risks and mitigation measures

	Risk ²⁷	Mitigation Measures	Technical Note
VDPVs	VDPV emergence related to use of OPV in populations with low immunity and areas prone to fecal-oral transmission	<ul style="list-style-type: none"> Withdraw bOPV Sustain high levels of population immunity to types 1 and 3 until bOPV cessation through RI and/or SIAs Maintain high quality for any mOPV SIAs for outbreak response. Develop alternative polio vaccines (e.g., nOPVs) 	<ul style="list-style-type: none"> Risk of VDPV circulation from OPV can continue for several years after cessation.²⁸ Failure to target high-risk groups and achieve adequate population immunity in pre-cessation SIAs can raise the threat of VDPV emergence and spread.²⁹ Risk of mOPVs resulting in VDPV transmission beyond an outbreak zone may increase with time after cessation.³⁰

²⁷ See Annex B for details on projected magnitude of risk for VAPP and VDPV in the post-certification era.

²⁸ Grassly NC. The final stages of the global eradication of poliomyelitis. *Phil. Trans. R. Soc. B* 2013 368, 20120140, published 24 June 2013. See also: Lyons, H, Famulare M, Chabot-Couture, G. OPV13 cessation and SIA planning. Presentation to the SAGE Polio Working Group, Geneva, September 2017.

²⁹ Pons-Salort M, et al. Preventing vaccine-derived poliovirus emergence during the polio endgame. *PLoS Pathog* 12(7): e100528. doi:10.1371/journal.ppat.100528.

³⁰ Tebbens RJD, et al. An economic analysis of poliovirus risk management policy options for 2013-2052. *BMC Infectious Diseases* (2015) 15:389.

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VDPVs (continued)	Importation of VDPVs into countries which have gaps in protection from types 1 and 3 and declining immunity due to early withdrawal of bOPV from RI prior to cessation	<ul style="list-style-type: none"> Synchronize cessation of bOPV for all countries using the vaccine at time of certification Initially provide priming and partial protection through IPV in RI 	<ul style="list-style-type: none"> IPV use with high coverage cannot prevent cVDPVs in areas with intense fecal-oral transmission.³¹ Depending on recipient age, one dose of IPV can seroconvert or prime majority of vaccine recipients.³² (See Objective 2.2 for long term projection)
VAPP	VAPP from continued use of OPV (either bOPV or mOPV used for outbreak response)	<ul style="list-style-type: none"> Withdraw bOPV Maximize prior IPV vaccination coverage and judiciously target use of mOPV for outbreak response Develop alternative polio vaccines such as new, safer OPV (nOPVs) 	<ul style="list-style-type: none"> See Goal 3 for further details on outbreak response and see Research Activities section for details on alternative polio vaccines.

bOPV= bivalent oral poliovirus vaccine; cVPDV= circulating vaccine-derived polioviruses; IPV= inactivated poliovirus vaccine; OPV= oral poliovirus vaccine; mOPV= monovalent oral poliovirus vaccine; nOPV= new oral poliovirus vaccine; RI= routine immunization; SIA= supplementary immunization activity; VDVP= vaccine-derived poliovirus; VAPP= vaccine-associated paralytic poliomyelitis

C. What Will Be Done

Activity 2.1.1 – Develop and implement plans (including pre-cessation SIAs) to withdraw bOPV from all use

While the GPEI established a general framework in 2005 for the eventual withdrawal of OPV after certification, the lessons learned from the tOPV switch provide supplemental guidelines for bOPV cessation. Withdrawing bOPV after global certification, however, represents a new challenge: the complete cessation, not simply a switch, of live polio vaccines.^{33,34}

Three core strategies can be identified for bOPV cessation, even as comprehensive operational details are still forthcoming.

1. Obtain clear commitment from all OPV-using countries to cease bOPV-use modeled after the endorsement of the switch at the World Health Assembly in May 2015,³⁵ and fully engage

³¹ Tebbens RJD, et al. Maintenance and intensification of bivalent oral poliovirus vaccine use prior to its coordinated global cessation. *J of Vaccines and Vaccination* 2016; 7:5, doi:10.4172/2157-75600.1'000340.

³² Bandyopadhyay AS, et al. Polio vaccination: past, present and future. *Future Microbiol.* 2015;10(5):791-808. doi: 10.2217/fmb.15.19. Epub 2015 Mar 31.

³³ World Health Organization. Cessation of routine oral polio vaccine (OPV) use after global polio eradication: Framework for national policy makers in OPV-using countries. Geneva, 2005.

³⁴ For extensive details on the lessons learned from the withdrawal of tOPV, see multiple articles in: *Polio Endgame and Legacy: Implementation, Best Practices and Lessons Learned. Journal of Infectious Diseases. Volume 216, Issue suppl_1, 1 July 2017.* https://academic.oup.com/jid/issue/216/suppl_1.

³⁵ World Health Organization, Sixty-Eighth World Health Assembly: Poliomyelitis: Report by the Secretariat. Available at http://apps.who.int/gb/ebwha/pdf_files/WHA68/A68_21-en.pdf.

stakeholders at all levels in the planning, preparation, implementation, and validation of global bOPV withdrawal.

2. Develop and aggressively implement pre-cessation risk mitigation measures necessary to meet multiple readiness criteria for full bOPV withdrawal.³⁶

Although not yet finalized, the proposed readiness criteria are:

- a. Pre-cessation immunity for types 1 and 3, see panel (at right)
- b. IPV supply and status of global introduction, see panel and Objective 2.2
- c. Poliovirus surveillance, see Objective 3.1
- d. Outbreak response capacity, see Objective 3.2
- e. Containment of poliovirus, see Goal 1
- f. Epidemiologic status, e.g., lack of persistent cVDPVs

Specific targets will be established for each criterion to reflect the parameters required at the global and/or country level to minimize and manage the risks associated with final bOPV cessation

Pre-Cessation Immunity

By inducing mucosal immunity for types 1 and 3, pre-cessation bOPV SIAs can maximize protection against future VDPVs. Not all areas may require such additional efforts. Priority should be given to achieving maximum quality SIAs in areas with high risk of infection and low routine immunization coverage. Further analysis of risk and local epidemiology will guide which implementation option will be most effective.

Countries using bOPV have been advised to introduce IPV to provide individual protection against paralysis. However, IPV use, even with high coverage, may not prevent cVDPVs in areas with intense fecal-oral transmission. Countries which have not been able to obtain adequate IPV supplies for all birth cohorts prior to cessation can also be more vulnerable after they stop bOPV. Additional IPV will be provided to 'catch-up' missed cohorts once supplies become available, but the timing and coverage of these efforts remain to be determined.

Sources: Tebbens RJD, et al. Maintenance and intensification of bivalent oral poliovirus vaccine use prior to its coordinated global cessation. *J of Vaccines and Vaccination* 2016; 7:5, doi:10.4172/2157-75600.1000340. Meeting of the strategic advisory group of experts on immunization, October 2016—conclusions and recommendations. *Wkly Epidemiol Rec* 2016; 91:561-584.

3. Implement the operational planning and withdrawal process based on clearly identified steps which actively mitigate the risks associated with cessation.

To maximize population immunity for types 1 and 3, country-level withdrawal of bOPV should be scheduled as soon as feasibly possible after global certification, ideally within 12 months. Global preparation for this operationally challenging event will need to begin well in advance (18-24 months) prior to implementation. Certification and other markers of epidemiologic achievement, such as the lack of persistent cVDPVs for at least six months, will need to be designated to activate both preparation and final planning.

³⁶ Based on criteria used for the switch. See: Meeting of the strategic advisory group of experts on immunization, October 2014—conclusions and recommendations. *Wkly Epidemiol Rec* 2014; 89:561–76.

Key strategies to mitigate risks associated with implementation include:

a. Synchronize bOPV cessation globally

Global synchronization of the withdrawal of bOPV after certification within a fixed two-week period should ensure that no country is inadvertently put at risk of importing Sabin OPV or VDPV from a country that continues to use bOPV in routine immunization.

b. Ensure complete withdrawal of bOPV at cessation

Direct communication with the public and healthcare providers should emphasize the need and importance of stopping all bOPV use. Additionally, a comprehensive monitoring and validation process should be put in place to confirm compliance with directives to collect and destroy all remaining vials from local providers and throughout the cold chain given the risks to containment and potential for emergence of VAPP/VDPVs from continued use.³⁷ Similar procedures will be needed for any remaining mOPV use in outbreak response. The GPEI will explore with relevant countries whether manufacturers should securely retain any remaining bOPV stocks until expiration for potential outbreak response or safely dispose at time of bOPV withdrawal.

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

A. Context

The plan to introduce at least one dose of IPV by mid-2016 in all 126 OPV-only using countries has been only partially implemented due to severe global constraints on IPV supply. To offset shortages, some countries have utilized fractional IPV (fIPV),³⁸ while others have either suspended IPV or deferred IPV introduction. High-income and many middle-income countries have already introduced IPV either as a stand-alone antigen or more commonly in a combination vaccine. In 2016, 42 countries reported using hexavalent (DTaP-Hib-HepB-IPV) and 39 reported using pentavalent (DTaP-Hib-IPV) in their EPI schedules.³⁹

B. Risks

Table 3 summarizes the risks faced in providing long term population protection against poliovirus re-emergence through vaccination and the technical challenges and measures proposed to mitigate these risks.

³⁷ New guidelines will be prepared prior to bOPV cessation. For switch guidelines see: World Health Organization. Guidance for implementing the switch.

http://www.who.int/immunization/diseases/poliomyelitis/endgame_objective2/oral_polio_vaccine/implementation/en/

³⁸ fIPV is defined as intradermal administration of 1/5th of the full dose given intramuscularly.

³⁹ See the World Health Organization's data for immunization, vaccines, and biologicals.

http://www.who.int/immunization/monitoring_surveillance/data/en/

Table 3. Vaccine protection and supply risks and mitigation measures

Risks	Mitigation Measures	Technical Notes
Limits to IPV protection	<ul style="list-style-type: none"> Develop global immunization policy which is programmatically feasible, flexible, and provides required individual protection Continue development of new polio vaccines 	<ul style="list-style-type: none"> IPV requires multiple doses, duration of protection for 2 doses is unknown, and vaccine has limited effectiveness against transmission and spread in high risk environments.⁴⁰ See Research Activities section for new poliovirus vaccine development.
Lack of adequate supply of affordable IPV for all countries	<ul style="list-style-type: none"> Determine demand for IPV and facilitate long-term supply Advocate for sustainable financing to support low-income countries Facilitate development of affordable formulations and efficient delivery options 	
High-risk populations are not adequately protected due to weak RI systems	<ul style="list-style-type: none"> Work with GVAP partners and other initiatives to strengthen RI and broader health systems Further strengthen current outreach and/or develop innovative strategies to reach high-risk populations with routine vaccines 	<ul style="list-style-type: none"> POL3 coverage in 2016 was estimated at 49% in Nigeria, 60% in Afghanistan, and 72% in Pakistan.⁴¹ See <i>GVAP 2011-2020</i> for proposed strategies to strengthen RI.⁴²

IPV= inactivated poliovirus vaccine; GVAP= Global Vaccine Action Plan; POL3= third dose of poliovirus-containing vaccine; RI= routine immunization

C. What Will Be Done

Activity 2.2.1 Implement future immunization policy to protect population against poliovirus

Future immunization policy and coverage targets in the post-certification era will be a consensus of guidelines and recommendations from advisory groups (Strategic Advisory Group of Experts on Immunization [SAGE] and Containment Advisory Group [CAG]) and global immunization objectives (Global Vaccine Action Plan [GVAP]) to achieve protection against poliomyelitis.

⁴⁰ Bandyopadhyay AS, et al. Polio vaccination: past, present and future. *Future Microbiol.* 2015;10(5):791-808. doi: 10.2217/fmb.15.19. Epub 2015 Mar 31.

⁴¹ WHO Unicef estimates of Pol3 coverage.

http://apps.who.int/immunization_monitoring/globalsummary/timeseries/tswucoveragepol3.html.

⁴² World Health Organization. *Global Vaccine Action Plan 2011-2020*. Available at http://www.who.int/immunization/global_vaccine_action_plan/GVAP_doc_2011_2020/en/

While specifics may change prior to certification based on additional research, SAGE put forward recommendations for future global polio vaccination policy which set expectations for national Expanded Programmes on Immunization (EPI) after global bOPV withdrawal (*see panel*).

This proposed schedule from SAGE 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 diphtheria–tetanus–pertussis (DTP) and measles.⁴³ The current recommendations apply to stand-alone IPV. Future recommendations will include specifics for combination vaccines containing IPV.

The recommendations from SAGE acknowledge the programmatic equivalency of fractional or full-dose IPV when the first dose is given at or after two months of age.⁴⁴ This policy provides countries with long-term options which could reduce costs and stretch vaccine supplies. Further research will be needed to determine the effectiveness and duration of immunity delivered by each delivery method (intramuscular for IPV and intradermal for iIPV). (See **Research Activities** section.)

The recommendation to use IPV for 10+ years addresses the need to provide long-term global protection, at least through the intermediate post-cessation period, against the small but continuing risk of poliovirus. The recommendation should also signal to vaccine manufacturers the potential future demand for IPV (*also see Activity 2.2.2*).

While the SAGE recommendations are focused on providing universal standards required for individual protection, the population immunity achieved through this schedule for a country or region will be dependent on the coverage that is attained. As currently set by GVAP, the coverage target for all vaccines in national immunization programmes is at least 90% national vaccination

SAGE Recommendations for Future Global Polio Vaccination Policy

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 if mandated by GAPIII to minimize poliovirus facility-associated risk.

Source: WHO. Meeting of the strategic advisory group of experts on immunization, April 2017—conclusions and recommendations. Wkly Epidemiol Rec 2017; 92:301-320

⁴³ For summary of IPV clinical trials, see: Estivariz CF, et al. Poliovirus vaccination options for achieving eradication and securing the endgame. *Current Opinion in Virology* 2013, 3:309-315.

⁴⁴ For summary analysis of iIPV, see: Okayasu H, et al. Intradermal administration of fractional doses of inactivated poliovirus vaccine: a dose-sparing option for polio immunization. *JID* 2017;216 (Suppl 1): S161-S167.

coverage and at least 80% vaccination coverage in every district or equivalent administrative unit.⁴⁵

GAPIII has also set specific coverage targets to reflect potentially higher risks for PEF-hosting countries.⁴⁶ After bOPV cessation, GAP III requires that countries with PEFs containing OPV/Sabin materials provide at least one dose of IPV (and attain coverage equal to DTP3) and countries with PEFs containing WPV materials provide at least three doses of IPV (and attain greater than 90% coverage). International advisory groups (such as SAGE, CAG, and the GCC) may choose to further refine the parameters and expected geographic scope of these recommendations.

Commented [BB16]: Edited to clarify further refinements.

Activity 2.2.2 Support the availability of affordable IPV and for effective, efficient delivery to facilitate high immunization coverage

In the post-certification era, attaining and sustaining high immunization coverage with IPV will require extensive coordination across global, national, and ultimately community levels. Specifically, high coverage will require: 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 acceptance for children to be vaccinated.

The strategies noted below are targeted to IPV; however, it should be noted that in the post-certification era, when polio immunization is globally integrated into routine programmes, these strategies should be part of a coherent set of activities which promote overall sustainability of immunization efforts and high coverage with all vaccines.

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

Gavi and the GPEI have updated the “The IPV Supply and Procurement Roadmap” that analyses the demand and supply dynamics of IPV for the longer term. The Roadmap aims to define actions which may positively impact the IPV market to achieve a healthy market over time, which is characterized by ensuring sufficient supply, improving pricing, and supporting the availability of new innovative vaccines.⁴⁷

While initially focused on solutions to the global supply shortage, recent updates of the Roadmap include longer-term projections covering the post-certification period based on broad-based scenarios and assumptions (see **Figure 4**). Assumptions in the August 2017 Roadmap relevant for the post-certification era include:

- Countries which have been using IPV for many years and are self-procuring (primarily upper-middle income countries) are expected to continue IPV vaccination using their own resources.
- For previously OPV-using countries, the long-term demand for IPV and IPV-combination vaccines will change over time and depend on multiple factors, including: the timing of global bOPV cessation and when countries will be expected to implement the two-dose regimen

⁴⁵ World Health Organization. *Global Vaccine Action Plan 2011-2020*. May 2012.
http://www.who.int/immunization/global_vaccine_action_plan/

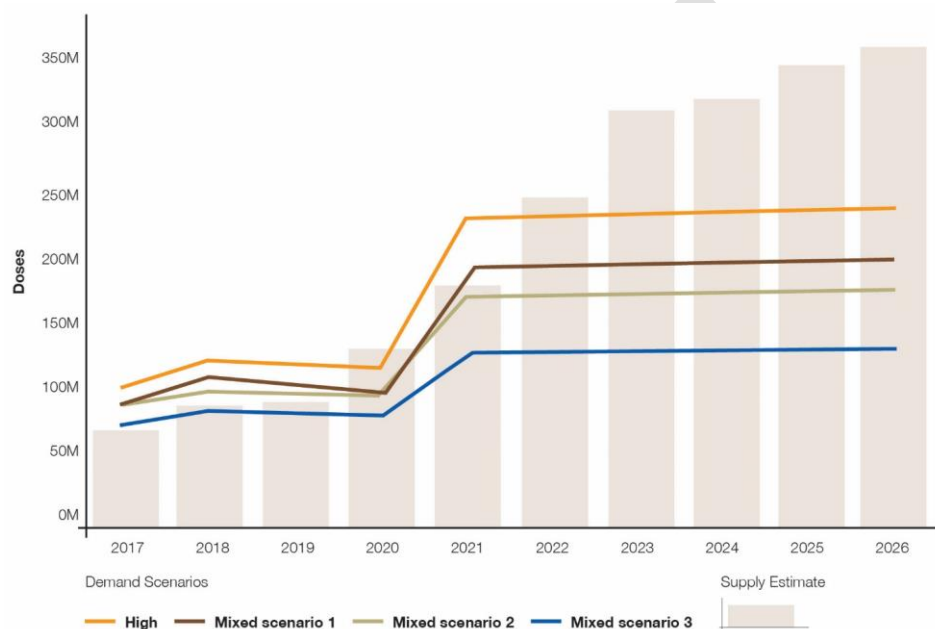
⁴⁶ World Health Organization. *GAPIII: WHO global action plan to minimize poliovirus facility-associated risk*. Geneva, Switzerland. http://polioeradication.org/wp-content/uploads/2016/12/GAPIII_2014.

⁴⁷ Gavi and Global Polio Eradication Initiative. *IPV supply and procurement roadmap-public summary*. August 2017.
<http://www.gavi.org/library/gavi-documents/supply-procurement/ipv-roadmap-public-summary/>

recommended by SAGE; pricing and available financing; national product preference and use of fractional doses; perceived future risk of poliomyelitis for their population; and availability of new or improved products.

- IPV supply should be sufficient to enable all countries to switch to two full IPV doses.

Figure 4. IPV demand scenarios and base case supply estimates



Demand estimates are based on four potential routine scenarios:

1. Routine High Demand (orange): one full dose for all countries in 2017-2020 and two full doses 2021+
2. Mixed Scenario 1 (dark brown): India, Sri Lanka, Bangladesh use two doses of fIPV. Remainder of countries have a full-dose schedule
3. Mixed Scenario 2 (light brown): India, Bangladesh, and Sri Lanka as well as 21 countries that haven't introduced IPV as of January 2017 on two doses of fIPV. Remainder on one full dose in 2017-2020 and two full doses 2021-2026
4. Mixed Scenario 3 (blue): Tier 1 countries on one full dose in 2017-2020 and 2 full doses from 2021. Remainder on two full doses.

Source: Gavi and GPEI. *IPV supply and procurement roadmap-public summary*. August 2017. Note: Projections cover the 126 countries which were using OPV in 2016.

The IPV Roadmap is updated in relation to major procurement activities such as new tenders and provides visibility to manufacturers and stakeholders on expectations related to supply and demand. All 126 countries which were using only tOPV committed to implement the SAGE recommendation (from October 2016) to introduce at least one IPV dose into RI.⁴⁸ However, long-term demand for IPV remains uncertain. Aside from countries with PEFs, which will be expected

⁴⁸ IVB/WHO Immunization Repository and Meeting of the Strategic Advisory Group of Experts on Immunization, October 2016—conclusions and recommendations. *Wkly Epidemiol Rec* 2016; 91:561-584.

to meet IPV-use requirements under GAPIII, other countries may take the SAGE recommendation into consideration as part of their own cost-benefit analysis on using IPV in the post-certification era. As such, demand forecasts should be regularly revised based on a study of country preferences and vaccination policies.

As countries make decisions on IPV use, they should be supported on the global level through communications about the role of IPV in protecting against the re-emergence of the virus. Similarly, ongoing engagements with incumbent and new IPV manufacturers should be continued to facilitate decisions on long-term supply.

Facilitate development of IPV products to stretch supply and maximize affordability

Several vaccine dose-sparing strategies have been developed and additional IPV products are in the pipeline which may stretch supply and maximize affordability. Two such approaches include: fractional IPV (fIPV) dosing and adjuvanted vaccines. The long-term global impact on IPV supply and cost of other options, such as combination vaccines or Sabin strain IPV (sIPV), remain to be determined.

Scientific data confirming the immunogenicity of intradermal (ID) fIPV and country experience demonstrating its operational feasibility provide strong evidence for the potential broader use of fractional dosing.⁴⁹ SAGE has endorsed the use of fractional dosing and encouraged countries to consider the use of fIPV based on their independent assessment of clinical data.⁵⁰ Although initially developed as a method to extend limited vaccine supplies, fIPV can also provide cost savings if appropriate vial sizes are available and ID delivery device costs can be decreased.⁵⁰ The use of fIPV, however, remains off-label, and active engagement with global and national regulators may be required to manage liability issues.

Adjuvanted vaccines are also being pursued to improve the intestinal mucosal immunity generated by IPV and to increase the vaccine's affordability by reducing the amount of poliovirus antigen needed per dose. Use of aluminium salts as IPV adjuvants has been shown to promote dose-sparing and is already widely used safely in other vaccines. Other novel adjuvants show promise to reduce the risk of shedding and environmental transmission of polioviruses. (See **Research Activities** section.)

Combining antigens can stimulate community demand and improve efficiency of delivery. Combination vaccines containing IPV and using acellular pertussis are currently widely used in developed countries, but are more expensive when compared with pentavalent vaccine plus stand-alone IPV. IPV combination vaccines using whole cell pertussis are under development. Whether this formulation will be sufficiently affordable to attract wide use is not yet known. By competing for the same bulk as stand-alone IPV, combination vaccines may also have a problematic impact on global IPV supply at least for the foreseeable future.

Since sIPVs use attenuated Sabin virus strains rather than WPV in production, they are less likely to cause problems for containment. While they may potentially provide more affordable, effective

⁴⁹ Okayasu H, et al. Intradermal administration of fractional doses of inactivated poliovirus vaccine: a dose-sparing option for polio immunization. *JID* 2017;216 (Suppl 1): S161-S167.

⁵⁰ World Health Organization. Meeting of the Strategic Advisory Group of Experts on Immunization, October 2016- conclusions and recommendations. *Wkly Epid Rec* 2016; 48:561-584.

options against stopping poliovirus transmission the costs, efficacy, and feasibility of large-scale production of these new vaccines are still being evaluated. (See **Research Activities** section.)

Advocate for sustainable financing of IPV

Low-income countries are expected to receive Gavi funding through 2020 to support the current SAGE recommendation for all countries to introduce a single full dose or two fractional doses of IPV for routine EPI. Decisions for funding Gavi-supported countries from 2021 onward are anticipated by the end of 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, and specifics on vaccine schedules 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 become globally available, some countries still may be in the process of fully integrating the vaccine into regular use. To successfully make this change to the EPI schedule, some key steps should be undertaken well in advance and implemented in close coordination with bOPV cessation. They include: training health workers, developing and implementing communications with caregivers and parents, instituting any required changes in cold-chain and vaccine management, and revising immunization records.

Intradermal (ID) fIPV in routine immunization has had success in some countries (such as India and Sri Lanka), though others have reservations about the increased operational requirements and training required for ID delivery. Several alternatives to the 0.1 ml syringe that is used for ID injection for fIPV have been developed and widely tested.⁵¹ These options are still relatively expensive and some require intensive re-training of healthcare workers. Nevertheless, they may present viable methods to increase the efficiency of ID delivery in the future. Field experience and collaboration with manufacturers should provide ways to bring down costs and increase acceptance among policy makers and healthcare workers. Additionally, studies are underway to determine the efficacy of fractional intramuscular (IM) dosing which would rely on regular syringes.

Commented [BB17]: Edited to clarify syringe size

The country transition planning process, supported by the GPEI, aims to identify how polio resources, human capacity, and knowledge can be directed to achieve 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 emergencies. As partners develop “GVAP 2.0,” sustaining polio eradication should be a core objective. The current GVAP Strategic Objective 3 highlights the requirement to ensure that the benefits of immunization are extended equitably to all people and it includes strategies for hard-to-reach communities.⁵² These generic strategies should be relevant for extending polio vaccination to populations at high risk for the re-emergence of polioviruses. Additional strategies for reaching these high-risk populations for poliovirus detection and outbreak response are explored in Goal Three.

⁵¹ Okayasu H, et al. Intradermal administration of fractional doses of inactivated poliovirus vaccine: a dose-sparing option for polio immunization. *JID* 2017;216 (Suppl 1): S161-S167.

⁵² World Health Organization. *Global Vaccine Action Plan*. Geneva, 2013.
http://www.who.int/immunization/global_vaccine_action_plan/en/



Detect and Respond

Main Objectives	Major Activities
Objective 3.1 –	Activity 3.1.1 –
To promptly detect any poliovirus in a human or in the environment through a sensitive surveillance system	Redefine poliovirus surveillance paradigm
	Activity 3.1.2 –
	Sustain adequate and technically qualified laboratory and surveillance infrastructure (including human capacity) and information systems
Objective 3.2 –	Activity 3.2.1 –
To develop and maintain adequate global and regional capacity and resources to support national efforts to rapidly and effectively contain any detected poliovirus and stop any poliovirus transmission	Identify future outbreak risks, develop and implement preparedness plans, and prepare response strategies
	Activity 3.2.2 –
	Sustain trained human capacity and create, maintain, and manage adequate stockpiles of polio vaccine and antivirals to appropriately respond

Commented [BB18]: Added

Commented [BB19]: Modified wording and structure in the text to focus Activity 3.2.1 on planning and strategy and shifted human and material capacity to Activity 3.2.2. Content remained unchanged.

Introduction

Comprehensive acute flaccid paralysis (AFP) surveillance and rapid response vaccination campaigns have been core strategies for polio eradication since the inception of the GPEI. In the post-certification era, minimizing the risks of delayed detection or inadequate response will involve building on current capacity and adapting to a new world where poliovirus is an eradicated pathogen.

In the post-certification era, the sensitivity and capacity for poliovirus surveillance will need to reflect the likelihood that poliovirus re-emergence risk will be highest immediately before and after bOPV cessation. Although this risk of re-emergence may decrease with time, some level of surveillance should continue since the severity of the consequences of any re-emergence will increase throughout the post-certification period. Countries will need to maintain their vigilance, outbreak preparedness, and capacity to respond effectively as required under the IHR and according to their assessed risk.⁵³

Commented [BB20]: Added para to reflect concept of change in risk and consequence over time.

⁵³ World Health Organization. International Health Regulations (2005), Third Edition. Geneva, 2016. <http://www.who.int/ihr/publications/9789241580496/en/>

Description of the Goal

Polio surveillance in the post-certification era will take a risk-based approach by prioritizing risks, clarifying risk tolerance, and developing risk mitigation measures. Using this approach, the goal of post-certification surveillance will be twofold:

1. For high-risk areas: Use sensitive surveillance strategies to rapidly identify any containment breach or human case of poliomyelitis and detect even low-level transmission in the environment. Target supplemental strategies to the most vulnerable populations.
2. For medium- and low-risk areas: Use a mix of strategies to detect clusters of potential poliomyelitis or evidence of relatively higher levels of transmission.

The public health infrastructure required to support the post-certification surveillance strategies of rapid detection, notification, and information sharing should also provide a robust response to prevent circulation (such as from a containment breach detected within a facility) or stop transmission (for example from a cVDPV detected in a human or the environment). Although primary responsibility for response rests at the country level, there should be adequate global and regional capacity and resources to support national efforts, especially in high-risk areas.

Commented [BB21]: Added examples

Objective 3.1: Prompt detection and sensitive surveillance

A. Context

Given the potentially severe threats to global health security from any public health emergency of international concern (PHEIC), such as poliovirus, the IHR requires that countries have the capacity to provide early warning and response (EWAR).⁵⁴ IHR monitoring protocols for infectious diseases, as supplemented by the Global Health Security Agenda (GHS), recommend that countries use indicator-based surveillance (IBS) systems from routine or sentinel site surveillance, and event-based surveillance (EBS) systems designed to detect and respond to signals from formal and informal sources of information.⁵⁵

AFP surveillance, backed by the Global Polio Laboratory Network (GPLN), is an example of an IBS system that has been the cornerstone of polio eradication. Countries which have experienced transmission within recent decades have established separate, vertical AFP surveillance structures alongside other multidisease IBS systems in order to provide rapid, case-based detection (see **Annex D**). AFP surveillance has been supplemented by environmental surveillance (ES) in selected countries. Developed countries have tended to rely on enterovirus surveillance (EVS) as the primary means to detect poliovirus among both paralysed and non-paralysed individuals.

Commented [BB22]: Edited to reflect that EVS is used to detect poliovirus among both paralyzed and non-paralyzed individuals.

⁵⁴ World Health Organization. *Early detection, assessment and response to acute public health events*. Geneva. WHO/HSE/GCR/LYO/2014.4.

⁵⁵ World Health Organization. *Protocol for assessing national surveillance and response capacities for the IHR* (2005). Geneva, 2010. http://www.who.int/ihr/publications/who_hse_ihr_201007_en.pdf. Also see GHS at <https://www.ghsagenda.org/>

B. Risks

There are a number of potential risks to poliovirus detection in the post-certification period. These and measures to mitigate the risks are presented in Table 4.

Table 4. Potential detection risks and mitigation measures

Risk	Mitigation Measures	Technical Note
Substantially delayed detection of poliovirus re-emergence or transmission	<ul style="list-style-type: none"> Initially continue active, case-based national AFP surveillance in high risk areas; gradually switch to focus on sentinel sites and passive surveillance Increase sensitivity of polio surveillance by utilizing a mix of surveillance systems (e.g., environmental, enterovirus, event-based, community-based) especially in high-risk areas Integrate AFP with other vaccine-preventable diseases (VPD) / communicable disease surveillance systems to sustain capacity 	<ul style="list-style-type: none"> There is an inherently limited sensitivity of AFP surveillance since the clear majority of polio infections are asymptomatic.⁵⁶ Low-level poliovirus transmission can continue undetected for many months in areas using only IPV.⁵⁷ In suitable locations, environmental surveillance can provide more sensitive detection of polioviruses than AFP surveillance alone.⁵⁸ AFP surveillance sensitivity can decline as countries shift to integrated systems or passive approaches where poliovirus detection is considered a relatively low priority. Integration has the potential to disrupt operational efficiency of vertical AFP surveillance systems. Timing of integration should be paced to maintain required sensitivity in high-risk areas.
Missed poliovirus cases/transmission among populations who are hard-to-reach, inaccessible, or who do not access health systems	<ul style="list-style-type: none"> Develop and implement specific strategies to reach high-risk populations 	<ul style="list-style-type: none"> These same populations may be highly vulnerable to polio infections due to low vaccination coverage, poor sanitation, etc.

AFP= acute flaccid paralysis; IPV= inactivated poliovirus vaccine; VPD= vaccine-preventable disease

⁵⁶ Grassly NC. The final stages of the global eradication of poliomyelitis. *Phil Trans R Soc B*. 2013; 368. 20120140.

⁵⁷ Kopel E, et al. Lessons from a Public Health Emergency — Importation of Wild Poliovirus to Israel. *N Engl J Med* 2014; 371:981-983 September 11, 2014. doi: 10.1056/NEJMp1406250

⁵⁸ Cowger TL, et al. (2017) The role of supplementary environmental surveillance to complement acute flaccid paralysis surveillance for wild poliovirus in Pakistan – 2011–2013. *PLoS ONE* 12(7):e0180608. <https://doi.org/10.1371/journal.pone.0180608>.

Risk (continued)	Mitigation Measures	Technical Note
Failure to rapidly detect primary immunodeficiency disease (PID) patients with subclinical poliovirus infection or poliovirus excretion	<ul style="list-style-type: none"> Develop sustainable PID surveillance system in high-risk areas to provide early detection of immunodeficiency-associated vaccine-derived poliovirus (iVDPV) 	<ul style="list-style-type: none"> Early identification of PID individuals can be problematic. Areas of high risk for iVDPV appear to be middle-income countries which are different from areas at risk for other poliovirus emergences.
Failure to detect containment breach in poliovirus-containing facility or surrounding community	<ul style="list-style-type: none"> Develop comprehensive detection plans specifically targeted to environments of poliovirus-containing facilities 	<ul style="list-style-type: none"> Complicated regulatory oversight and containment requirements (see Goal 1).

iVDPV= immunodeficiency-associated vaccine-derived poliovirus; PID= primary immunodeficiency disease

C. What Will Be Done

The PEESP already recommends surveillance strategies for reaching WPV eradication. To have confidence in this milestone, the GCC and RCCs may expand upon or otherwise refine surveillance standards for certification. The forthcoming *Global Polio Surveillance Action Plan* (GPSAP) will provide additional technical guidance to assist countries with implementing the strategies and standards expected from the PEESP to achieve global certification, including strategies for inaccessible areas and high-risk populations.⁵⁹ The PCS builds on current strategies and standards by providing broad global recommendations for poliovirus surveillance required after certification.

Commented [BB23]: Clarified scope of GPSAP vis a vis PEESP and PCS.

Activity 3.1.1. – Redefine the polio surveillance paradigm

The current paradigm for poliovirus surveillance will need continual refinements to address new and evolving challenges to mitigating the risk of delayed detection. The specific strategies and standards applicable at the country level in the future will evolve from current practices based on their risk of poliovirus re-emergence. The system for classifying each country's risk allows for risk to be dynamic, with countries or large areas moving between risk strata over time and risk differing by poliovirus category (e.g., WPV, cVDPV, or iVDPV). (See **Annex C**.)

The future paradigm not only reframes risk, but also modifies specific approaches for AFP surveillance and incorporates key additional strategies required in the post-certification period (see **Table 5**). The proposed approaches and strategies attempt to balance multiple considerations: the probability and consequences of poliovirus re-emergence, intensity of effort required to maintain standards, and evolution of risk over time.

⁵⁹ Global Polio Eradication Initiative. *Global Polio Surveillance Action Plan*. (In preparation).

Table 5. Current and redefined paradigms for poliovirus surveillance

	Current paradigm	Redefined paradigm
Strategies in focus areas	<u>Countries in non-certified regions</u> <ul style="list-style-type: none"> Primarily active, case-based AFP surveillance with multiple facility & community reporting sites; often separate from other IBS systems Supplemented by ES 	<u>High-risk areas</u> <ul style="list-style-type: none"> Priority on AFP surveillance but continued integration with other VPD surveillance and IBS systems Gradual shift from active AFP surveillance to sentinel sites and then to passive approaches Increasing reliance on ES; mix of strategies evolving over time; supplement with EBS
Strategies in other areas	<u>Countries in certified regions</u> <ul style="list-style-type: none"> Mix of AFP, ES, and EVS 	<u>Medium- and low-risk areas</u> <ul style="list-style-type: none"> Mix of AFP, ES, EVS strategies based on risk Continue integrating AFP within IBS at a pace that maintains required poliovirus surveillance standards Incorporate poliovirus detection into global and national level EBS
Global Polio Laboratory Network (GPLN) organization	<ul style="list-style-type: none"> Polio-specific laboratories linked in a tiered network with designated capacities 	<ul style="list-style-type: none"> Maintain GPLN; polio-specific laboratories continue at global/regional levels, but become integrated virology laboratories at national level Potential for improved, faster diagnostics; more stringent containment requirements
Key additional strategies	<ul style="list-style-type: none"> Limited iVDPV global registry Ad hoc surveillance strategies around PEFs 	<ul style="list-style-type: none"> Develop more comprehensive surveillance for PID patients to detect iVDPV Develop global standards for community surveillance around PEFs

AFP= acute flaccid paralysis; CBS= community-based surveillance; EBS= event-based surveillance; ES= environmental surveillance; EVS= enterovirus surveillance; GPLN= Global Polio Laboratory Network; IBS= indicator-based surveillance; iVDPV= immunodeficiency-associated vaccine-derived poliovirus; PEF=poliovirus-essential facility; PID=primary immunodeficiency disease; VPD= vaccine-preventable disease

The Redefined Polio Surveillance Paradigm: Five Essential Strategies

Beyond the minimum capacity to provide early warning for global public health security threats as required for all countries under IHR, post-certification poliovirus surveillance systems will modify, reprioritize, or expand current strategies to meet future risks. The redefined paradigm incorporates five essential strategies to ensure specific detection of any poliovirus re-emergence. (See **Annex E, Table E1** for details on appropriate strategies and standards recommended for each country-risk category over time.)

1. Implement an appropriate mix of AFP surveillance, environmental surveillance, and enterovirus surveillance, with supplemental activities for high-risk, hard-to-reach populations or areas

Commented [BB24]: Moved all detailed tables to Annex E.

AFP Surveillance

Except for low-risk countries with highly developed health systems, AFP should remain a priority disease or condition with a standardized syndromic definition under any comprehensive routine or early warning surveillance system. Particularly in hospitals with neurology and pediatric neurology services, special attention should be paid to include surveillance for conditions which are the main differential diagnoses of poliomyelitis (such as Guillain-Barre syndrome, transverse myelitis, and traumatic neuritis). Each AFP case must be immediately reported to national authorities and investigated at the local level with stool collection and follow-up. Specific parameters for AFP surveillance (e.g. active vs. passive, population-based vs. sentinel sites, community- vs. facility-based, or integrated vs. single-disease structure) should be tailored to a country's risk status. Additionally, surveillance standards (such as NPAFP rate and stool adequacy percent) will evolve over time and by country risk category to meet required levels of sensitivity. If a poliovirus re-emergence is detected at any time, the affected area should employ surveillance strategies and standards at the levels of sensitivity required for high-risk countries during the three years post-certification.

Commented [BB25]: Added to highlight required attention for AFP surveillance

Commented [BB26]: Added to clarify the need to potentially re-introduce highly sensitive surveillance in response to a polio virus detection.

Environmental Surveillance

Since 2015, Environmental Surveillance (ES) has expanded among polio-endemic and high-risk countries where it is used to detect low-level transmission or provide an early indication of importation, especially in areas with possible gaps in AFP surveillance.⁶⁰ Because the benefits of ES will increase as the detectable paralysis-to-infection ratio of polio decreases⁶¹, the GPEI is preparing a revised long-term strategy to reflect increased reliance on this method.⁶²

In the post-certification era, the projected roles for ES include:

- Track the elimination of Sabin viruses after bOPV cessation or use of mOPV
- Support early detection of poliovirus circulation
- Monitor the geographic extent of transmission
- Guide outbreak response planning and monitor efficacy

Whereas current ES site selection is driven by the epidemiology of poliovirus circulation, in the post-certification era it will be based on areas or populations deemed vulnerable for re-emergence. Future site selection for both national and subnational locations should be based on comprehensive risk analysis, with consideration to the surveillance and laboratory capacity required to sustain quality. However, ES has potential limitations in terms of geographic locations where it can be applied, interpretation of findings, and technical implementation.⁶³

⁶⁰ World Health Organization. Polio environmental surveillance expansion plan. Geneva: April 2015. http://polioeradication.org/wp-content/uploads/2016/07/GPLN_ExpansionPlanES.pdf

⁶¹ 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

⁶² GPEI. Long-term Strategy for Poliovirus Environmental Surveillance. (In preparation).

⁶³ Asghar A, et al. Environmental surveillance for polioviruses in the global polio eradication initiative. *JID* 2014;210 (Suppl 1), S294-303.

Enterovirus Surveillance

Enterovirus surveillance (EVS) is primarily a passive, laboratory-based system which collects stool, respiratory specimens, or cerebral spinal fluid from a range of patients showing clinical symptoms of EV infection, including AFP. Though not polio-specific, EVS can be a useful auxiliary system, for example with specific high-risk urban populations or subpopulation groups. However, to be an effective tool for poliovirus surveillance, an EVS system should have known sensitivity and specificity.⁶⁴ Given the challenges in meeting these criteria, future use of EVS may be restricted to countries with relatively well-established health systems.

Supplemental Surveillance Activities for High-Risk Populations and Areas

Geographic, political, and social constraints create surveillance challenges with populations who either cannot or chose not to access health services.⁶⁵ These challenges can limit the value and sensitivity of any surveillance system including AFP. To address these challenges, supplemental strategies have been implemented at the national and subnational level.⁶⁶ The forthcoming GPSAP provides more details and guidance on implementing supplemental activities. In the post-certification era, these efforts will be intensified, especially the use of community-based surveillance (CBS) among hard-to-reach populations, such as is currently widely used in Afghanistan (see *Annex D* for general information on CBS). Global and regional efforts should be directed toward coordination, communication, and outreach tactics for intensified surveillance in high-risk intercountry areas (such as Lake Chad) or conflict zones.

Commented [B827]: Added example

2. Use event-based surveillance for early warning of potential poliovirus circulation

Event-based surveillance (EBS) is the organized collection, monitoring, assessment, and interpretation of mainly unstructured ad hoc information regarding health events which may represent an acute risk to human health.⁶⁷

For polio surveillance, triggers relevant to the re-emergence of polioviruses (such as media reports of clusters of paralysed children) will need to be introduced into the algorithms tracking ad hoc, informal sources. EBS can assist with early detection of possible re-emergence and thereby increase the overall sensitivity of polio surveillance. Countries can also add indirect and direct reports from the community, NGOs, informal community healthcare providers, or other sources of information such as social media or a national hotline.⁶⁸

⁶⁴ WHO EURO and US CDC. *Enterovirus surveillance guidelines*. Copenhagen, 2015

⁶⁵ These groups include: populations inaccessible due to insecurity or geographic isolation; failed states; ethnic minorities; migrants or nomads; internally displaced persons or refugees; or those living in densely populated urban areas, particularly slums.

⁶⁶ World Health Organization. *Outbreak surveillance and response in humanitarian emergencies: guidelines for EWAR implementation*, Geneva, 2012. http://whqlibdoc.who.int/hq/2012/WHO_HSE_GAR_DCE_2012_1_eng.pdf. And Hamisu AW, et al. *Strategies for improving polio surveillance performance in the security-challenged Nigerian states of Adamawa, Borno, and Yobe during 2009-2014*. *J Infect Dis*. 2016 May 1; 213(Suppl 3): S136–S139. *Global Polio Surveillance Action Plan*. (In preparation).

⁶⁷ World Health Organization. *Early detection, assessment and response to acute public health events: implementation of early warning and response with a focus on event-based surveillance*. Geneva. WHO/HSE/GCR/LYO/2014.4.

⁶⁸ WHO/WPRO. *Guide to establish event-based surveillance*. 2014. http://www.wpro.who.int/emerging_diseases/documents/docs/eventbasedsurv.pdf

Signals from EBS will require investigation and laboratory confirmation, but filters will be needed to avoid overwhelming the system with false-positives. The IHR authorizes WHO to review unofficial reports of public health events and obtain verification from Member States concerning such events.⁶⁹ As part of national early warning and response systems in high-risk countries, Emergency Operations Centers (EOCs) at the national or provincial level should include AFP as part of their regular monitoring of both IBS and EBS for signals of potential public health threats.

3. Develop surveillance among individuals with primary immunodeficiency diseases (PID) to detect and treat poliovirus excretors

Countering iVDPV risks requires early identification and treatment of individuals with PID who are excreting poliovirus. Since 2005, there has been a marked increase in known iVDPV cases, identified primarily in middle-income countries. However, the current and future prevalence of asymptomatic iVDPV excretors is difficult to estimate. While there is a potential for community spread of iVDPV, there has been no documented occurrences to date. Risks of transmissibility from asymptomatic long-term iVDPV excretors are also not fully known. The possibility that one or more PID patients may continue to excrete iVDPVs for several years after bOPV cessation represents a possible, but highly uncertain risk for re-emergence.⁷⁰ (See also **Activity 3.2.1.**)

The identification of iVDPV excretors without paralysis shows that AFP surveillance alone is not sufficient. Other options that are currently being piloted include: (1) identifying excretors among patients with PID (particularly B-cell deficiencies or combined immunodeficiencies) through immunology networks,⁷¹ and (2) **conducting clinical screening and then immunologic testing for those that meet the definition of possible PID in all children with or without paralysis younger than 15 years of age and attending a health facility within an AFP-reporting network.**⁷²

Commented [BB28]: Added detail.

Better understanding of the risk, including prevalence and survivability of PID patients and the transmissibility of iVDPV, will help determine a long-term strategy. Further development of bedside quantitative immunoglobulin testing also has the potential to greatly facilitate screening. Countries assessed as high-risk for iVDPV excretors will most likely require some measure of continued periodic screening of PID patients and follow-up of any identified chronic excretors. The extent to which this strategy is adopted by other countries will depend on tolerance towards undetected iVDPV excretion. Enhanced surveillance (e.g., frequent active surveillance, increased number of target facilities, expanded age groups) may be required during Years 6-9 post-certification when iVDPV are assumed to be the primary risk for poliovirus re-emergence.

4. Develop plans to detect any containment breach with potential community exposures

As part of the primary safeguards mandated under GAPIII, all poliovirus-essential facilities (PEFs) must develop a risk assessment plan to detect any breach within their facility that may

⁶⁹ World Health Organization. *International Health Regulations (2005)*, 3rd Edition. Geneva, 2016, Part II, Article 9.

⁷⁰ Duintjer Tebbens et al. Modeling the prevalence of immunodeficiency-associated long-term vaccine-derived poliovirus excretors and the potential benefit of antiviral drugs. *BMC Infectious Diseases* (2015) 15:379.

⁷¹ Aghamohammadi A, et al. Patients with primary immunodeficiencies are a reservoir of poliovirus and a risk to polio eradication. *Front. Immunol.*, 13 June 2017. <https://doi.org/10.3389/fimmu.2017.00685>.

⁷² El-Sayed ZA, et al. Poliovirus Excretion among Persons with Primary Immune Deficiency Disorders: Summary of Data from Enhanced Poliovirus Surveillance in Egypt, 2011-2014. *J Vaccines Vaccin* 2016, 7:4.

expose the surrounding community, including either a poliovirus release/spill or a worker exposure. To minimize risks, GAPIII also suggests locating PEFs in areas with effective AFP and environmental surveillance and efficient public health and response capacity. Given the potential consequences of a containment breach, additional global guidance will be developed by WHO to provide PEFs and national authorities with appropriate surveillance requirements. National authorities for containment (NACs) may also develop country-specific guidelines for community surveillance.

5. Maintain core polio laboratories and enhance innovations for rapid, reliable confirmation

All polio laboratories should continue to follow WHO-validated, standardized methodologies which will be continually updated to reflect the changing epidemiology of polio.

Future laboratory innovations and activities include:

- *Improve sample collection, transport, and processing methods.* After certification, the number of stool samples from AFP cases may decline; however, the ES workload will likely increase as this system gains use. Maintaining or improving laboratory efficiency will require innovations in the concentration and processing of ES samples (see **Research Activities** section). Even in locations without ES, containment requirements will necessitate some new approaches (see **Goal 1, Table 1**).
- *Improve diagnostics and testing algorithms.* Cell culture provides the highest diagnostic sensitivity and should be retained for processing stool samples in high-risk areas, as well as for all ES samples until other methods have been validated. Direct detection methods are now being tested which have the potential to provide faster results and simpler processing. As these methods become validated, they can be phased into wider use.
- *Continue global accreditation to ensure quality control.* Confidence in results from the GPLN has been dependent on a rigorous accreditation process for all laboratories. In the post-certification period, global experts should continue annual reviews to ensure quality assurance and control.⁷³

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

Global/regional surveillance responsibilities

Expectations for global and regional level surveillance activities are outlined in **Annex E, Table E2**. The scope and intensity of global support will gradually decrease over time, but the capacity to monitor quality and provide expert advice should be maintained. Regional capacity and support will depend on the risk level of their countries. Regions with multiple high-risk countries should

⁷³ For additional details and proposed operational strategies for the post-certification period, see *Global Polio Laboratory Network Strategic Plan. (In preparation)*.

pay attention to cross-border areas and may need to directly support active sentinel site surveillance, at least through Year 5 post-certification.

National level surveillance responsibilities

In keeping with the IHR expectation that each country should have core capacity to detect any potential PHEIC, primary responsibility for poliovirus surveillance lies at the national level. However, in the post-certification era, surveillance capacity required beyond this core level will depend on individual country risk. (See *Annex E, Table E2.*)



Integrating AFP surveillance systems with other vaccine-preventable disease (VPD) or communicable disease surveillance will be essential in order to sustain poliovirus surveillance.⁷⁴ The process of integration includes both expanding the scope (e.g., including other VPDs as targets of surveillance) and, if required, shifting management (e.g., from primarily WHO-led vs. MoH to MoH-led IBS systems). Even most high-risk countries have already added detection of measles/rubella and neonatal tetanus as part of AFP surveillance. Surveillance officers will be able to gradually shift focus from poliovirus detection to other diseases as the risk of re-emergence declines. While the ultimate objective should be to incorporate all surveillance management responsibilities into a consolidated government system, the timing of this transition will depend heavily upon national capacities.

Commented [BB29]: Added para with further clarification on the concept of integration.

Laboratory capacity and infrastructure

After certification, the GPLN must retain the capability to sustain polio eradication by testing stool and environmental samples and providing molecular epidemiological data. All countries should be able to confirm poliovirus either through national laboratories or efficient transportation

⁷⁴ Wassilak SG et al. Using Acute Flaccid Paralysis Surveillance as a Platform for Vaccine-Preventable Disease Surveillance. *JID*. 2017;216(S1):S293–8.

channels to reference laboratories. Sequencing will be increasingly important but not required in all locations. Economic, epidemiological, and containment considerations will influence the number, location, and diagnostic capacities at the global, regional, and national levels (see **Annex E, Table E2**). The GPLN will propose specific requirements for the global and regional levels, but each country will need to determine its own laboratory structure. As with other aspects of AFP surveillance, laboratory testing capacity for poliovirus should be integrated with other VPD laboratories as far as possible.⁷⁵

Information management

Access to reliable, quality, and timely AFP, laboratory, and environmental surveillance data, currently provided by the web-based polio information system (POLIS), will continue to be a strategic priority. High-quality data is critical not only to detect infections; it also helps in monitoring risk and surveillance performance.

Depending on levels of responsibility, future public health staff will need ready access to AFP reporting, linked laboratory/case-based data, IPV coverage data, and streamlined indicators of any supplementary immunization activity (SIA) implementation. Especially wherever passive AFP is the primary mode of surveillance, clinicians and community informants will need to be efficiently linked to central public health infrastructures to report suspicions of AFP cases. Mobile phones are already widely used, and there should be full utilization of new technologies in mobile health ("mHealth") and innovations such as Auto-Visual AFP Detection and Reporting (AVADAR).⁷⁶

Just as AFP reporting is globally standardized, it will become increasingly important in the post-certification period to develop similar standardized approaches for ES data. There also will be a need to maintain a global repository of poliovirus nucleotide sequences to facilitate tracking any detected poliovirus.

At the country level, any information system in the post-certification period should account for the specific data requirements related to country risk. High-risk countries should be able to continue reporting case-based AFP data to regional and global levels at least through Year 5 post-certification.

Global options for meeting these requirements include: (1) using POLIS as a platform for other VPDs with common data requirements, such as measles/rubella; (2) integrating polio data into an "EPI Information System" for all VPDs; or (3) relying on broader communicable disease monitoring under integrated disease surveillance and response (IDSR) systems. Some combination of approaches may be an option, though data validation will be required and a centralized global database for AFP should be maintained.

⁷⁵ Diop OM et al. The Global Polio Laboratory Network as a Platform for the Viral Vaccine-Preventable and Emerging Diseases Laboratory Networks. *JID*. 2017;216(S1):S299–307. Mulders MN et al. Expansion of Surveillance for Vaccine-preventable Diseases: Building on the Global Polio Laboratory Network and the Global Measles and Rubella Laboratory Network Platforms. *JID* 2017;216(S1):S324–330.

⁷⁶ World Health Organization. *mHealth: new horizons for health through global technologies*. Geneva, 2011. http://www.who.int/goe/publications/goe_mhealth_web.pdf

Objective 3.2: Adequate response capacity

A. Context

In order to respond promptly and effectively to public health risks and PHEICs as required by the IHR (2005), countries should develop preparedness plans and the capacity to implement public health emergency response operations, including risk communication.⁷⁷ The IHR obligates WHO to assist country capacity and provide support if local resources are insufficient.

B. Risks

The risks associated with developing an adequate response capacity along with the relevant mitigation measures and technical challenges are outlined in Table 6.

Table 6. Response risks and mitigation measures

Risk	Mitigation Measures	Technical Note
Delayed or ineffective response due to lack of proper risk assessment or preparedness	<ul style="list-style-type: none"> Identify future poliovirus outbreak risks through ongoing global, regional, and national assessments Develop global, regional, and national polio outbreak preparedness plans, including outbreak simulation exercises 	<ul style="list-style-type: none"> Comprehensive risk models have been developed, but their predictive value remains to be determined.⁷⁸
Failure to prevent transmission due to inadequate response strategies or capacity	<ul style="list-style-type: none"> Develop global protocol for polio outbreak response specific to post-certification era Develop specific community response strategies for containment breaches, humanitarian emergencies, and iVDPV excretors Maintain adequate global, regional, and national technical, operational, and management capacity as required by IHR + polio specific expertise to mount aggressive response 	<ul style="list-style-type: none"> Capacity to plan and implement a supplemental immunization activity (SIA) in response to an outbreak may rapidly diminish as experienced staff retire or move to other programmes.

IHR= International Health Regulations; iVDPV= immunodeficient vaccine-derived poliovirus; SIA= supplementary immunization activity

Commented [BB30]: Added technical notes

⁷⁷ World Health Organization. Protocol for assessing national surveillance and response capacities for the IHR (2005). Geneva, 2010. http://www.who.int/ihr/publications/who_hse_ihr_201007_en.pdf. Also see GHSA at <https://www.ghsagenda.org/>

⁷⁸ O'Reilly KM et al. An assessment of the geographical risks of wild and vaccine-derived poliomyelitis outbreaks in Africa and Asia. *BMC Infectious Diseases* (2017) 17:367. DOI 10.1186/s12879-017-2443-4

Risk (continued)	Risk Mitigation Measures	Technical Note
Failure to prevent transmission due to ineffective or insufficient vaccine or antiviral supply	<ul style="list-style-type: none"> Create and manage adequate stockpiles of mOPV and IPV Develop adequate supply of safe, effective, polio antiviral drugs (PAVDs) Develop alternative poliovirus vaccines and/or delivery systems which can increase effectiveness and/or supply 	<ul style="list-style-type: none"> IPV is highly effective in protecting individual recipients through humoral immunity, but role in stopping fecal-oral transmission is more limited; duration of protection of two-dose schedule is unknown.⁷⁹ Forecasting stockpile requirements for mOPV and IPV can be problematic. PAVDs under development show promise of efficacy; however, at least two drugs with differing mechanisms of action will most likely be required to minimize drug resistance.⁸⁰ See Research Activities section for new vaccines, Activity 2.2.2 for enhanced delivery methods.
Generation of new poliovirus outbreak if mOPV infects PID patients or is exported outside the outbreak zone into populations with decreasing mucosal immunity after bOPV cessation	<ul style="list-style-type: none"> Develop alternative polio vaccines (preferably oral) which prevent poliovirus transmission without risks of current Sabin vaccines Maximize SIA quality and consider 'ring' strategy with IPV around outbreak 	<ul style="list-style-type: none"> mOPV can present a risk for VAPP and VDPVs in a low-immunity setting.⁸¹ See Research Activities section for details on new poliovirus vaccines.

bOPV= bivalent oral poliovirus vaccine; IPV= inactivated poliovirus vaccine; mOPV= monovalent oral poliovirus vaccine; PAVDs= polio antiviral drugs; PID= primary immunodeficiency disease; SIA= supplementary immunization activity; VAPP= vaccine-associated paralytic poliomyelitis; VDPV= vaccine-derived poliovirus

C. What Will Be Done

Activity 3.2.1. Identify future outbreak risks, develop and implement preparedness plans, and prepare response strategies

Future outbreak risks

Continued global and regional forecasting based on AFP-based susceptibility indicators and other information (such as IPV coverage, migration data, or presence of humanitarian emergencies)

⁷⁹ Bandyopadhyay AS, et al. Polio vaccination: past, present and future. *Future Microbiol.* 2015;10(5):791-808. doi: 10.2217/fmb.15.19. Epub 2015 Mar 31.

⁸⁰ McKinlay MA, et al. Progress in the development of poliovirus antiviral agents and their essential role in reducing risks that threaten eradication. *J Infect Dis.* 2014 Nov 1;210 Suppl 1: S447-53. 3.

⁸¹ Estivariz CF, et al. Paralytic poliomyelitis associated with Sabin monovalent and bivalent oral polio vaccines in Hungary. *Am J Epidemiol.* 2011 Aug 1;174(3):316-25. Epub 2011 Jun 17.

should help identify countries or areas at risk for either immediate or long-term possible poliovirus re-emergence. Further analysis, including type-specific risks, trends, and quantification of potential emergences, should be periodically conducted to provide additional guidance on future programme priorities and resource requirements (see **Annex B**). Country risk assessments should also be used to drive preparedness and response strategies (see **Annex C**).

Preparedness plans

Global public health staff should develop and regularly update technical support plans and poliovirus-specific outbreak response guidelines. All countries should include detection of poliovirus as a possible scenario in their communicable disease outbreak preparedness response plans. Countries assessed as high-risk should develop and regularly review detailed polio-specific guidelines and periodically conduct a polio outbreak simulation exercise (POSE) at least through Year 3 post-certification.

Response strategies

The basis for responding to a possible outbreak should be the standard response procedures of verifying a global threat, conducting an immediate risk assessment, and establishing an Incident Management System (IMS) to guide operational support.⁸²

Country-level response strategies should follow global and regional guidelines. Existing standard operating procedures which provide guidance on risk assessment, control measures, and monitoring specific for responding to detection of a verified poliovirus will be updated prior to certification to reflect lessons learned, new considerations for poliovirus as an eradicated pathogen, and unprecedented low global population immunity.⁸³

Vaccine response strategies

Vaccine response strategies required after bOPV cessation should be proposed now in order to determine requirements for vaccine stockpiles (see **Activity 3.2.2**).

IPV should be used to respond in the unlikely event of a poliovirus detected in a country with good sanitation. If poliovirus is detected in areas where primary transmission is expected to be fecal-oral, vaccine response will be the homotypic mOPV related to the detected poliovirus, even if IPV has already been introduced into RI. As time after bOPV cessation increases and population mucosal immunity decreases, there is a risk that mOPV use could trigger new cVPDs outside

⁸² World Health Organization. *Emergency Response Framework*, 2nd edition. Geneva, 2017. <http://apps.who.int/iris/bitstream/10665/258604/1/9789241512299-eng.pdf>; 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.

⁸³ World Health Organization. *Standard Operating Procedures for responding to a poliovirus event or outbreak, Parts 1 and 2*. Geneva, 2017; and World Health Organization. *A guide for investigation of Sabin Like 2 (SL2) poliovirus in a human or in the environment*. Geneva, 2017.

the outbreak zone.⁸⁴ Adding IPV preemptively as a ring around an initial SIA target population is a potential strategy to reduce this risk that needs further research.⁸⁵

Given the risks of mOPV use and the limitations of IPV in areas with poor sanitation, developing alternative vaccines such as nOPV is critical for sustaining eradication. (See **Research Activities section**.)

Special response considerations

Hard-to-reach populations. Vaccination responses in areas of conflict, refugee camps, or dense urban communities may require modifications to the general guidelines to maximize SIA quality.⁸⁶

PID patients and iVPDV. Treating PID patients with an effective polio antiviral drug (PAVD) or combination of two drugs with a high potential to stop excretion and low risk for generating resistant variants will be critical to protecting them from VAPP and protecting the community from iVPDV.

The majority of OPV-infected PID patients spontaneously stop excreting any poliovirus in fewer than 6 months. A minority of PID patients excrete iVDPVs for ≥ 6 months and even fewer excrete chronically (>5 years).⁸⁷ These groups of prolonged excretors pose the primary risk for potential community transmission and are the priority for treatment. PAVDs currently under development show promising results—and one agent, pocapavir, is presently available for compassionate use while the ultimate combination antiviral product is developed (see **Research Activities section**). Further information on the specific types of PID most prone to excretion and the risk of iVPDV transmissibility will guide development of strategies for where, when, and how to most effectively treat PID patients excreting poliovirus.

In addition to treating individuals, community-based strategies should be introduced to reduce the risk of transmission. Detection of an iVDPV excretor should prompt vaccination of close contacts with IPV. If laboratory methods permit identification of a VDPV in an environmental sample as an iVDPV, public health officials should initiate a local search in the community and local health facilities. Until further information about iVDPV transmissibility is available, a decision whether to initiate a community vaccination response will depend on risk analysis of the source of the poliovirus (e.g., human vs. environment), and risk of further spread based on local force of infection, population immunity, and time since bOPV cessation.

Containment breach. All PEFs should have plans for responding to a containment breach in their facilities. GAPIII (or future editions) as well as national authorities for containment (NACs) should provide clear expectations for the speed, scope, and type of activities required. Global guidelines should advise all countries with a PEF on response in the event of potential community exposure following a poliovirus spill or exposure of facility staff (see also **Goal 1**).

⁸⁴ Famulare M, et al. Assessing the stability of polio eradication after the withdrawal of oral polio vaccine. <http://dx.doi.org/10.1101/084012>. doi: bioRxiv preprint first posted online 27 Oct 2016.

⁸⁵ Tebbens DJD and Thompson KM. Costs and benefits of including inactivated in addition to oral poliovirus vaccine in outbreak response after cessation of oral poliovirus vaccine use. *Medical Decision-Making Policy and Practice* 2017; doi:10.1177/2381468317697002 (published online 1 March 2017).

⁸⁶ See *Vaccination in humanitarian emergencies: implementation guide*. Geneva, 2017. http://www.who.int/immunization/documents/general/who_ivb_17.13/en/

⁸⁷ Tebbens RJD, Pallansch M, and Thompson KM. Modeling the prevalence of immunodeficiency-associated long-term vaccine-derived poliovirus excretors and the potential benefit of antiviral drugs. *BMC Infectious Diseases* (2015) 15:379.

Commented [BB31]: Edited to clarify potential use of IPV



Activity 3.2.2. Sustain trained human capacity and create, maintain, and manage adequate stockpiles of polio vaccine and antivirals for an appropriate response

Functional and human capacities

The critical functions required for responding to a poliovirus re-emergence are based on the core generic requirements for responding to any global health security threat.⁸⁸ To ensure technical quality in implementation, polio-specific components will be needed for selected functions, time periods, and geographic areas (see **Annex E, Table E3**).

If the response to a poliovirus detection is assessed as exceeding local capacity, the Global Outbreak Alert and Response Network (GOARN) should be mobilized to coordinate international support from multiple partners. Some polio-specific capacity within multidisciplinary response teams should be maintained at the global level within implementing agencies for at least 10 years after certification. Regional capacities should mirror the global level with requirements based on national capacities, especially of high-risk countries. High-risk regions have leadership and operational responsibilities for multicountry or border outbreaks and may require subregional staff to support both surveillance and outbreak response. Any global roster to provide surge capacity in the event of global emergencies should include public health experts with polio response experience.

High-risk countries should retain polio-specific capacities in Rapid Response Teams for critical responsibilities (such as planning and implementing an SIA) through Year 10 post-certification. Medium-risk countries should retain similar capacity through Year 5 post-certification. The breadth of this capacity and how it will be organized depends on individual country situations. Especially

⁸⁸ World Health Organization. *Emergency Response Framework, 2nd Edition*. Geneva, 2017.

for high-risk countries, Joint External Evaluations (JEE) assessing national capacity should identify areas in need of strengthening to maximize readiness for a poliovirus outbreak.⁸⁹

Polio vaccine stockpile

Maintaining appropriately sized stockpiles of IPV and type-specific mOPV is an essential mitigation strategy for risks of outbreaks. Determining the necessary doses for each type is complicated by uncertainty around the probability and size of future outbreaks, the type of vaccine for any outbreak response after bOPV withdrawal, and the anticipated shelf life of the stored vaccine. Modeling based on analysis of type 2 outbreaks following tOPV withdrawal will be informative, but decisions on required stockpile size ultimately will depend on risk tolerance for responding to outbreaks and avoiding stock-outs. Stockpiles of Sabin mOPV (bulk or prefilled) will need to be stored in facilities with the containment safeguards required by GAPIII. Stockpile management will also need to provide clear decision-making for vaccine release.

Antivirals

Although the number of PID patients requiring PAVDs is expected to be small, creating an antiviral supply could be an important mitigation measure for an unlikely, but highly consequential risk to sustained eradication.⁹⁰ Once the efficacy of PAVDs is confirmed and protocols for their use are determined, public communication tools and management parameters will need to be developed as part of a long-term strategy to ensure global accessibility.

⁸⁹ World Health Organization Joint external evaluation tool: International Health Regulations (2005). Geneva, 2016. http://apps.who.int/iris/bitstream/10665/204368/1/9789241510172_eng.pdf

⁹⁰ Duintjer Tebbens et al. Modeling the prevalence of immunodeficiency-associated long-term vaccine-derived poliovirus excretors and the potential benefits of antiviral drugs. *BMC Infectious Diseases* (2015) 15:379.

Polio research and development requires not only substantial resources, but also a forum to identify knowledge gaps and a mechanism for translating data into public health and immunization policy.



Research Activities

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

The GPEI partners maintain independent but highly collaborative polio research programs. The Polio Research Committee (PRC), which includes the GPEI partners and ex-officio representatives from the National Institutes of Health (NIH), the Food and Drug Administration (FDA), PATH, and WHO regional offices, serves as a forum to identify research needs, review current research activities, and support a competitive extramural research program. 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.

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 5**.)

Polio-focused research and development not only requires substantial resource allocation; because of its unique mission, it also 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 versions of the PCS will reflect stakeholder discussions and decisions on the status of the PRC, research oversight, and support after the closure of the GPEI at certification.

Goal 1: Contain Polio Sources

Poliovirus-essential facilities (PEF) include vaccine manufacturers, public health testing facilities, and academic laboratories which 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 release 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.

Restrictions on the use of all wild and Sabin polioviruses in clinical research will seriously limit the use of tests essential to assess population immunity as well as immunogenicity and efficacy of vaccines and antivirals. New assays for determination of serum antibodies and for assessment of mucosal immunity are in development.⁹¹ Also, if alternative poliovirus strains prove to be safe to

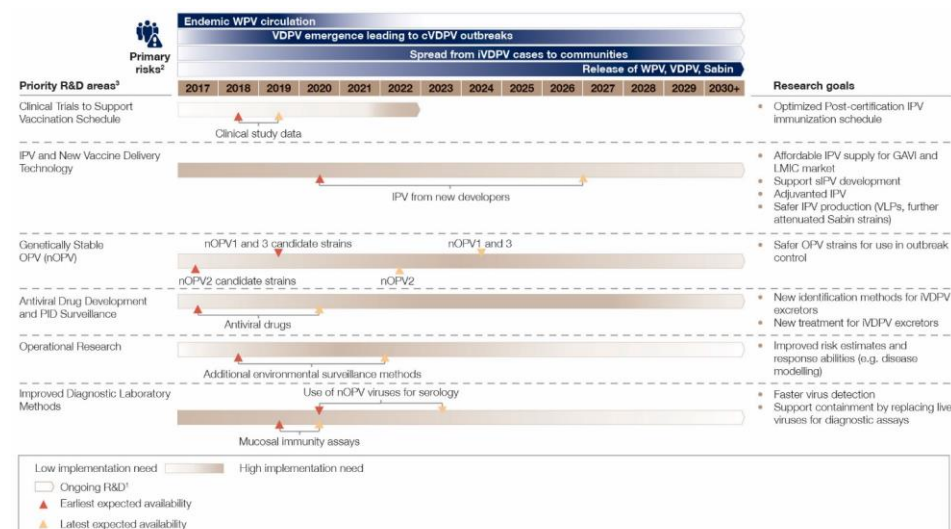
⁹¹ Wright PF, Connor RI, Wieland-Alter WF, et al. Vaccine-induced mucosal immunity to poliovirus: analysis of cohorts from an open-label, randomised controlled trial in Latin American infants. *Lancet Infect Dis* 2016; 16:1377-

Commented [BB32]: Research section has been edited to balance technical and general readership objectives and slightly re-formatted to better reflect linkages to Goals.

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use in the community (i.e., under deliberate release), they may be permitted to be deployed in open clinical trials that require OPV challenge tests to assess mucosal immunity elicited by a vaccine or efficacy of an antiviral drug.

Figure 5: Polio research and development



1. R&D to introduce new products may not always be complete before implementation need begins;
2. Timeline of risks assumes current certification timeline – research will continue regardless of certification timeline changes;
3. Specific research projects that are listed are examples, not an exhaustive list

IPV= inactivated poliovirus vaccine; iVDPV= immunodeficiency-associated vaccine-derived poliovirus; LMIC= Low and middle income countries; MAP IPV=IPV administered by microarray patches; nOPV=new OPV; OPV= oral poliovirus vaccine; PID=primary immunodeficiency disease; QIG=quantitative immunoglobulin; R&D= Research and development; sIPV= Sabin inactivated poliovirus vaccine; VLPs=virus-like particles

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.

Optimize individual protection with currently marketed IPV vaccines — SAGE recommended a two-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 are underway that will provide more information on the optimal full dose and fractional dose IPV schedules for primary

8410.1016/S1473-3099(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.

immunization by early 2019. These studies are complemented by operational research on delivery, feasibility, and costs associated with intradermal IPV administration.

New IPV development — Projected demand and supply for IPV are shown in **Figure 4** (see Goal Two). 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.⁹² 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 or virus-like particles (VLPs), and vaccines that include novel adjuvants like oil-in-water emulsions, E. coli double-mutant labile toxin (dmLT) and toll-like receptor (TLR) agonists.⁹³ 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 stand-alone 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.⁹⁴ Their future utility is uncertain due to the added costs of the devices and healthcare worker training, and because SAGE does not currently recommend IPV for campaigns or for outbreak control.

Microarray patches (MAPs) that deliver vaccine directly into the dermis can be applied quickly and easily by minimally trained healthcare 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

⁹² 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.

⁹³ 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.

⁹⁴ 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.

outbreak control. To date, MAPs suitable for clinical study have not been produced by any of the developers and future of MAP technology for polio immunization is uncertain.

Work continues on delayed-release IPV formulations 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 2024 or later.

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, innovations in environmental surveillance, and rapid diagnostics for identifying and characterizing polioviruses in the field and in the laboratory. Additional research on new poliovirus vaccines for outbreak response and development of antiviral drugs to clear infection in long-term, immunodeficient iVDPV excretors will also be critical to sustain a polio-free world.

Risk assessment and Modeling — Forecasting of short- and long-term risks will require development of models to predict the absolute and relative risks from WPV, cVDPV and iVDPV in all regions and over time until all credible threats to eradication are irreducible.⁹⁵ Post-certification, it will be critically important to continuously re-evaluate assumptions and update models based on past and current experience.

Ongoing modeling can assist in surveillance planning as the program adapts to changing risks over time and in different geographies by improving site selection, sampling frequency, and other operational facets of environmental surveillance. Modeling can also inform outbreak response planning and assess the impact of new surveillance tools and new vaccines and vaccine strategies.

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 standardized serological assays that are easy to perform and do not require live virus should improve timeliness, reduce costs, and mitigate the containment requirements of the current serum neutralization assay.

Operational research to improve surveillance and outbreak response — Operational research on surveillance and 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. Innovations on risk communication and community mobilization are being developed to address evolving perceptions about poliovirus among both health providers and the public.

Environmental surveillance — The world will rely on ES to detect new outbreaks, monitor persistent transmission, and provide evidence of the disappearance of Sabin poliovirus after the

⁹⁵ For examples see: 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; 4. O'Reilly KM et al. An assessment of the geographical risks of wild and vaccine-derived poliomyelitis outbreaks in Africa and Asia. *BMC Infectious Diseases* (2017) 17:367. DOI 10.1186/s12879-017-2443-4. Famulare M, et al. Assessing the stability of polio eradication after the withdrawal of oral polio vaccine. <http://dx.doi.org/10.1101/084012doi: bioRxiv preprint first posted online 27 Oct. 2016>.

withdrawal of bOPV or mOPV use.⁹⁶ Improvements to environmental surveillance will require research on optimization of site selection through modeling, demography, and use of GIS technology; and continued innovation of specimen collection, sample concentration, and molecular detection methods to distinguish and characterize poliovirus isolates from individual excretors in the sample population.

Rapid diagnostic tests — Development of rapid diagnostic tests that can be applied in the field for quick, point-of-care (POC) testing could enhance both AFP and environmental surveillance in the future.

Genetically stable new OPV — To mitigate the risk of mOPV use seeding a new VDPV outbreak, Sabin-derivative OPV strains modified to increase genetic stability and reduce neurovirulence compared with the Sabin viruses are under development. Two new OPV type 2 (nOPV2) candidate strains have been manufactured for clinical study and human trials are now underway. Proof of concept is anticipated by 2019 and, if successful, nOPV2 could be available as early as 2021. New OPV1 and OPV3 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.

Identification of iVDPV excretors — The risk from iVDPV excretors will be reduced only with effective surveillance and treatment protocols. Recent prevalence surveys found a 1% iVDPV excretion prevalence among patients with hereditary immunodeficiency syndromes in selected middle-income countries in Africa, the Middle East and Asia. A study assessing the feasibility of extending surveillance beyond the centralized immunology clinics in Egypt found mixed success. The objectives, scope, strategies, and operational requirements for pre- and post-eradication PID surveillance are now under active review.

Antiviral drugs — 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, pocapavir, a capsid inhibitor, and the 3C protease inhibitor V-7404.^{97,98} Assuming successful completion of clinical trials, ViroD7000 (a combination of pocapavir and V-7404) will be available for distribution under named-patient protocol and further assessed for efficacy in a concurrent Phase II challenge study in 2019. However, antiviral drug development will inevitably extend into the post-certification era.

⁹⁶ 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.

⁹⁷ 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.

⁹⁸ Collett MS, Hincks JR, Oberste MS, van der Avoort HGM. Anti-poliovirus activity of pocapavir in a human mOPV1 challenge model. In: 53rd Interscience Conference on Antimicrobial Agents and Chemotherapy. (Denver). 2013.



Annex A

Annex A

PCS Engagement List

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The GPEI engaged a broad set of stakeholders as an opportunity to gather input and begin reviewing the critical functions that will be needed to continue after certification to maintain a polio-free world. These stakeholders and organizations include:⁹⁹

- WHO Member States and Executive Board
- WHO and UNICEF regional office focal points for Polio and EPI
- WHO Regional Committees
 - Regional Committee for the Americas
 - Regional Committee for the Eastern Mediterranean
 - Regional Committee for the Western Pacific
- Technical Advisory Groups
 - Regional Immunization Technical Advisory Group for the African Region
 - Immunization Technical Advisory Group for the South-East Asia Region
 - Technical Advisory Group on Immunization and Vaccine-Preventable Diseases in the Western Pacific Region
- Polio Partners Group in 2017 (additional touch points with Co-Chairs and major donors)
- Transition Independent Monitoring Board (TIMB)
- Global Commission for the Certification of Poliomyelitis Eradication (GCC)
- Strategic Advisory Group of Experts on Immunization (SAGE)
- SAGE Polio Working Group
- Measles and Rubella Initiative
- Yellow Fever Initiative
- WHO Focal Point for Smallpox
- Kid Risk modeling group
- Imperial College modeling group

⁹⁹ A full list by organization and focal point can be shared upon request.

- Institute for Disease Modeling polio team
- Gavi, the Vaccine Alliance
- CORE (Coalition of NGOs)
- GPEI Partners (Polio and Immunization teams at global and regional levels)
- GPEI Management Groups and Task Teams
- Polio Oversight Board (POB)
- Global Polio Laboratory Network (GPLN)
- WHO Health Emergencies Program

The PCS team conducted two rounds of consultations during which a wide range of stakeholders were given the opportunity to review and provide feedback on drafts of the strategy (see Figure 6). Some groups, such as the PPG and SAGE, were consulted at multiple touch points beyond the consultation rounds. Details on the first round of consultations can be found in the PCS consultation report.¹⁰⁰

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Figure 6. Consultation summary provided to the Polio Oversight Board

	Participants	Results
First Consultation Round (August 2017)	<ul style="list-style-type: none"> Major donors Polio Partners Group (PPG) Co-chairs Transition Independent Monitoring Board (TIMB) members GCC, SAGE chair, SAGE Polio Working Group chair Disease modeling agencies (Kid Risk, Imperial College, IDM¹) Gavi, the Vaccine Alliance, Measles & Rubella & Yellow Fever Initiatives GPEI partnership agencies, including WHO and UNICEF regional offices Smallpox focal points for lessons learned 	<p>The team received feedback from 50+ respondents from across a wide range of stakeholders.</p>
Second Consultation Round (November 2017)	<ul style="list-style-type: none"> All participants from First Consultation Round Global groups (IHR EC², GHS³, GVAP⁴ working group members) Non-polio donors (e.g. Sweden, Denmark) Full Polio Partners Group Polio transition priority countries Core NGO group focal points Member states and immunization stakeholders 	<p>Consolidated feedback from 15+ organizations / agencies, including:</p> <ul style="list-style-type: none"> • 3 Major Donors • 3 WHO and UNICEF regional offices and regional technical advisory groups • 1 TIMB member • Gavi, SAGE, GCC

¹ Institute for Disease Modeling; ² International Health Regulations Emergency Committee; ³ Global Health Security; ⁴ Global Vaccine Action Plan

¹⁰⁰ Report of the first stakeholder consultation on the draft polio Post-Certification Strategy, November 2017.
<http://polioeradication.org/wp-content/uploads/2017/11/polio-post-certification-strategy-1st-report-august-2017.pdf>.

Annex B

Annex B

Risk Analysis

The annex provides additional technical explanation and analysis on the risk categories identified in the *Post-Certification Strategy* (PCS).

Beyond familiar outbreak risk factors, the future poses new challenges amidst uncharted terrain. After eradication and bOPV cessation, population mucosal immunity will eventually be low across all ages, a situation unprecedented in recorded history. Future high birth cohort rates may translate into an exponentially increasing number of children requiring vaccination. Placing further stress on health systems, a worldwide increase in political and economic migrants who often live in urban areas without access to clean water will have significant epidemiological effects. Climate change adds to these difficulties through extreme weather conditions and rising temperatures, which not only contributes to disease spread and geographic changes in disease distribution but also produces famine and malnutrition, thereby weakening population immunity. Addressing the specifics of these risks and their impact are beyond the scope of the PCS.

The amount of time since bOPV cessation has already been identified as a key determinant of risk for poliovirus re-emergence in the post-certification period, which impacts the proposed mitigation strategies. Several other factors influence the likelihood of re-emergence and the severity of an outbreak. These include: virus category (transmissibility and neurovirulence differ by WPV and VDPVs vs. Sabin/OPV), population characteristics (size, density, mobility, and accessibility), environmental variables (sanitation and climate), health infrastructure capacities, and the broader geopolitical context.¹⁰¹

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Future outbreak risks

Risk Category #1: Risks due to continued use of OPV

The risk of vaccine-associated paralytic poliomyelitis (VAPP) following exposure to trivalent OPV (tOPV) has been well documented, but the risk from monovalent OPV (mOPV) in countries with high fecal-oral transmission of poliovirus is unknown.¹⁰² There is evidence that mOPV use can be associated with VAPP, particularly mOPV3, so the risk is expected to continue as long as any

¹⁰¹ For detailed review see Fine PEM and Ritchie S. *Perspective: Determinants of the Severity of Poliovirus Outbreaks in the Post Eradication Era. Risk Analysis*, Vol. 26, No. 6, 2006, 1533-1540.

¹⁰² Bandyopadhyay AS, et al. *Polio vaccination: past, present and future. Future Microbiol.* 2015;10(5):791-808. doi: 10.2217/fmb.15.19. Epub 31 Mar 2015.

OPV is used in outbreak response.¹⁰³ However, vaccination with IPV as proposed for routine immunization use after certification could protect against VAPP.¹⁰⁴

Models and prior experience with vaccine-derived poliovirus (VDPV) emergence provides imperfect though useful estimates of the future number of VDPVs. Uncertain risk factors (e.g., type-specific population immunity, population mixing and mobility, and local environmental factors influencing the propensity for fecal-oral transmission) translate into wide ranges for predicted future emergences—though these ranges can be instructive for vaccine stockpile needs and other response strategies and requirements (see **Activity 3.2.2**).

The number of type 2 emergences in the first year post-tOPV withdrawal have been at the high end of what models predicted.¹⁰⁵ The number and geographic distribution have highlighted the importance of high-quality surveillance and pre-cessation SIAs; they also demonstrate the continued susceptibility of populations in insecure or inaccessible areas. Nevertheless, the risk for type 2 cVDPVs associated with tOPV use should decline rapidly and the probability of further outbreaks by certification should be very low. However, low-quality outbreak response with mOPV2 to the type 2 cVDPV outbreaks to date could imply continued transmission of the cVDPV virus or emergence of new cVDPVs.

Experience to date with type 2 can help guide estimations of future risk from types 1 and 3, though there are differences in virulence, reversion patterns, transmissibility, and secondary immunity benefits of OPV which need to be considered. Since cVDPVs were first characterized in 2000, 87% of cVDPVs detected through October 2017 have been type 2 with only 12% type 1 and 1% type 3.¹⁰⁶ (Prior to the shift from tOPV to mOPV and bOPV for SIAs starting in 2005, the majority of VDPVs were type 1.) The historical predominance of type 2 cVDPVs may be attributed to several factors: (a) differences in OPV reversion rates (OPV2>OPV1>OPV3); (b) improved cVDPV surveillance accompanied by the change to a more sensitive case definition of type 2 cVDPVs than type 1 and 3 cVDPVs; and (c) the lack of competition for susceptible individuals given the global eradication of WPV type 2 in 1999.

While specifics surrounding future outbreaks are unknown, the risk of cVDPV 1 and 3 post-bOPV cessation should be similar to, or even smaller than, the risk for type 2 after tOPV withdrawal.¹⁰⁷ Failure to maintain routine bOPV coverage until cessation, introduce IPV, or conduct high-quality pre-cessation SIAs in areas with low RI coverage could increase the risks of cVDPV (particularly type 1) emergences.¹⁰⁸

IVDPV

The global prevalence of B-cell related PID patients is uncertain due to variabilities in diagnosis, reporting, and survival rates. PID patients are expected to have a lower survival rate in low-income countries which tend to use OPV although recent cases have been identified. Although OPV use

¹⁰³ Estivariz CF et al. Paralytic poliomyelitis associated with Sabin monovalent and bivalent oral polio vaccines in Hungary. *Am J Epidemiol.* 2011 Aug 1;174(3):316-25. doi: 10.1093/aje/kwr070. Epub 2011 Jun 17.

¹⁰⁴ Bandyopadhyay AS, et al. Polio vaccination: past, present and future. *Future Microbiol.* 2015;10(5):791-808. doi: 10.2217/fmb.15.19. Epub 2015 Mar 31.

¹⁰⁵ Kroiss S, et al. OPV2 cessation risks. Presentation to Cessation Risk Task Team, Atlanta, 13 June 2017.

¹⁰⁶ Compiled from WHO database of poliovirus cases, 17 October 2017.

¹⁰⁷ Lyons H et al. OPV13 cessation and SIA planning. Presentation to Polio SAGE WG, September 2017, Geneva.

¹⁰⁸ Duintjer Tebbens et al. Maintenance and intensification of bivalent oral poliovirus vaccine use prior to its coordinated global cessation. *Journal of Vaccines and Vaccination* 2016;7(5):340.

would put these countries at the highest risk for transmission from iVDPV excretors, decreased survival of these patients reduces the risk to communities. PID patients in high-income countries have much better survival rates but, as these countries stopped OPV use or are transitioning to IPV-only use, the risk for new iVDPVs is decreasing with time. The primary risk for iVDPVs and the source of most reported cases since 2005 has been from middle-income countries.

A recent study from 13 OPV-using countries found 2% of PID patients excreted poliovirus and only 0.8% of patients (all with combined immunodeficiency) were iVDPV excretors.¹⁰⁹ The vast majority of OPV-infected PID patients spontaneously stop excreting in less than six months. Another summary of screening studies among PID patients reported 2.7% with poliovirus excretion and 0.1% with documented iVDPV excretion >6 months.¹¹⁰ Among the 101 iVDPV cases in the WHO global registry of iVDPV cases detected between 1962-2016, average excretion duration has been approximately one year; only 7 (7%) were chronic (e.g. >5 years) excretors. Only 8 excretors (one chronic excretor) are alive and excreting at last specimen.¹¹¹

The risks for new iVDPVs should continue to decline as countries with the highest rates of PID survivability stop using OPV. Nevertheless, any iVDPV excretors could present a potential reservoir for transmission of neurovirulent poliovirus and a potential threat to sustaining polio eradication.

Evidence of iVDPV transmission among family contacts or into the community is very rare and no poliomyelitis outbreaks have been attributed to iVDPV.^{112,113}

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

Risk Category #2: Risks due to unsafe handling

As explained in the context of Goal One, the likelihood of poliovirus release from a facility depends on the number of facilities handling polioviruses and the adherence of those facilities to international biorisk management standards during storage and manipulation of poliovirus-harboring materials. The potential for poliovirus released from facilities reinitiating circulation in surrounding communities will depend on the type of material released and the presence of population and environmental factors that facilitate poliovirus transmission.^{114,115}

The highest risk of community exposure is through facility personnel who are unknowingly contaminated or infected with poliovirus. Community exposure through ingestion of water or food

¹⁰⁹ Aghamohammadi A, et al. Patients with primary immunodeficiencies are a reservoir of poliovirus and a risk to polio eradication. *Frontiers in Immunology*. 8:685. Doi:10.103389/fimmu.2017.00685.

¹¹⁰ Duintjer Tebbens RJ, et al. Modeling the prevalence of immunodeficiency-associated long-term vaccine-derived poliovirus excretors and the potential benefits of antiviral drugs. *BMC Infectious Diseases* 2015;15:379

¹¹¹ Macklin G, et al. Prolonged Excretion of Poliovirus among Individuals with Primary Immunodeficiency Disorder: An Analysis of the World Health Organization Registry. *Front. Immunol.*, 25 September 2017. Available at <https://doi.org/10.3389/fimmu.2017.01103>

¹¹² Avellon A, et al. Paralysis Case and Contact Spread of Recombinant Vaccine-derived Poliovirus, Spain. *Emerging Infectious Diseases*. (2008) 14:1807-09.

¹¹³ Transmission of Imported Vaccine-Derived Poliovirus in an Undervaccinated Community in Minnesota <https://academic.oup.com/jid/article-lookup/doi/10.1086/596052>

¹¹⁴ 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(6):1449-69.

¹¹⁵ Fine PE, Ritchie S, Fine PEM, Ritchie S. Perspective: determinants of the severity of poliovirus outbreaks in the post eradication era. *Risk Anal* 2006; 26(6):1533-40.

contaminated with liquid effluents will depend on the poliovirus content of facility spill, the integrity and type of sewerage system, and the potential for human consumption.¹¹⁶ Deliberate release of wild, vaccine- or genetically-engineered polioviruses is also possible.¹¹⁷ Although polioviruses are currently considered a low threat agent for a biological weapon because they cause low morbidity and mortality and are too fragile to disperse in an effective manner, the consequences of a deliberate release may be very serious with time.

A small number of containment failures have been reported in the last 25 years, but only one was associated with paralytic cases. During the 1990s, WPV used for vaccine manufacturing was isolated in one child in the Netherlands and one child in France. The father of one child worked in an IPV manufacturing plant but an epidemiological link could not be identified for the second child.¹¹⁸ Between 2000 and 2003, a type 2 poliovirus used exclusively for IPV manufacture and quality control (MEF-1) was isolated from nine children with AFP in India. The same type was found in vials of a single batch of tOPV.¹¹⁹ In 2014, a vaccine production plant in Belgium accidentally released into the sewage system 45 liters of vaccine concentrate containing 10^{13} infectious WPV type 3 particles, which subsequently discharged into rivers and the North Sea at concentrations high enough to cause infection from swimming or consuming raw shellfish for several days.¹²⁰ Finally in 2016, a worker was infected following an accidental spillage in a Dutch vaccine manufacturing plant.¹²¹

A modeling analysis found that a poliovirus release from vaccine production sites into countries with high transmission risk several years after bOPV cessation could result in uncontrollable transmission that would require OPV restart.¹²² This situation was found in one out of 100 iterations of the model, whereas introduction of VDPV1 by a long-term PID excretor caused the other iteration associated with an uncontrollable outbreak.

Risk Category #3: Risk due to undetected transmission

The last detected case of WPV2 was in 1999, and in September 2015 the Global Commission for the Certification of Poliomyelitis Eradication (GCC) confirmed that wild type 2 poliovirus has been globally eradicated. In July 2017, the GCC noted that modeling suggests that, in the presence of high-quality AFP surveillance and high population immunity, a period of three years without

¹¹⁶ See Dowdle W, van der Avoort H, de Gourville E, et al.

¹¹⁷ Cello J, Paul AV, Wimmer E. Chemical synthesis of poliovirus cDNA: generation of infectious virus in the absence of natural template. *Science* 2002; 297(5583): 1016-8.

¹¹⁸ Mulders MN, van Loon AM, van der Avoort HG, et al. Molecular characterization of a wild poliovirus type 3 epidemic in The Netherlands (1992 and 1993). *J Clin Microbiol* 1995; 33(12): 3252-6.

¹¹⁹ World Health Organization. Update on actions taken following the isolation of MEF-1 reference poliovirus associated with acute flaccid paralysis cases in India in late 2002 and early 2003. *Wkly Epidemiol Rec* 2003; 78(32): 284.

¹²⁰ Duizer E, Rutjes S, Husman AMR, Schijven J. Risk assessment, risk management and risk-based monitoring following a reported accidental release of poliovirus in Belgium, September to November 2014. *Eurosurveillance* 2016; 21(11): pii=30169.

¹²¹ Duizer E, Ruijs WL, van der Weijden CP, Timen A. Response to a wild poliovirus type 2 (WPV2)-shedding event following accidental exposure to WPV2, the Netherlands, April 2017. *Eurosurveillance* 2017; 22(21).

¹²² 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: 389.

detection of both WPV types 1 and 3 provides high confidence (95%) for concluding the eradication of both types.¹²³

Given that the GCC is expected to require strict surveillance and immunity standards prior to declaring global eradication, the magnitude of risk for continuing circulation of WPV types 1 or 3 after certification should be quite small and diminish rapidly, as long as surveillance quality remains high. After five years without detecting cases the probability of undetected transmission drops to 0.1-1%.¹²⁴

¹²³ Global Commission for the Certification of Poliomyelitis Eradication. Report from the Sixteen Meeting, Paris, France, 4-5 July 2017. For modeling to support their assessment, see: Eicherner M and Dietz K. Eradication of poliomyelitis: when can one be sure that polio virus transmission has been terminated? *Am J Epidemiol.* 1996 Apr 15;143(8):816-22; and Kalkowska DA, et al. Modeling undetected live poliovirus circulation after apparent interruption of transmission: implications for surveillance and vaccination. *BMC Infectious Disease* 2015; 15:66. Doi 10.1186/s12879-015-0791-5. McCarthy et al. A spatial model of Wild Poliovirus Type 1 in Kano State, Nigeria: calibration and assessment of elimination probability. McCarthy et al. *BMC Infectious Diseases* (2016) 16:521. Famulare M. Has Wild Poliovirus Been Eliminated from Nigeria? *PLoS ONE* 10(8): e0135765. doi:10.1371/journal.pone.0135765.

¹²⁴ Dietz K. Eradication of poliomyelitis: when can one be sure that polio virus transmission has been terminated? *Am J Epidemiol.* 1996 Apr 15;143(8):816-22.

Annex C

Country Risk Classification

In the post-certification era, a risk-based surveillance approach is recommended to maintain a polio-free world. Classification of a country's risk is based on the three risk categories: (1) continued OPV use; (2) unsafe handling of polioviruses; and (3) undetected transmission.

Shedding of immunodeficiency-associated vaccine-derived poliovirus (iVDPV) among primary immunodeficiency disease (PID) patients may also result from continued OPV use; this is not addressed in the classification scheme. Further research is needed to better understand the prevalence of PID and transmissibility of iVDPV, as well as to identify effective surveillance strategies for detection. These findings and recommendations will be published in a future version of the *Post-Certification Strategy* (PCS). Finally, development of vaccine-associated paralytic poliomyelitis (VAPP) is a risk of continued OPV use but is not addressed in the classification scheme.

Ambiguous vaccine-derived polioviruses (aVDPV) also pose a potential threat to a polio-free world after certification. The origin and properties of aVDPVs are unclear but are believed to be closer to cVDPV than to Sabin viruses. aVDPVs may die out spontaneously or may be the first indication of a cVDPV outbreak and, due to this uncertainty, aVDPVs are treated as cVDPVs for country risk classification purposes.

Rationale for Risk Classification Criteria

1. Continued OPV use: The risks associated with continued OPV use are further classified to address type-specific difference in OPV use.
 - Emergence of cVDPV1 or 3 (bOPV use in routine immunization): Factors included as part of the classification criteria are bOPV use, vaccine coverage, and country income-level (as a surrogate for health and sanitation infrastructure). Only bOPV use in routine immunization is a consideration due to the absence of tOPV and mOPV1 or 3 use. Vaccine coverage and country income-level are used to roughly estimate population immunity. Vaccination coverage alone is inadequate because effectiveness of OPVs can be reduced depending on country circumstances. Country-income level is used to account for these country-specific factors.
 - Emergence of cVDPV2 (mOPV2 use for outbreak response): mOPV2 use and IPV coverage are factors used in the classification criteria. mOPV2 is the only Type 2-containing OPV that will be used prior to certification. Although the overall risk of cVDPV2 at the time of certification will be low, the risk will be higher in countries that

used mOPV2 for outbreak response. IPV coverage is used as a proxy for population immunity to Type 2.

2. Unsafe handling of polioviruses: Any country with a poliovirus-essential facility (PEF) will be at risk of an unintentional release of poliovirus. The country risk classification criteria are based on factors that increase the risk of transmission following release which are (a) amount of virus released and (b) population vulnerability.
 - a. Amount of virus released: Vaccine manufacturing PEFs will have higher volumes and concentrations of poliovirus in materials than laboratory PEFs.
 - b. Population vulnerability: High IPV coverage in a country with a vaccine manufacturing PEF can protect vaccinated individuals from paralysis and mitigate the risk of transmission from a release in areas where oropharyngeal transmission predominates. Furthermore, country income-level is used as a proxy for health and sanitation infrastructure, which are linked to routes of transmission and transmissibility.

Categories of virus (WPVs, VDPVs, Sabin viruses) were not distinguished because release of any poliovirus poses a serious threat even though transmissibility differs by category. Intentional release of poliovirus is not addressed because of its unpredictability.

3. Undetected transmission: Continued circulation of a previously identified cVDPV is of concern because it is unknown when extinction of the virus occurs. Modeling results of cVDPV type 2 suggests extinction occurs if it has not been detected within three years of last detection even in the presence of poor surveillance.¹²⁵ The time periods used for each risk group reflects a cautious interpretation of modeling results including extrapolation to cVDPV types 1 and 3.

Final Determination of Country Risk Classification

The categories and criteria for risk classification for poliovirus re-introduction are summarized in Table 10. A country should assess each of the risk categories independently as it may be high risk for one risk category and low risk for another. A single high-risk determination leads to a preliminary classification as a high-risk country. In the absence of any high risk, a single medium risk determination leads to a preliminary medium risk classification. In the absence of any high or medium risk, a country is preliminarily classified as low risk.

Final determination and classification of country risk will be completed in collaboration with WHO regional offices. In some large countries, the preliminary assessment may apply to only certain provinces or geographic areas (usually population blocks of at least 10 million). Countries also need to consider the risks posed by bordering countries. This multinational approach is intended to ensure continuity of surveillance activities across high-risk border areas (e.g., Lake Chad).

¹²⁵ Kalkowska DA, et al. Modeling undetected live poliovirus circulation after apparent interruption of transmission: implications for surveillance and vaccination. *BMC Infectious Disease* 2015; 15:66. Doi 10.1186/s12879-015-0791-5.

Surveillance Strategies

Countries should adopt a mix of strategies appropriate for their corresponding finalized country risk classification that is reflective of the changing potential re-emergence of poliovirus post-certification (see **Figure 2** and **Annex E, Table E1**). This will efficiently address the varying risks across all risk categories and avoid the complexities associated with changing surveillance strategies over a short period of time.

Poliovirus Outbreaks

Poliovirus outbreaks outside of high-risk countries will immediately lead to reclassification of the country as high-risk, which will require changes to its long-term surveillance strategies and activities. This will also necessitate WHO regional office consultation to determine if reclassification of neighbouring countries will be needed. The use of mOPV as part of outbreak response activities will necessitate high-risk surveillance strategies (e.g., active surveillance) to continue for at least two years after last mOPV2 use to detect any emergence of VDPVs.

Country Risk Classification over Time

Prior to certification, all countries should assess their future risk for the re-introduction of poliovirus using the most current version of the PCS. After certification, the PCS is anticipated to be updated prior to each post-certification stage (see **Annex E, Table E1**). This presents an opportunity to re-assess and re-tool the country risk classification criteria. Countries are expected to re-evaluate their risks using the updated risk classification criteria, potentially resulting in a move from one risk classification category to another. This is expected and countries need to ensure their surveillance strategies are appropriate for their new risk classification.

Of note, a number of the criteria used for the country risk classification are based on time since an important milestone. For example, Table C1 is based on time since certification. With subsequent updates of the PCS, other milestones will be used such as bOPV cessation.

Table C1. Summary of risk categories and criteria for country risk classification

Risk Categories	Country Risk Classification			
	High Risk	Medium Risk	Low Risk	Negligible Risk
Emergence of cVDPV1 or 3⁺: bOPV use in routine immunization	bOPV used in the 5 years prior to certification AND OPV3 coverage (5-year median): <65% in middle-income country* OR <80% in low-income country*	bOPV used in the 5 years prior to certification AND OPV3 coverage (5-year median): <80% in high-income country* OR 65-79% in middle-income country* OR 80-89% in low-income country*	bOPV used in the 5 years prior to certification AND OPV3 coverage (5-year median): ≥80% in high- or middle-income country* OR ≥90% in low-income country*	No bOPV used in the 5 years prior to certification
Emergence of cVDPV2⁺: mOPV2 use for outbreak response	Used mOPV2 in the 5 years prior to certification and IPVfinal [^] coverage (5-year median) <80%	Used mOPV2 in the 5 years prior to certification and IPVfinal [^] coverage (5-year median) 80-89%	Used mOPV2 in the 5 years prior to certification and IPVfinal [^] coverage (5-year median) >90%	No mOPV2 used prior to certification
Unsafe handling of polioviruses	Vaccine manufacturing PEF located in a low-income country*	Vaccine manufacturing PEF located in a middle-income country* AND most recent national IPVfinal [^] coverage <90% OR Laboratory PEF located in a low-income country*	Vaccine manufacturing PEF located in a high- or middle-income country* AND most recent national IPVfinal [^] coverage ≥90% OR Laboratory PEF located in a high- or middle-income country*	Country with no PEFs
Undetected cVDPV⁺ transmission	Last cVDPV detected in the country was ≤ 5 years before certification	Last cVDPV detected in the country was 6-8 years before certification	Last cVDPV detected in the country was ≥9 years prior to certification	cVDPV was never detected in the country

*Country income according to World Bank classification of high-, middle- and low-income countries. Coverage rates based on country specific WHO/UNICEF immunization coverage estimates (or reliable data relevant to specific areas).

[^]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.

*aVDPV to be treated as cVDPV when conducting the country risk classification

Annex D

Other Relevant Surveillance Systems

Most countries have established 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. (Acute flaccid paralysis [AFP] surveillance is an example.) Although standardized IBS approaches for both global¹²⁶ and regional levels (e.g., Integrated Disease Surveillance and Response in Africa¹²⁷) 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 programme 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.

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

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 programme impact. Polio eradication efforts are also unique among programmes 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 diseases such as viral hemorrhagic fevers, meningitis, cholera, Zika, etc.) utilizes a mix of surveillance strategies based on risk level in order to achieve programme

¹²⁶ World Health Organization. *Recommended Surveillance Standard*, 2nd ed. Geneva, WHO; 1999.

¹²⁷ *Technical Guidelines for Integrated Disease Surveillance response in the African Region*, 2nd ed. Brazzaville, Atlanta: Who Regional Office for Africa, CDC; (2010).

objectives to control or eliminate epidemics. Case-based surveillance reporting from health facilities is generally used in high-risk countries and a sentinel surveillance approach in moderate-risk countries. Low-risk countries tend to have more developed health systems and can rely on routine surveillance but may develop targeted systems if an unusual threat arises in a particular subnational area. 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, the focus is on passive reporting from district or tertiary healthcare 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 poliovirus surveillance or found it difficult to sustain the expected AFP quality indicators over time. Enterovirus surveillance is commonly utilized in Europe to passively 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. which may be caused by a wide variety of agents.¹²⁸ At clinician discretion, laboratories collect and process stool, respiratory, or cerebral spinal fluid specimens. In the United States, the National Enterovirus Surveillance System (NESS) is a passive, voluntary surveillance system that monitors sentinel-site laboratory detections of enteroviruses and human parechoviruses. A cluster of suspicious EV cases, such as acute flaccid myelitis, may prompt more active case investigation and enhanced surveillance.¹²⁹

Community-based surveillance (CBS) – Community informants or village based volunteers have been used in many countries as informal sources of information on AFP cases. On a wider scale, CBS can be a useful source of event-based surveillance (EBS) to track disease trends or identify unusual health events at the local level by detecting clusters of people with similar signs and symptoms. 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 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 usually are paid a small stipend to monitor trends and detect clusters of various syndromes, including paralysis, in their districts through regular interviews of village leaders.¹³⁰ 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.

¹²⁸ CDC and WHO Regional Office for Europe. *Enterovirus surveillance guidelines: guidelines for enterovirus surveillance in support of the Polio Eradication Initiative*. Copenhagen. 2015.

¹²⁹ Sejvar JJ, et al. *Acute Flaccid Myelitis in the United States, August–December 2014: Results of Nationwide Surveillance*. *Clinical Infectious Diseases*, Volume 63, Issue 6, 15 September 2016, Pages 737–745, <https://doi.org/10.1093/cid/ciw372>.

¹³⁰ IFRC. *Community based surveillance: guiding principles*. Geneva, March 2017.

Annex E

Additional Goal Three Tables

The tables in this annex are a companion to the information presented in Goal Three. They appear here to support the implementation of the *Post-Certification Strategy*.

Table E1. Summary of surveillance standards & operational strategies by post-certification stage and country risk

	Stage I Certification to bOPV Cessation (0-1-year post-certification)	Stage II Immediate Post-Cessation (2-5 yrs. post-certification)	Stage III Intermediate Post-Cessation (6-9 yrs. post- certification)	Stage IV Longer term (≥10 yrs. post- certification)
Primary global risk	cVDPV 1 or 3	cVDPV1 or 3	iVDPV1 or 3	Containment breach
Secondary risks	cVDPV2, iVDPV Containment breach	Sabin 1 or 3, iVDPV, Containment breach	iVDPV2, Containment breach	iVDPV
Polio High-Risk Countries				
Strategies	Active AFP surveillance ES CBS EBS	<u>Years 2-3 post-certification</u> Active AFP surveillance Enhanced efforts among high-risk populations <u>Years 4-5 post-certification</u> Passive AFP + active sentinel site surveillance in specific areas <u>All Years 2-5 post-certification</u> ES CBS EBS	Passive AFP surveillance ES CBS EBS	
Minimum Standards	NPAFP rate ≥2/100K <15 years + stool adequacy ≥80% at <u>first admin level</u>	NPAFP rate ≥2/ 100K <15 years + stool adequacy ≥80% at <u>national level and for selected sentinel sites</u>	NPAFP rate ≥2/100k <15 years + stool adequacy ≥80% at <u>national level</u>	

Table E1 cont'd. Summary of surveillance standards & operational strategies by post-certification stage and country risk

	Stage I Certification to bOPV Cessation (0-1-year post-certification)	Stage II Immediate Post-Cessation (2-5 yrs. post-certification)	Stage III Intermediate Post-Cessation (6-9 yrs. post- certification)	Stage IV Longer term (≥10 yrs. post- certification)
Polio High-Risk Countries				
Strategy and standard for iVDPV detection*	PID surveillance		PID surveillance with increased frequency and intensity in targeted areas	PID surveillance
Laboratory	Continue current cell culture algorithms until other methods are fully validated. 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,			
Polio Medium-Risk Countries				
Strategies	Active and passive AFP surveillance ES as required EBS	<u>Years 2-3 post-certification</u> Passive AFP surveillance Include active sentinel site AFP surveillance in subnational areas of risk (e.g., bordering high risk country) or among high risk populations (e.g. refugees from high risk country). ES EBS <u>Years 4-5 post-certification</u> Passive AFP surveillance ES as required EBS	Passive AFP surveillance ES as required EBS	
Minimum Standards	NPAFP rate ≥2/100K <15years + stool adequacy ≥ 80% at <u>national level</u>	NPAFP rate ≥1/100K <15years + stool adequacy ≥80% at <u>national level</u>		
Laboratory	Potential to shift to direct detection (if validated in low-risk countries). Depending on anticipated demand and national resources, rely on neighbouring country or maintain ≥1 laboratory with VI and ITD diagnostic capacity integrated into multidisease platform along with efficient referral system for sequencing.			

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	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 yrs. post-certification)
Polio Low-Risk Countries				
Strategies	Mix of passive AFP, ES, EVS and EBS			
Minimum Standards	NPAFP rate $\geq 1/100k$ <15years + stool adequacy $\geq 80\%$ at <u>national level</u>			
Laboratory	Countries could be early adopters of direct detection methods (if validated) for initial VI and ITD. Countries (especially with small populations) may rely on neighbouring country laboratories.			

AFP=acute flaccid paralysis; CBS= community-based surveillance; EBS= event-based surveillance; ES = environmental surveillance; EVS = enterovirus surveillance; ITD= intratypic differentiation; NPAFP= non-polio acute flaccid paralysis; PID= Primary Immunodeficiency Diseases; TBD=to be determined ; VI= virus isolation

*Surveillance strategies for PID patients may differ from AFP surveillance although AFP and ES could still be used to detect some iVDPV.

NOTE: Surveillance standards for ES and PID surveillance remain to be determined. For 12 months post any outbreak, NPAFP rate should be $\geq 3/100k$ <15 years per year.

Table E2. Functional detection capacities required at global, regional, and national levels (unless noted, capacities should be sustained through Year 10 post-certification)

	Surveillance-Detection	Laboratory
Global	<ul style="list-style-type: none"> • Generic capacity to implement EBS w/ signals for AFP • Maintain core staff of polio expertise with capacity to: <ul style="list-style-type: none"> – Provide TA/training – Develop updated guidance on PV surveillance – Conduct risk forecasting on countries or areas that require priority monitoring – Conduct regular analysis of AFP and ES data and manage global data information – Rapidly respond to conduct or support AFP case/event investigations if required – Monitor quality & periodically evaluate national systems – Conduct research to guide operational and policy changes 	<ul style="list-style-type: none"> • Maintain global specialized laboratories plus polio virologists with capacity to: <ul style="list-style-type: none"> – Provide TA/training – Prepare & distribute reagents – Perform viral isolation, ITD, and sequencing – Conduct QA/QC along with accreditation – Conduct research on improved diagnostics, new vaccines, etc. – Develop guidance, procedures, and recommendations to maintain the coherence and safety of the GPLN – Coordinate with other WHO-led laboratory networks
Regional	<ul style="list-style-type: none"> • All regions should have staff with general epidemiologic capacity to: <ul style="list-style-type: none"> – Assist with TA, training, updating surveillance guidance, risk forecasting, data analysis and information management, and monitoring. • In addition, regions with high-risk areas should maintain polio specific technical expertise at regional and/or sub-regional level through Year 9 with capacity to: <ul style="list-style-type: none"> – Coordinate and monitor surveillance in high risk cross border areas. – Conduct or assist national staff with active AFP surveillance in sentinel sites – Rapidly respond to conduct or support case/event investigations if required 	<ul style="list-style-type: none"> • Maintain regional reference laboratories and polio virologists with capacity to: <ul style="list-style-type: none"> – Assist with TA, training, analysis, monitoring (depending on regional requirements) – Perform VI, ITD, and sequencing while safely containing polioviruses – Assist with QA/QC – Coordinate with other regional laboratory networks

AFP=acute flaccid paralysis; EBS=event-based surveillance; ES=environmental surveillance; GPLN= Global Polio Laboratory Network; ITD=intratypic differentiation; TA=technical assistance; QA/QC=quality assurance/quality control; VI=viral isolation; VPD=vaccine-preventable disease.

Surveillance-Detection (continued)		Laboratory (continued)
National —		
The expected scope and intensity of surveillance will depend on the assessed risk; however, all countries regardless of risk, should maintain a core capacity to detect poliovirus with reliable access to a WHO-accredited laboratory to test for polioviruses.		
High Risk	<ul style="list-style-type: none"> Integrate scope and management of polio surveillance with VPD or communicable disease surveillance but maintain polio specific technical expertise at national level at least through Year 5 with capacity to: <ul style="list-style-type: none"> Identify subnational high-risk areas or populations Implement case-based, event-based, and supplemental surveillance as required by stage, including AFP/event investigation Conduct polio-specific data analysis and information management from AFP, ES, or EBS, including monitoring performance indicators. Evaluate significance of compatible AFP cases (e.g. Expert Review Committees) 	Depending on anticipated demand, maintain access to ≥ 1 accredited national polio laboratory with at least VI and ITD capacity along with efficient referral system for sequencing.
Medium Risk	<ul style="list-style-type: none"> Integrate scope and management of polio surveillance with VPD or communicable disease surveillance but maintain polio specific technical expertise at national level through Year 3 with capacity to: <ul style="list-style-type: none"> Implement appropriate mix of strategies depending on stage, Conduct polio-specific data analysis from AFP, ES, or EBS, including monitoring performance indicators. After Year 1 may rely on global or regional support to conduct AFP case or event investigations 	<ul style="list-style-type: none"> For all countries, depending on anticipated demand, maintain, or have access to ≥ 1 polio laboratory with VI and ITD diagnostic capacity along with efficient referral system for sequencing if required.
Low Risk	<ul style="list-style-type: none"> Integrate scope and management of polio surveillance with VPD or communicable disease surveillance with capacity to: <ul style="list-style-type: none"> 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 	<ul style="list-style-type: none"> Countries (especially those with small populations) may rely on neighbouring country laboratories to process stool samples. Countries with laboratories maintain VI and ITD diagnostics.

AFP= acute flaccid paralysis; EBS= event-based surveillance; ES= environmental surveillance; ITD= intratypic differentiation; TA= technical assistance; QA/QC= quality assurance/quality control; VI= viral isolation; VPD= vaccine-preventable disease

Table E3. Functional capacities for preparedness and response required at global, regional, and national levels (unless noted, capacities should be sustained through Stage IV—10 years post certification)

Generic functional capacity: *	Polio-specific functional capacity
Global	
<ul style="list-style-type: none"> Leadership (incident management, security, external relations, EOC management) 	<ul style="list-style-type: none"> Technical input to incident management system and EOC Decision making on stockpile release of vaccines and PAVDs
<ul style="list-style-type: none"> Partner coordination/liaison (GOARN, etc.) 	<ul style="list-style-type: none"> Mobilize global roster for surge capacity
<ul style="list-style-type: none"> Information & planning (generic preparedness tools, global communication and planning in response situations) 	<ul style="list-style-type: none"> Technical guideline development or revisions
<ul style="list-style-type: none"> Health operations & technical expertise (risk communication, technical guidance, training) 	<ul style="list-style-type: none"> Training, communication, social mobilization
<ul style="list-style-type: none"> Operational & logistic support—including vaccine & antiviral stockpile management; syringe deployment 	<ul style="list-style-type: none"> Technical assistance to future determination of polio vaccine stockpile requirements
<ul style="list-style-type: none"> Finance & administration (budget, procurement, HR for immediate response) 	<ul style="list-style-type: none"> Vaccine and antiviral procurement as required; Identify pool of funds to support outbreak operational costs
<ul style="list-style-type: none"> IHR monitoring and administration 	<ul style="list-style-type: none"> 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 multicountry 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	
<ul style="list-style-type: none"> Leadership (activate EOC, etc.) 	<ul style="list-style-type: none"> Technical input to incident management system and EOC
<ul style="list-style-type: none"> Partner coordination 	<ul style="list-style-type: none"> Identify in-country polio-specific expertise that could be mobilized if required
<ul style="list-style-type: none"> Information & planning 	<ul style="list-style-type: none"> Preparedness planning & periodic simulation exercises; Conduct rapid assessment
<ul style="list-style-type: none"> Health operations & technical expertise 	<ul style="list-style-type: none"> Plan, organize, and implement outbreak response
<ul style="list-style-type: none"> Operational & logistic support 	<ul style="list-style-type: none"> Polio vaccine management, including collection/destruction of residual mOPV doses
<ul style="list-style-type: none"> Finance & administration 	<ul style="list-style-type: none"> Process and release funds Identify national resources that could be mobilized for outbreak response activities at lower administrative levels

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<ul style="list-style-type: none"> <i>IHR monitoring and administration</i> (monitor development of minimum core capacity; notify WHO of verified poliovirus detection) 	<ul style="list-style-type: none"> Monitor outbreak response as part of JEE, ensure adequate polio-specific capacity
Medium Risk	
Should at least develop IHR minimum expected capacities, including notification to WHO if poliovirus detected	Mirror High Risk capacity for Stage I-II; utilize 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 poliovirus detected	Utilize global and/or regional surge capacity if required for outbreak support.

* Based on WHO. *Emergency Response Framework, 2nd Edition*. Geneva, 2017. EOC=Emergency Operations Center; GOARN= Global Outbreak Alert and Response Network; HR= human resources; IHR=International Health Regulations (2005); JEE= Joint External Evaluation; PAVDs=polio antiviral drugs

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