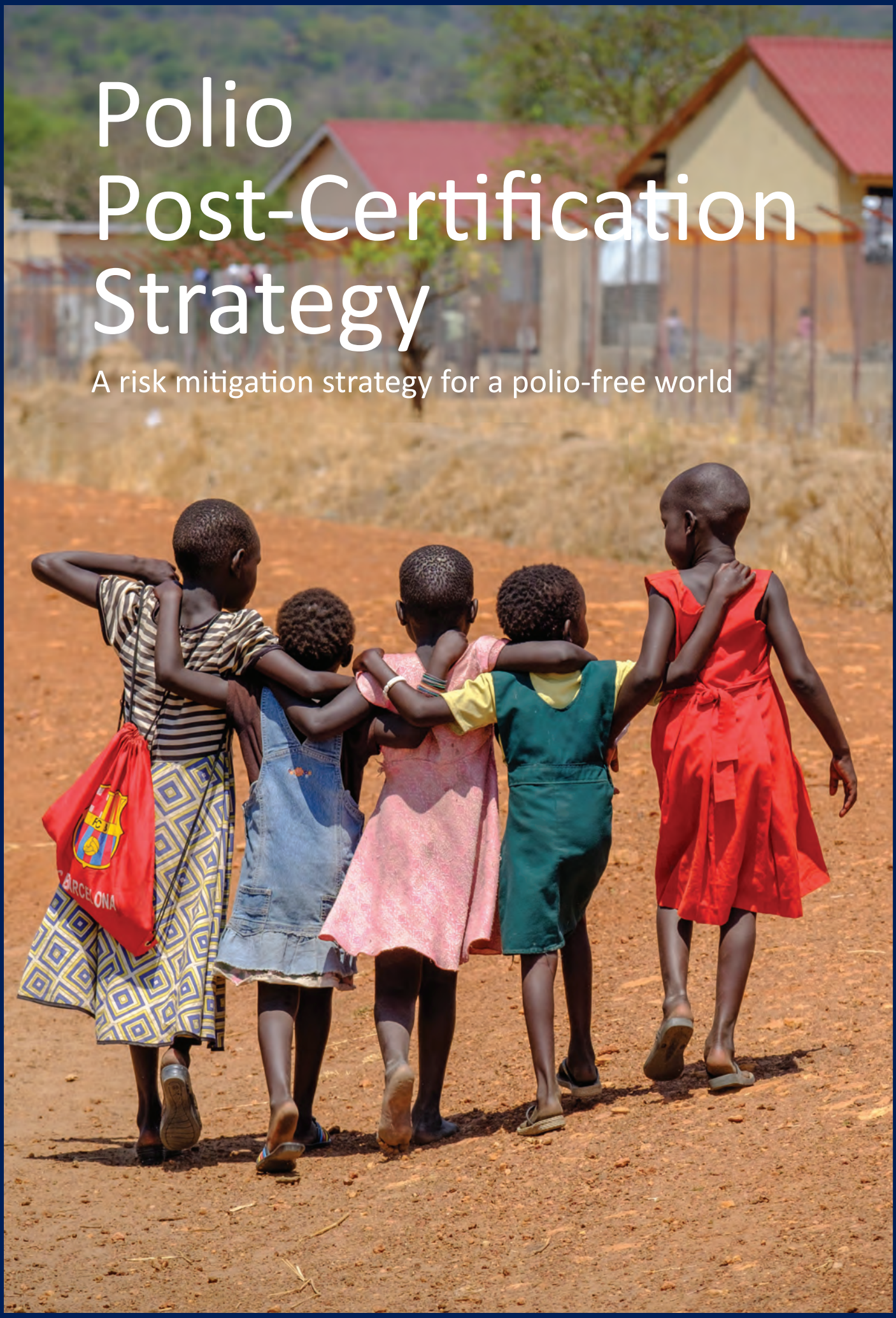
Polio Post-Certification Strategy

A risk mitigation strategy for a polio-free world



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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 Children's Fund (UNICEF), and the Bill & Melinda Gates Foundation.

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Contents

Foreword

As the world draws closer to eradicating polio, we must start planning how we will protect our hard-won progress for a polio-free world. Future governance and coordination will be needed to preserve the gains that generations have worked so hard to secure – and to ensure that polio remains defeated.

Developed in 2017, the Post-Certification Strategy (PCS) is a risk mitigation strategy that defines the functions and standards required to sustain a polio-free world through three goals: containing polioviruses, protecting populations, and detecting and responding to a sudden, resurgent polio outbreak.

From the start, the Strategy – which will be presented at the upcoming Seventy-first World Health Assembly in May 2018 – has been a collaborative effort, developed by partners within the Global Polio Eradication Initiative (GPEI), along with technical experts, regional and country polio and immunization focal points, funders, advisory groups, and modelling groups.

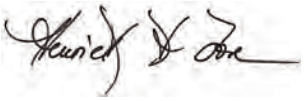
This commitment to collaboration must continue even after polio has been defeated. The Strategy calls on governments to lead the way by shaping health-sector plans that reflect the activities essential to ensure a polio-free world. Support to implement the Strategy must also continue from global donors, nongovernmental organizations, technical advisory groups, and partners such as Gavi, the Vaccine Alliance, the Measles and Rubella Initiative, and the current GPEI core partners.

As we refine and implement the Strategy, we must never lose sight of why we are doing so: to achieve the first polio-free generation in history.

We are also honoring the efforts of those who have spent the last three decades in the pursuit of eradicating polio: a group of 20 million dedicated volunteers who have vaccinated more than 2.5 billion children worldwide against polio, saving 17 million people from this paralysing disease.

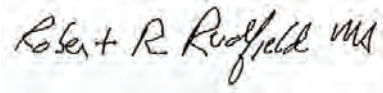
As we finish the job and look to the work ahead, let us renew our commitment to vigilance in sustaining their inspiring legacy and make real our shared dream of a polio-free world for today's children – and tomorrow's.

Dr. Chris Elias
Chairman, Polio Oversight Board
President, Global Development
Bill & Melinda Gates Foundation



Ms. Henrietta H. Fore
Executive Director
United Nations Children's Fund (UNICEF)

Mr. John G. Germ
President, 2016-2017
Rotary International



Robert R. Redfield, MD
Director
U.S. Centers for Disease Control and Prevention

Dr. Tedros Adhanom Ghebreyesus
Director General
World Health Organization

Acronyms and abbreviations

A	
AFP	Acute flaccid paralysis
aVDPV	Ambiguous vaccine-derived poliovirus
B	
bOPV	Bivalent oral poliovirus vaccine
C	
CAG	Containment Advisory Group
CBS	Community-based surveillance
CDC	U.S. Centers for Disease Control and Prevention
cVDPV	Circulating vaccine-derived poliovirus
cVDPV2	Circulating vaccine-derived poliovirus type 2
CWG	Containment Working Group
E	
EBS	Event-based surveillance
EOC	Emergency Operations Center
EPI	Expanded Programme on Immunization
ES	Environmental surveillance
EVS	Enterovirus surveillance
EWAR	Early warning and response
F	
fIPV	Fractional inactivated poliovirus vaccine
G	
GAPIII	Global Action Plan to minimize poliovirus facility-associated risk (Third Edition)
GCC	Global Commission for the Certification of Poliomyelitis Eradication
GHSA	Global Health Security Agenda
GIS	Geographic information system
GOARN	Global Outbreak Alert and Response Network
GPEI	Global Polio Eradication Initiative
GPLN	Global Polio Laboratory Network
GPSAP	Global Polio Surveillance Action Plan
GVAP	Global Vaccine Action Plan
I	
IBS	Indicator-based surveillance
IFRC	International Federation of Red Cross and Red Crescent Societies
IDSR	Integrated disease surveillance and response
IHR	International Health Regulations
IMS	Incident Management System
IPV	Inactivated poliovirus vaccine
ITD	Intratypic differentiation
iVDPV	Immunodeficiency-associated vaccine-derived poliovirus
iVDPV2	Immunodeficiency-associated vaccine-derived poliovirus type 2
J	
JEE	Joint External Evaluations
M	
MAPs	Microarray patches
mOPV	Monovalent oral poliovirus vaccine
mOPV1, 2, 3	Monovalent oral poliovirus vaccine, types 1, 2, 3
N	
NAC	National authority for containment
NCC	National Certification Committee
nOPV	New oral poliovirus vaccine
NPAFP	Non-polio acute flaccid paralysis
NPCC	National polio containment coordinator
O	
OPV	Oral poliovirus vaccine
OPV1, 2, 3	Oral poliovirus vaccine, types 1, 2, 3
P	
PAVD	Polio antiviral drug
PCS	Post-Certification Strategy
PEESP	Polio Eradication & Endgame Strategic Plan
PEF	Poliovirus-essential facility
PHEIC	Public Health Emergency of International Concern
PID	Primary immunodeficiency disease
POB	Polio Oversight Board
POL3	Poliovirus-containing vaccine, third dose
POLIS	Polio information system
POSE	Polio outbreak simulation exercise
PPG	Polio Partners Group
PRC	Polio Research Committee
Q	
QA/QC	Quality assurance/quality control
R	
RCC	Regional Certification Commission
RI	Routine immunization
S	
SAGE	Strategic Advisory Group of Experts on Immunization
SIA	Supplementary immunization activity
sIPV	Sabin strain inactivated poliovirus vaccine
T	
TA	Technical assistance
TAG	Technical advisory group
tOPV	Trivalent oral poliovirus vaccine
U	
UNICEF	United Nations Children's Fund

V

VAPP	Vaccine-associated paralytic poliomyelitis
VDPV	Vaccine-derived poliovirus
VI	Virus isolation
VLPs	Virus-like particles
VPD	Vaccine-preventable disease

W

WHO	World Health Organization
WPV	Wild poliovirus
WPV2	Wild poliovirus type 2

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.*

UNICEF / Donaig Le Du (Central African Republic)

Executive summary

The world is making tremendous progress towards eradicating a human disease for only the second time in history. The fewest number of wild poliovirus (WPV) cases were recorded in 2017, and only three countries are defined as endemic, where the virus may continue to circulate in these populations. National ministries of health and government leadership are critical to interrupting the circulation of WPV, the goal of eradication.

Founded in response to the 1988 World Health Assembly resolution that declared a commitment to the global 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 Children's Fund (UNICEF), and the Bill & Melinda Gates Foundation, working closely with countries, donors, foundations, nongovernmental organizations, and industry. The GPEI will accomplish its 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 the Regional Certification Commissions (RCCs) for polio eradication; and (3) issuing, if and when appropriate, a final report to the WHO Director-General, 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 were to show the absence of WPV from cases of acute flaccid paralysis (AFP, suspected 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, public and private partners, regional colleagues, donors, and other health initiatives to gather input and define the technical standards to sustain a polio-free world – 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.

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

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.

As per the decision of 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 is important to start implementation planning now as the GPEI partnership will dissolve at certification. Following the POB's review and endorsement of the PCS, 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 refers 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, the Measles and Rubella Initiative), vaccine manufacturers, 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).

Over the course of the polio eradication effort, the resources supporting polio activities at the global, regional, and country levels have also supported broader health initiatives, such as measles accelerated control or elimination activities, surveillance for vaccine-preventable diseases such as yellow fever, outbreak

WHO / L. Dore

[2] See the minutes of the October 2017 Polio Oversight Board meeting (http://polioeradication.org/wp-content/uploads/2016/07/pob-meeting-minutes-02102017.pdf).

[3] World Health Organization. Global Polio Eradication Initiative. Polio Eradication & Endgame Strategy 2013–2018. February 2013 (http://polioeradication.org/wp-content/uploads/2016/07/PEESP_EN_A4.pdf).

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 either to groups that will support maintaining a polio-free world, or to groups that have relied on polio resources to accomplish their health goals.

The Post-Certification Strategy: Risk mitigation

The following three goals have been identified to mitigate the current and future risks to maintaining 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	**Activity 1.1.1**
To achieve and sustain the containment of polioviruses in laboratories, vaccine manufacturing and other facilities	Support the global reduction of facilities storing and handling poliovirus
	Activity 1.1.2
	Implement and monitor long-term poliovirus containment in facilities with appropriate safeguards
Goal Two: Protect populations	
Objective 2.1	**Activity 2.1.1**
To protect populations from VDPVs and VAPP by effectively preparing and implementing the globally synchronized withdrawal of bOPV	Develop and implement plans (including pre-cessation supplementary immunization activities) to withdraw bOPV from all use
Objective 2.2	**Activity 2.2.1**
To provide access to safe, effective polio vaccines for the long-term protection of global populations	Implement future immunization policy to protect populations 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	**Activity 3.1.1**
To promptly detect any poliovirus in a human or in the environment through a sensitive surveillance system	Redefine the 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

bOPV= bivalent oral poliovirus vaccine; IPV= inactivated poliovirus vaccine; VAPP= vaccine-associated paralytic poliomyelitis; VDPV= vaccine-derived poliovirus.
Source: WHO, Post-Certification Strategy.

Cross-cutting research on new diagnostic tests, 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.

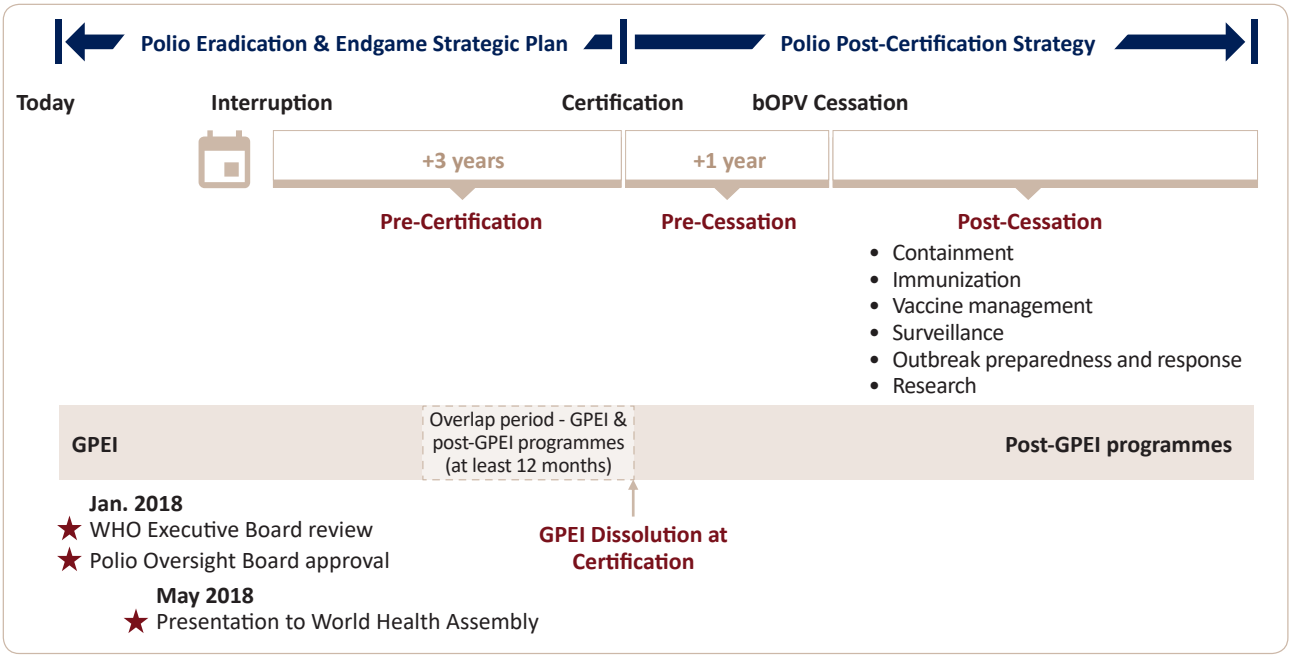
[4] For examples of activities and time spent towards broader immunization and healthcare goals, see Van den Ent MM, Swift RD, Anaokar S, Hegg LA, Eggers R, Cochi SL. Contribution of Global Polio Eradication Initiative – Funded Personnel to the Strengthening of Routine Immunization Programs in the 10 Focus Countries of the Polio Eradication and Endgame Strategic Plan, J Infect Dis. 2017;216(S1):S244–9 (https://doi.org/10.1093/infdis/jiw567).

This document does not address governance, management, financial estimates, or monitoring elements, all of 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 national ministries of health and finance that 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 the integration of polio activities and strengthen immunization and surveillance systems.

It is critical to identify the future owners and initiate the planning process by the Seventy-first World Health Assembly in May 2018, 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 handoff 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 estimated costs for activities performed at the country level.

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



bOPV= bivalent oral poliovirus vaccine.
Source: WHO, Post-Certification Strategy.

[5] For more on the decision to dissolve the partnership at certification, see the minutes of the April 2017 Polio Oversight Board meeting (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 Polio Eradication & Endgame Strategic Plan 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.

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.

The Bill & Melinda Gates Foundation (Nigeria)

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* 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 Post-Certification Strategy (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 of 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 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. The GVAP offers a framework for global equity by focusing on risks that impede universal access to public health programmes, as it endeavours 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.

PCS engagement and audience

The PCS was developed through an iterative consultative process with experts within and beyond the Global Polio Eradication Initiative (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, which will be expected to sustain a polio-free world. (*See* **Annex A** – *Post-Certification Strategy engagement list*.)

Source: WHO, Post-Certification Strategy.

[6] While there is an epidemiological difference between "emergence" (in the case of a new vaccine-derived poliovirus [VDPV]), "re-emergence" (from previously identified circulating vaccine-derived polioviruses [cVDPVs]), and "reintroduction" (of WPV, VDPV, or Sabin from release), for the purposes of this strategy and to suit 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 (2005), Third Edition. Geneva: WHO; 2016 (http://www.who.int/ihr/publications/9789241580496/en); Global Health Security Agenda [website] (https://www.ghsagenda.org/about); Global Vaccine Action Plan 2011–2020. Geneva: WHO; 2013 (http://www.who.int/immunization/global_vaccine_action_plan).

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 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 in the polio programme, will include national governments (ministries of health and finance), nongovernmental organizations, technical advisory groups (the Global Commission for the Certification of Poliomyelitis Eradication [GCC], the Strategic Advisory Group of Experts on Immunization [SAGE]), global immunization and other public health development partnerships (Gavi, the Vaccine Alliance, and the Measles and Rubella Initiative), donors, and the current GPEI implementing partners.

Scope

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

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 on how these functions should be incorporated within national health systems.

Country transition plans should propose how to mainstream the implementation of the required functions both by building long-term capacity and by assuming a progressively greater percentage of costs within the 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 the PCS provides.

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 under way at the agency level for each of the GPEI partners and at the country level, with particular focus on 16 priority countries that represent the largest footprint for GPEI support.

Source: WHO, Post-Certification Strategy.

[8] Global Polio Eradication Initiative. Polio Transition Planning Framework. March 2017.

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 the possible inadequate use of the bivalent oral poliovirus vaccine (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 four months after the last use of monovalent oral poliovirus vaccine [mOPV] or post-bOPV cessation) must be notified to WHO. Depending on the risk of international spread and other factors, the detection could constitute 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.

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 the re-emergence of VDPVs – which will gradually decline with time after the last use of OPV.

[9] WPV type 2 eradication has been certified since September 2015. The use of monovalent oral poliovirus vaccine type 2 (mOPV2) is expected to have stopped well before certification, unless current circulating vaccine-derived poliovirus type 2 (cVDPV2) outbreaks have spread further or have not been stopped at that time. Chronic excretion of an immunodeficiency-associated vaccine-derived poliovirus type 2 (iVDPV2) is possible (though a low risk) with countries that used mOPV2 less than five years prior to certification.

[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.

- **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 vaccine-derived polioviruses [cVDPVs]). Additionally, immunodeficiency-associated vaccine-derived polioviruses (iVDPVs) can result when patients with primary immunodeficiency diseases (PIDs) 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 vaccine-derived poliovirus [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 non-immune 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. Facilities may also exist 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.

Risk category 3: Undetected transmission

The risk of undetected transmission also remains since poliovirus can circulate in communities at low levels without resulting in cases of paralysis. With sensitive global surveillance at the time of certification, confidence will be high 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 the cVDPV was last detected. Sustaining sensitive global surveillance for poliovirus will be required as long as the risk of any poliovirus re-emergence remains.

Assessing risk over time

The primary risk and source of re-emergence is expected to vary over time after bOPV cessation. While **Figure 2** 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 of 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 the PCS goals, as well as in **Annex B**.

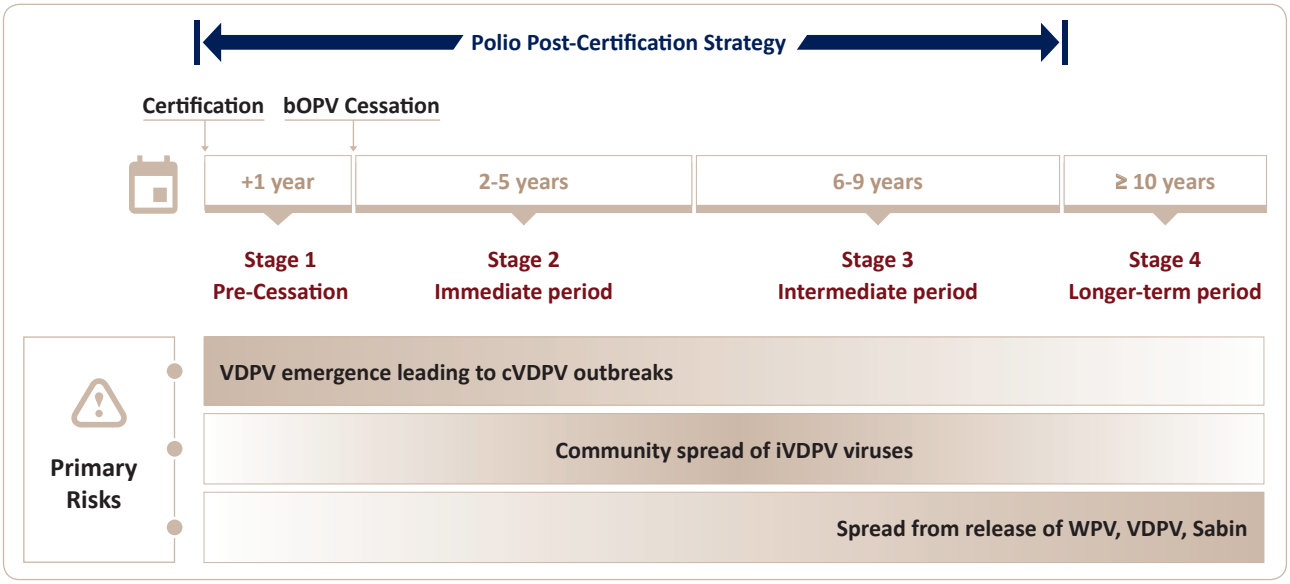
Evolution of risk across post-certification stages

- 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 (zero to one year post-certification) and immediate post-cessation periods (two to five 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]

[11] Grassly NC. The final stages of the global eradication of poliomyelitis. Phil Trans R Soc B. 2013;368. 20120140; Duintjer Tebbens RJ, Pallansch MA, Cochi SL, Wassilak SG, Thompson KM. 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.

Figure 2. Risk of poliovirus re-emergence over time



bOPV= bivalent oral poliovirus vaccine; cVDPV= circulating vaccine-derived poliovirus; iVDPV= immunodeficiency-associated vaccine-derived poliovirus; VDPV= vaccine-derived poliovirus; WPV= wild poliovirus.
Source: WHO, Post-Certification Strategy.

- Intermediate post-cessation period

  As the risk of cVDPV wanes, the primary risk for poliovirus re-emergence in the intermediate post-cessation period (six to nine years post-certification) will come from an iVDPV spreading within a community. No poliomyelitis outbreaks to date have been attributed to iVDPV; nevertheless, this possibility needs to be considered. While the 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 under-immunized 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 or a manufacturing or research facility is unlikely. However, such events have happened, and the possibility of a new occurrence 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 period 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.

[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).

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 reintroduction in a polio-free world. The key focus areas will be to reduce the number of facilities storing and handling poliovirus globally, and to implement and monitor appropriate safeguards in those facilities that retain poliovirus.
2. **Protect populations**. Goal Two is to protect populations from vaccine-derived polioviruses (VDPVs) and vaccine-associated paralytic poliomyelitis (VAPP) by preparing and coordinating the global withdrawal of bOPV, and from any poliovirus re-emergence by providing access to safe, effective vaccines.
3. **Detect and respond to a polio event**. The focus of Goal Three 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 Polio Eradication & Endgame Strategic Plan. 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 occur a year prior to certification, after bOPV cessation, and at the midterm of the PCS's 10-year duration – the future owners of the PCS will be the ones who will re-evaluate the strategy, as and when appropriate.

Next steps

This document is one step towards 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, the strategy will be presented to the Seventy-first World Health Assembly in May 2018.

[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 PCS would begin in 2021 and continue until 2030.

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

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

World Health Organization

GOAL 1 Contain polioviruses

Main objectives	Major activities
Objective 1.1	**Activity 1.1.1**
To achieve and sustain the 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 poliovirus containment in facilities with appropriate safeguards

Source: WHO, Post-Certification Strategy.

Introduction

After the global interruption of wild poliovirus (WPV) transmission and the cessation of bivalent oral poliovirus vaccine (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 Polio Eradication & Endgame Strategic Plan. The global strategies and mechanisms to achieve effective poliovirus containment were outlined in the third edition of the Global Action Plan to minimize poliovirus facility-associated risk (GAPIII), 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 reintroducing poliovirus from laboratories or vaccine manufacturing facilities into a polio-free world. The major principles of poliovirus containment are: (1) a minimal number of facilities storing and handling poliovirus infectious and potentially infectious materials; (2) a minimal risk of exposure for the worker or community as a result of operations; (3) the minimal susceptibility of workers to poliovirus infection; and (4) minimal consequences of release in the community.

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-harbouring 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]

[14] World Health Organization. GAPIII: WHO Global Action Plan to minimize poliovirus facility-associated risk, Third edition. Geneva: WHO; 2015 (http://polioeradication.org/wp-content/uploads/2016/12/GAPIII_2014.pdf).
[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. Bulletin of the World Health Organization. 2004;82(1):40–6.

The potential for polioviruses released from facilities to reinitiate transmission in surrounding communities will depend on several factors.[19,20] The first is the category of poliovirus-containing material released, as WPV and vaccine-derived polioviruses (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 a >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 the provision of inactivated poliovirus vaccine (IPV) through routine immunization will protect against paralysis and transmission of reintroduced polioviruses through the oropharyngeal route, it will confer very limited protection against intestinal infection and transmission through the faecal-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.

Potential for polioviruses released from facilities to reinitiate transmission

This eventuality 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 capabilites

Source: WHO, Post-Certification Strategy.

Considering these factors, a modelling 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, 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 could only be eliminated if all polioviruses stored in laboratories and biomedical facilities were destroyed, and if polioviruses could not be artificially synthesized. Unfortunately, this cannot be achieved because polioviruses are necessary for vaccine production and other functions. However, effective containment can decrease the risk to acceptable levels. GAPIII proposes two main 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.

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

Source: WHO, Post-Certification Strategy.

To reduce the number of facilities harbouring poliovirus, all countries need to conduct surveys and inventories of all laboratories and biomedical facilities, public and private, that may be storing polioviruses. The facilities in which storing and handling poliovirus are not critical will need to destroy (or transfer to

[19] Dowdle W, van der Avoort H, de Gourville E, Delpeyroux F, Desphande J, Hovi T et al. Containment of polioviruses after eradication and OPV cessation: characterizing risks to improve management. Risk Anal. 2006;26(6):1449–69.
[20] 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.

poliovirus-essential facilities [PEFs]) 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 harbouring 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 harbouring poliovirus (e.g., from areas with a new outbreak), and destroy, transfer, or contain those specimens if the presence of the virus is confirmed.

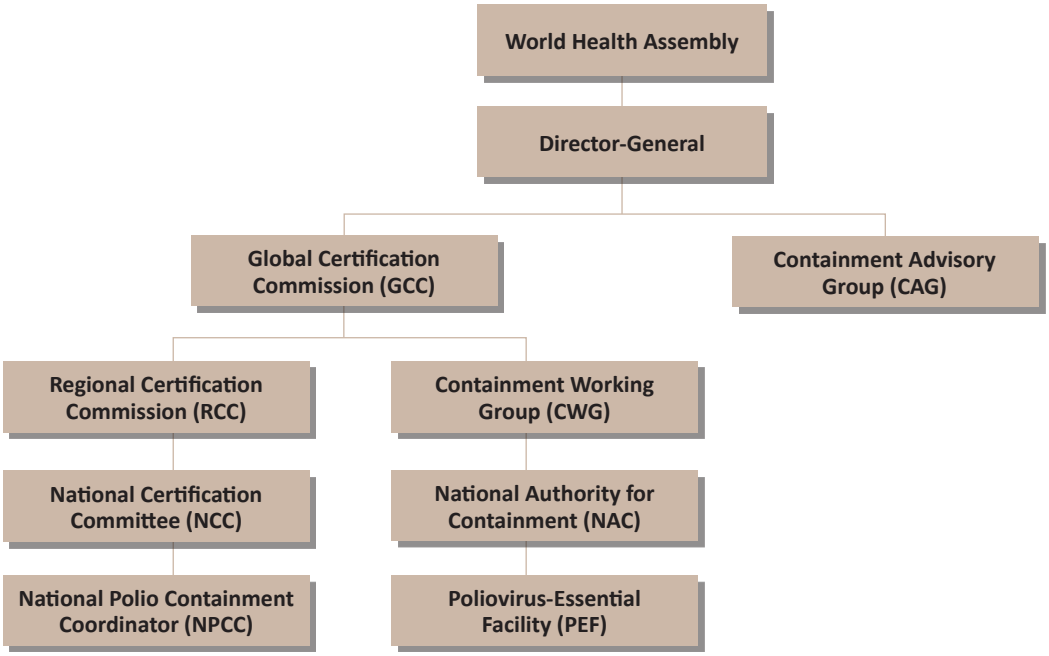
PEFs that need to store and handle polioviruses to perform critical functions, and their host countries, should implement and comply with several containment safeguards. Safeguards will be more stringent for WPV/VDPV than for OPV/Sabin poliovirus.

- **Primary safeguards** reduce the risk of accidental or intentional poliovirus release from a facility. Key elements include modifications to 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.
- **Tertiary safeguards**, required only for facilities handling and storing WPV/VDPV, 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 oversee the implementation of containment measures at the national and global levels (*see **Figure 3***).[23]

Figure 3. Current oversight structure of containment activities



Source: WHO, Post-Certification Strategy.

[22] World Health Organization. Guidance for non-poliovirus facilities to minimize risk of sample collections potentially infectious for polioviruses. Geneva: WHO; 2018 (http://polioeradication.org/wp-content/uploads/2018/04/polio-containment-guidance-for-non-poliovirus-facilities-20180410-en.pdf).

[23] World Health Organization. Containment Certification Scheme to support the WHO Global Action Plan for Poliovirus Containment. Geneva: WHO; 2017 (http://polioeradication.org/wp-content/uploads/2017/02/CCS_2016EN.pdf).

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

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 Commission for the Certification of Poliomyelitis Eradication (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 GCC acts as the oversight body to confirm the achievement of the 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 the sequential removal of poliovirus types contained in OPV.[24] Phase I includes an inventory and reduction of facilities holding poliovirus type 2 materials; Phase II refers to poliovirus type 2 containment; and Phase III refers to the containment of all polioviruses. Phases I and II were to be implemented around the certification of WPV type 2 (WPV2) eradication in 2015 and after trivalent oral poliovirus vaccine (tOPV) withdrawal in April–May 2016, respectively. Phase III implementation is expected to begin by the time all six WHO regions are certified as polio-free.

The 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 Strategy period, the Global Polio Eradication Initiative (GPEI) has increased technical support and funding for communications, advocacy, and the training of stakeholders, including NACs and PEFs. CAG recommendations and 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 to continue the process of reducing the number of facilities retaining polioviruses, and to oversee the implementation of safeguards and continuously monitor compliance with containment requirements in facilities retaining poliovirus and in their host countries.

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

- Although GAPIII is expected to be revised during the Endgame Strategy period before certification, the revisions will likely address specific questions and challenges to implementation procedures, while 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.

[24] World Health Organization. GAPIII: WHO Global Action Plan to minimize poliovirus facility-associated risk. Geneva: WHO; 2015 (http://polioeradication.org/wp-content/uploads/2016/12/GAPIII_2014.pdf).

[25] World Health Organization. Guidance for non-poliovirus facilities to minimize risk of sample collections potentially infectious for polioviruses. Geneva: WHO; 2018 (http://polioeradication.org/wp-content/uploads/2018/04/polio-containment-guidance-for-non-poliovirus-facilities-20180410-en.pdf).

- 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 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 storing and handling poliovirus

In preparation for bOPV withdrawal, countries will need to identify all facilities retaining any infectious or potentially infectious OPV/Sabin type 1 and 3 materials by updating the facility surveys conducted for type 2 poliovirus, which may also help to find 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.[26] These activities should be coordinated with the withdrawal and destruction of bOPV stocks as outlined in Goal Two.

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 be responsible for ensuring compliance through regulatory or other types of mandate. The implementation of containment for all polioviruses (WPV, VDPV, and Sabin) may affect polio surveillance, vaccine production, outbreak response, and research activities (*see* ***Table 1***).

Any country that experiences a poliovirus outbreak will have to update their facility survey to include laboratories that may have collected specimens harbouring polioviruses and facilities that may have vaccine stocks – and destroy or contain those materials. An international oversight body will monitor these activities to certify the 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 levels will conduct the following activities:

- Develop guidelines and training on surveys and containment reports, and share them 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 the submission of country reports to the RCC and the GCC (or other oversight bodies)
- Provide technical assistance (TA) on containment to countries facing outbreaks after certification
- Coordinate meetings of oversight bodies with countries and regions to monitor the progress of 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 the 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 the* ***Research activities*** *section.*)

[26] Ibid.

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

The risk of poliovirus reintroduction after a containment breach will decrease with time after certification, as the number of facilities retaining polioviruses declines and as those facilities handling poliovirus implement safeguards appropriately. However, the potential consequences of a breach will rise as population immunity decreases with time.[27] 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 GAPIII 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 bodies).

At the global and regional levels, 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 TA and expert containment advice on certification processes and questions related to poliovirus containment (*see **Table 1** for links with other polio activities*)
- Maintain and regularly update a global inventory of PEFs
- Provide regular training on containment certification processes
- Support GCC-CWG activities, including training members, organizing meetings, and preparing the documentation necessary to review containment certificate requests
- Provide secretariat functions to expert committees and oversight bodies (such as CAG, GCC)
- Provide TA in investigating and responding to containment breaches in coordination with PEFs and outbreak response groups (national and international).

The GCC-CWG will continue performing the verification of containment certificates issued for new or existing PEFs until the certification of the global containment of all poliovirus following bOPV cessation. 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 the case with smallpox.

[27] 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

Effect of containment implementation	Action to address these effects
Vaccine manufacture and stockpile	
• 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.	• Consider the containment requirements for manufacture during the estimation of polio vaccine supplies • Consider these requirements while planning the location of national and international mOPV stockpiles
Surveillance	
• Regulations for the international shipment of samples that contain or may contain poliovirus will be more stringent and will increase costs and complexity.	• Ship poliovirus RNA (considered to have lower infectious risk) instead of poliovirus isolates or stools to reference labs • Update laboratory and field guidelines to include procedures for the shipment of samples • Account for extra costs/delays of sample shipments when planning surveillance activities
• 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.	• 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 the limited number of laboratories with testing capacity • Replace WPV/Sabin strains with highly attenuated strains for serological testing when assays are available
Outbreak response	
• Shipment of mOPV to respond to outbreaks may have stricter restrictions and take longer.	• Maintain global capacity to support country authorities with import permits and shipments
• A new WPV/VDPV outbreak and the use of OPV to interrupt transmission will reintroduce polioviruses in facilities without appropriate containment safeguards.	• Update outbreak guidelines to ensure that samples potentially harbouring poliovirus and vaccine stocks are destroyed or contained after closing the outbreak
Research	
• Laboratories conducting experimental research or supporting testing for vaccine clinical trials will need to be certified as PEFs.	• Ensure adequate test capacity when planning poliovirus-related research
• The use of live vaccines in clinical trials will not be available or will be very restricted for: – administration to individuals in study arms – challenge with OPV to assess mucosal immunity – determination of antibody levels by microneutralization to assess efficacy.	• Adjust resources, time, and designs for clinical trials of new vaccines • Support the development of new diagnostic tools to facilitate research on new polio vaccines

GAPIII= Global Action Plan to minimize poliovirus facility-associated risk (Third Edition); IPV= inactivated poliovirus vaccine; OPV= oral poliovirus vaccine; mOPV= monovalent oral poliovirus vaccine; PEF= poliovirus-essential facility; VDPV= vaccine-derived poliovirus; WPV= wild poliovirus.

Source: WHO, Post-Certification Strategy.

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

The Bill & Melinda Gates Foundation

GOAL 2 Protect populations

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

bOPV= bivalent oral poliovirus vaccine; IPV= inactivated poliovirus vaccine; VAPP= vaccine-associated paralytic poliomyelitis; VDPV= vaccine-derived poliovirus.

Source: WHO, Post-Certification Strategy.

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 the 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 poor sanitation settings 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 to eliminate all paralytic polio disease and sustain WPV eradication ultimately requires stopping all use of bivalent oral poliovirus vaccine (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 (RI) 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 WPV2 global eradication in September 2015, the Global Polio Eradication Initiative (GPEI) initiated sequential steps to withdraw OPV. The first of these was the global withdrawal of the type 2-containing vaccine, trivalent oral poliovirus vaccine (tOPV), and the switch to 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 that impact how these measures will be implemented. Further details are provided in Section C below.

Table 2. Vaccine-derived poliovirus and vaccine-associated paralytic poliomyelitis: risks and mitigation measures

	Risk[28]	Mitigation measures	Technical note
VDPVs	VDPV emergence related to the use of OPV in populations with low immunity and areas prone to faecal-oral transmission	• 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)	• Risk of VDPV circulation from OPV can continue for several years after cessation.[29] • Failure to target high-risk groups and achieve adequate population immunity in pre-cessation SIAs can raise the threat of VDPV emergence and spread.[30] • Risk of mOPVs resulting in VDPV transmission beyond an outbreak zone may increase with time after cessation.[31]
	Importation of VDPVs into countries that have gaps in protection from types 1 and 3 and declining immunity due to early withdrawal of bOPV from RI prior to cessation	• Synchronize the cessation of bOPV for all countries using the vaccine at the time of certification • Initially provide priming and partial protection through IPV in RI	• IPV use with high coverage cannot prevent cVDPVs in areas with intense faecal-oral transmission.[32] • Depending on recipient age, one dose of IPV can seroconvert or prime the majority of vaccine recipients.[33] (*See* ***Objective 2.2*** *for long-term projection.*)
VAPP	VAPP from continued use of OPV (either bOPV or mOPV used for outbreak response)	• Withdraw bOPV • Maximize prior IPV vaccination coverage and judiciously target the use of mOPV for outbreak response • Develop alternative polio vaccines (e.g., safer nOPVs)	• See ***Goal Three*** for further details on outbreak response and see the ***Research activities*** section for details on alternative polio vaccines.

bOPV= bivalent oral poliovirus vaccine; cVDPV= circulating vaccine-derived poliovirus; 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; VAPP= vaccine-associated paralytic poliomyelitis; VDVP= vaccine-derived poliovirus.

Source: WHO, Post-Certification Strategy.

C. What will be done

Activity 2.1.1 – Develop and implement plans (including pre-cessation supplementary immunization activities) 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.[34,35]

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, modelled after the endorsement of the switch at the World Health Assembly in May 2015,[36] and fully engage stakeholders at all levels in the planning, preparation, implementation, and validation of global bOPV withdrawal

[28] See *Annex B* for details on the projected magnitude of risk for VAPP and VDPVs in the post-certification era.
[29] Grassly NC. The final stages of the global eradication of poliomyelitis. Phil Trans R Soc B. 2013;368. 20120140. See also: Lyons H, Famulare M, Chabot-Couture G. OPV13 cessation and SIA planning. Presentation to the SAGE Polio Working Group, Geneva, September 2017.
[30] Pons-Salort M, Burns CC, Lyons H, Blake IM, Jafari H, Oberste MS et al. Preventing Vaccine-Derived Poliovirus Emergence during the Polio Endgame. PLoS Pathog. 2016;12(7):e100528. doi:10.1371/journal.ppat.1005728.
[31] 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.
[32] Duintjer Tebbens RJ, Hampton LM, Wassilak SGF, Pallansch MA, Cochi SL, Thompson KM. Maintenance and Intensification of Bivalent Oral Poliovirus Vaccine Use Prior to its Coordinated Global Cessation. J Vaccines Vaccin. 2016;7(5):340. doi:10.4172/2157-75600.1000340.
[33] Bandyopadhyay AS, Garon J, Seib K, Orenstein WA. Polio vaccination: past, present and future. Future Microbiol. 2015;10(5):791–808. doi: 10.2217/fmb.15.19.
[34] 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: WHO; 2005.
[35] For extensive details on the lessons learned from the withdrawal of tOPV, see multiple articles in: Polio Endgame & Legacy: Implementation, Best Practices, and Lessons Learned. J Infect Dis. 2017;216(S1):S1–8 (https://academic.oup.com/jid/issue/216/suppl_1).
[36] World Health Organization. Sixty-Eighth World Health Assembly: Poliomyelitis: Report by the Secretariat. 1 May 2015 (http://apps.who.int/gb/ebwha/pdf_files/WHA68/A68_21-en.pdf).

2. Develop and aggressively implement **pre-cessation** risk mitigation measures necessary to meet multiple readiness criteria for full bOPV withdrawal[37]

   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 One***

   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 levels to minimize and manage the risks associated with final bOPV cessation.

3. Implement the operational planning and withdrawal process based on clearly identified steps that 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 before 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.

   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 RI.

   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

Pre-Cessation Immunity

By inducing mucosal immunity for types 1 and 3, pre-cessation bOPV supplementary immunization activities (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 at high risk of infection and low RI 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 faecal-oral transmission. Countries that 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: Duintjer Tebbens RJ et al. Maintenance and Intensifi\cation of Bivalent Oral Poliovirus Vaccine Use Prior to its Coordinated Global Cessation. J Vaccines Vaccin. 2016;7(5):340. Meeting of the Strategic Advisory Group of Experts on Immunization, October 2016 – conclusions and recommendations. Wkly Epidemiol Rec. 2016;91:561–84.

[37] 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.

and the potential for emergence of VAPP/VDPVs from continued use.[38] 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 of them at the 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 was only partially implemented due to severe global constraints on IPV supply. To offset shortages, some countries have used fractional inactivated poliovirus vaccine (fIPV),[39] 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 the hexavalent (DTaP-Hib-HepB-IPV[40]) combination vaccine and 39 reported using pentavalent (DTaP-Hib-IPV[41]) vaccine in their Expanded Programme on Immunization (EPI) schedules.[42]

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.

Table 3. Vaccine protection, supply risks and mitigation measures

Risk	Mitigation measure	Technical note
Limits to IPV protection	• Develop global immunization policy that is programmatically feasible and flexible and provides required individual protection • Continue the development of new polio vaccines	• IPV requires multiple doses, the duration of protection for two doses is unknown, and the vaccine's effectiveness against transmission and spread in high-risk environments is limited.[43] (*See the **Research activities** section for new poliovirus vaccine development information.*)
Lack of adequate supply of affordable IPV for all countries	• Determine demand for IPV and facilitate long-term supply • Advocate for sustainable financing to support low-income countries • Facilitate the development of affordable formulations and efficient delivery options	
Inadequate protection of high-risk populations due to weak RI systems	• 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	• POL3 coverage in 2016 was estimated at 49% in Nigeria, 60% in Afghanistan, and 72% in Pakistan.[44] • See *GVAP 2011–2020* for proposed strategies to strengthen RI.[45]

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

Source: WHO, Post-Certification Strategy.

[38] 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).
[39] fIPV is defined as intradermal administration of 1/5th of the full dose given intramuscularly.
[40] Diphtheria-tetanus-acellular pertussis–*haemophilus influenzae* type B–hepatitis B vaccine–inactivated poliovirus vaccine.
[41] Diphtheria-tetanus-acellular pertussis–*haemophilus influenzae* type B–inactivated poliovirus vaccine.
[42] See the World Health Organization's data for Immunization, Vaccines and Biologicals (http://www.who.int/immunization/monitoring_surveillance/data/en).
[43] Bandyopadhyay AS, Garon J, Seib K, Orenstein WA. Polio vaccination: past, present and future. Future Microbiol. 2015;10(5):791-808. doi: 10.2217/fmb.15.19.
[44] WHO–UNICEF esimates of POL3 coverage (http://apps.who.int/immunization_monitoring/globalsummary/timeseries/tswucoveragepol3.html).
[45] World Health Organization.Global Vaccine Action Plan 2011–2020. Geneva: WHO; 2013 (http://www.who.int/immunization/global_vaccine_action_plan/GVAP_doc_2011_2020/en).

C. What will be done

Activity 2.2.1 – Implement future immunization policy to protect populations 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.

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

This proposed schedule from SAGE is designed to achieve durable individual immunity by providing at least 90% seroconversion and robust antibody titres to all three poliovirus serotypes. The designated age at first IPV dose and dosing interval will offer maximum vaccine efficacy and accommodate existing EPI contacts for diphtheria–tetanus–pertussis and measles.[46] 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 two fractional doses versus one full-dose IPV when the first dose of IPV is given at or after two months of age.[47] This policy provides countries with long-term options that could reduce costs and stretch vaccine supplies. Further research will be needed to determine the effectiveness and duration of immunity provided by each delivery method (intramuscular for IPV and intradermal for fIPV). (*See the **Research activities** section.*)

SAGE recommendations for future Global Polio Vaccination Policy

1. Countries should include at least two doses of IPV in their RI 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 around four months after the first dose, administered either as full or fractional doses.
2. Countries without poliovirus-essential facilities (PEFs) should maintain IPV in their RI schedule for at least 10 years after global OPV withdrawal to address immediate (VDPVs), intermediate (immunodeficiency-associated vaccine-derived poliovirus), 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: World Health Organization. Meeting of the Strategic Advisory Group of Experts on Immunization, April 2017 – conclusions and recommendations. Wkly Epidemiol Rec. 2017;92:301-20.

The recommendation to use IPV for more than 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 depend on the coverage that is attained. As currently set by the GVAP, the coverage target for all vaccines in national immunization programmes is at least 90% national vaccination coverage and at least 80% vaccination coverage in every district or equivalent administrative unit.[48]

[46] For a summary of IPV clinical trials, see Estivariz CF, Pallansch MA, Anand A, Wassilak, SGF, Sutter RW, Wenger J et al. Poliovirus vaccination options for achieving eradication and securing the endgame. Current Opinion in Virology. 2013;3:309–315.

[47] For a summary analysis of fIPV, see Okayasu H, Sein C, Chang Blanc D, Ramirez Gonzalez A, Zehrung D, Jarrahian C et al. Intradermal Administration of Fractional Doses of Inactivated Poliovirus Vaccine: A Dose-Sparing Option for Polio Immunization. J Infect Dis. 2017;216(S1):S161–7.

[48] World Health Organization. Global Vaccine Action Plan 2011–2020. Geneva: WHO; 2013 (http://www.who.int/immunization/global_vaccine_action_plan).

GAPIII has also set specific coverage targets to reflect potentially higher risks for countries hosting poliovirus-essential facilities (PEFs).[49] After bOPV cessation, GAPIII requires that countries with PEFs containing OPV/Sabin materials provide at least one dose of IPV (and attain coverage equal to three doses of diphtheria–tetanus–pertussis), 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 Global Commission for the Certification of Poliomyelitis Eradication [GCC]) may choose to further refine the parameters and expected geographic scope of these recommendations.

Activity 2.2.2 – Support the availability of affordable IPV and its 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 outlined 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 that promote the overall sustainability of immunization efforts and high coverage with all vaccines.

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

Gavi and the GPEI have updated 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 that may positively impact the IPV market to achieve a healthy market over time, characterized by ensuring sufficient supply and affordable pricing and supporting the availability of new innovative vaccines.[50]

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

- Countries that 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 countries previously using OPV, 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 recommended by SAGE; pricing and available financing; national product preference and the use of fractional doses; the perceived future risk of poliomyelitis for their population; and the availability of new or improved products.
- IPV supply should be sufficient to enable all countries to switch to two full IPV doses.

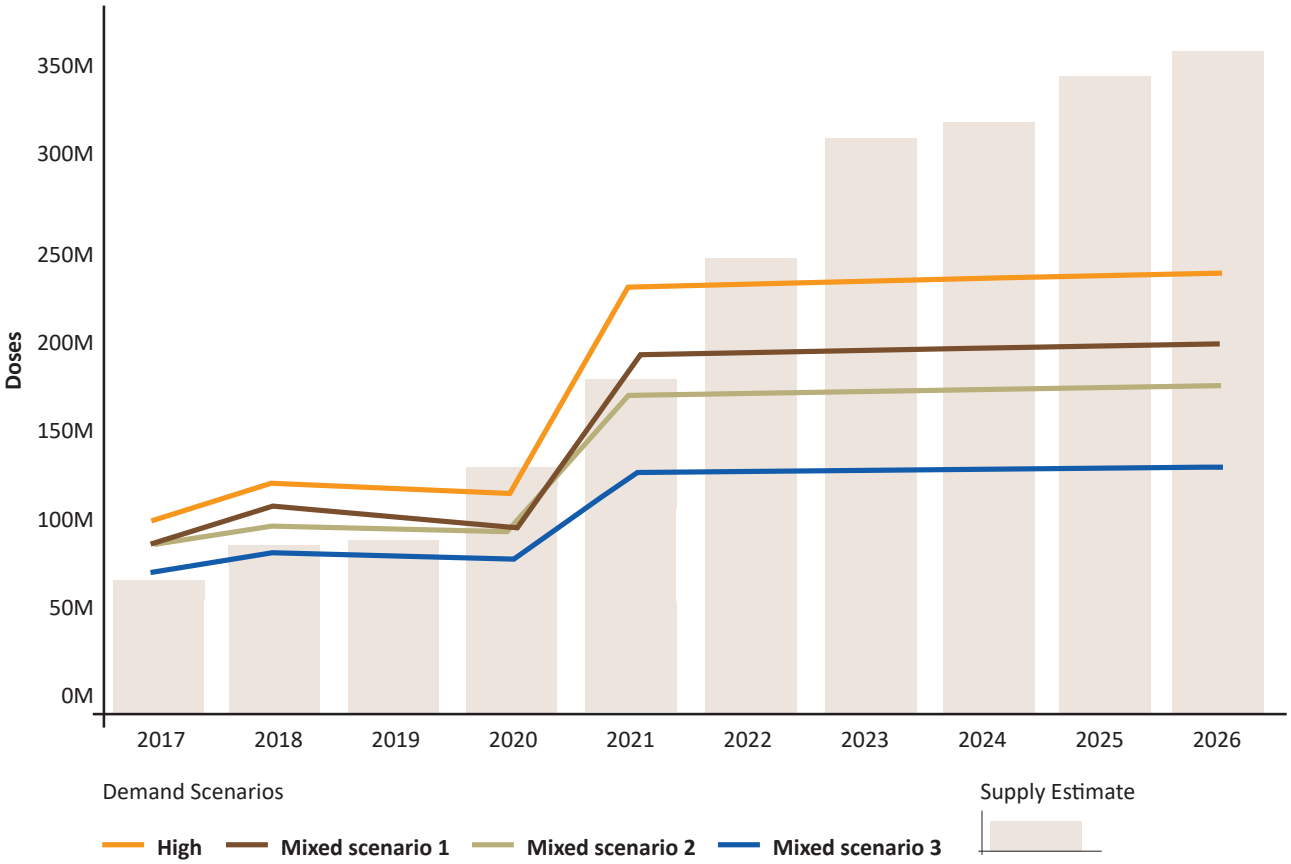
The IPV Supply and Procurement Roadmap is updated in relation to major procurement activities, such as new tenders, and provides visibility to manufacturers and stakeholders on expectations regarding supply and demand, with demand scenarios based on accurate forecasting at the country level and vaccine supply based on realistic industrial scenarios. All 126 countries using only tOPV committed to implement the SAGE recommendation (from October 2016) to introduce at least one IPV dose into RI.[51] However, long-term demand for IPV remains uncertain. Aside from countries with PEFs, which will be expected 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.

[49] World Health Organization. GAPIII: WHO Global Action Plan to minimize poliovirus facility-associated risk. Geneva: WHO; 2015 (http://polioeradication.org/wp-content/uploads/2016/12/GAPIII_2014.pdf).

[50] 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).

[51] World Health Organization Immunization, Vaccines and Biologicals Repository, and Meeting of the Strategic Advisory Group of Experts on Immunization, October 2016 – conclusions and recommendations. Wkly Epidemiol Rec. 2016;91:561–84.

Figure 4. Demand scenarios and base-case supply estimates for inactivated poliovirus vaccine, 2017–2026



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 from 2021.
2. Mixed Scenario 1 (dark brown): India, Sri Lanka, and Bangladesh use two doses of fIPV. Remainder of countries have a full-dose schedule.
3. Mixed Scenario 2 (light brown): India, Sri Lanka and Bangladesh, as well as 21 countries that have not introduced IPV as of January 2017, use two doses of fIPV. The remainder are on one full dose in 2017–2020 and two full doses in 2021–2026.
4. Mixed Scenario 3 (blue): Tier 1 countries use one full dose in 2017–2020 and two full doses from 2021. The remainder are on two fIPV doses.

Projections cover the 126 countries using OPV in 2016; M=millions.

Source: Gavi and GPEI. IPV Supply and Procurement Roadmap – Public Summary. August 2017.

As countries make decisions on IPV use, they should be supported at 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 through appropriate visibility into supply and demand evolution.

Facilitate the development of sufficient IPV products to meet country requirements at a price acceptable to countries and manufacturers

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

Scientific data confirming the immunogenicity of intradermal fIPV and country experience demonstrating its operational feasibility provide strong evidence for the potential broader use of fractional dosing. 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.[52] Although initially developed as a method to

[52] Okayasu H, Sein C, Chang Blanc D, Ramirez Gonzalez A, Zehrung D, Jarrahian C et al. Intradermal Administration of Fractional Doses of Inactivated Poliovirus Vaccine: A Dose-Sparing Option for Polio Immunization. J Infect Dis. 2017;216(S1):S161–7.

extend limited vaccine supplies, fIPV can also provide cost savings if appropriate vial sizes are available and intradermal delivery device costs can be decreased.[53] 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 the environmental transmission of polioviruses. (*See the **Research activities** section.*)

Combining antigens can stimulate community demand and improve the 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 (with whole cell pertussis) 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.

Sabin IPVs may potentially provide more affordable, effective options against stopping poliovirus transmission, the costs, efficacy, and feasibility of these new vaccines' large-scale production are still being evaluated. (*See the **Research activities** section.*)

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Withdrawing bOPV and extending widespread IPV use will mitigate the risks from VDPVs and VAPP and protect against the possible re-emergence of WPV.

[53] World Health Organization. Meeting of the Strategic Advisory Group of Experts on Immunization, October 2016 – conclusions and recommendations. Wkly Epidemiol Rec. 2016;48:561–84.

Advocate for sustainable financing of IPV

Low-income countries are expected to receive Gavi funding through 2020 to support the current SAGE recommendation that all countries 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. Including IPV as a "global public good" under a new Vaccine Investment Strategy is being considered. The number and type of dosing, length of funding, and specifics on vaccine schedules all remain to be determined.

Facilitate the 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 may still be in the process of fully integrating the IPV 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 fIPV in RI has been deployed in some countries (such as India, Bangladesh, and Sri Lanka), though others have reservations about the increased operational requirements and training required for intradermal delivery. Several alternatives to the 0.1 ml syringe that is used for intradermal injection for fIPV have been developed and widely tested.[54] These options are still relatively expensive and some require the intensive retraining of healthcare workers. Nevertheless, they may present viable methods to increase the efficiency of intradermal 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 under way to determine the efficacy of fractional intramuscular dosing that would rely on regular syringes.

The country transition planning process, supported by the GPEI, aims to identify how polio resources, human capacity, and knowledge can be directed to achieve the GVAP and broader public health goals. The overall strengthening of RI must be a critical priority to attain these broader goals, as well as sustaining the functions essential to protecting populations from future polio emergences. As partners develop "GVAP 2.0," sustaining polio eradication should be a core objective. 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.[55] 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.

[54] Okayasu H, Sein C, Chang Blanc D, Ramirez Gonzalez A, Zehrung D, Jarrahian C et al. Intradermal Administration of Fractional Doses of Inactivated Poliovirus Vaccine: A Dose-Sparing Option for Polio Immunization. J Infect Dis. 2017:216 (S1):S161–7.

[55] World Health Organization. Global Vaccine Action Plan 2011–2020. Geneva: WHO; 2013 (http://www.who.int/immunization/global_vaccine_action_plan/en).

Polio surveillance in the post-certification era will take a risk-based approach by prioritizing risks, clarifying risk tolerance, and developing risk mitigation measures.

World Health Organization / S. Ramo (Afghanistan)

GOAL 3 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 the poliovirus surveillance paradigm
	Actvitiy 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

Source: WHO, Post-Certification Strategy.

Introduction

Comprehensive acute flaccid paralysis (AFP) surveillance and rapid response vaccination campaigns have been core strategies for polio eradication since the inception of the Global Polio Eradication Initiative (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 International Health Regulations (IHR) and according to their assessed risk.[56]

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 circulating vaccine-derived poliovirus [cVDPV] detected in a human or the environment). Although primary responsibility for response rests at the country level, the global and regional capacity and resources should be adequate to support national efforts, especially in high-risk areas.

[56] World Health Organization. International Health Regulations (2005), Third Edition. Geneva: WHO; 2016 (http://www.who.int/ihr/publications/9789241580496/en).

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).[57] IHR monitoring protocols for infectious diseases, as supplemented by the Global Health Security Agenda (GHSA), 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.[58]

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 that 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.

B. Risks

A number of potential risks to poliovirus detection exist 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 measure	Technical note
Substantially delayed detection of poliovirus re-emergence or transmission	• 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 (VPDs) / communicable disease surveillance systems to sustain capacity	• The sensitivity of AFP surveillance is inherently limited since the clear majority of polio infections are asymptomatic.[59] • Low-level poliovirus transmission can continue undetected for many months in areas using only IPV.[60] • In suitable locations, environmental surveillance can provide more sensitive detection of polioviruses than AFP surveillance alone.[61] • 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 the operational efficiency of vertical AFP surveillance systems. The timing of integration should be paced to maintain required sensitivity in high-risk areas.
Missed poliovirus cases/ transmission among populations that are hard-to-reach, inaccessible, or that do not access health systems	• Develop and implement specific strategies to reach high-risk populations	• These same populations may be highly vulnerable to polio infections due to low vaccination coverage, poor sanitation, etc.
Failure to rapidly detect primary immunodeficiency disease patients with subclinical poliovirus infection or poliovirus excretion	• Develop a sustainable PID surveillance system in high-risk areas to provide early detection of immunodeficiency-associated vaccine-derived poliovirus (iVDPV)	• Early identification of PID patients 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 a containment breach in a poliovirus-containing facility or surrounding community	• Develop comprehensive detection plans specifically targeted to environments of poliovirus-containing facilities	• The regulatory oversight and containment requirements are complicated (*see **Goal One***).

AFP= acute flaccid paralysis; IPV= inactivated poliovirus vaccine; VPD= vaccine-preventable disease; iVDPV= immunodeficiency-associated vaccine-derived poliovirus; PID= primary immunodeficiency disease.

Source: WHO, Post-Certification Strategy.

[57] 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; 2014 (http://www.who.int/ihr/publications/WHO_HSE_GCR_LYO_2014.4/en).

[58] World Health Organization. Protocol for Assessing National Surveillance and Response Capacities for the International Health Regulations (2005). Geneva, WHO; 2010 (http://www.who.int/ihr/publications/who_hse_ihr_201007_en.pdf); also see Global Health Security Agenda [website] (https://www.ghsagenda.org).

[59] Grassly NC. The final stages of the global eradication of poliomyelitis. Phil Trans R Soc B. 2013,368. 20120140.

[60] Kopel E, Kaliner E, Grotto, I. Lessons from a Public Health Emergency – Importation of Wild Poliovirus to Israel. N Engl J Med. 2014;371:981–3. doi: 10.1056/NEJMp1406250.

[61] Cowger TL, Burns CC, Sharif S, Gary Jr HE, Iber J, Henderson E et al. The role of supplementary environmental surveillance to complement acute flaccid paralysis surveillance for wild poliovirus in Pakistan – 2011–2013. PLoS ONE. 2017;12(7):e0180608 (https://doi.org/10.1371/journal.pone.0180608).

C. What will be done

The Polio Eradication & Endgame Strategic Plan (PEESP) already recommends surveillance strategies for reaching WPV eradication. To have confidence in this milestone, the Global Commission for the Certification of Poliomyelitis Eradication (GCC) and the Regional Certification Commissions (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 help countries implement the strategies and standards expected from the PEESP to achieve global certification, including strategies for inaccessible areas and high-risk populations.[62] The Post-Certification Strategy (PCS) builds on current strategies and standards by providing broad global recommendations for poliovirus surveillance after certification.

Activity 3.1.1 – Redefine the polio surveillance paradigm

The current paradigm for poliovirus surveillance will need continual refinement 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, including the probability and consequences of poliovirus re-emergence, the intensity of effort required to maintain standards, and the evolution of risk over time.

Table 5. Current and redefined paradigms for poliovirus surveillance

	Current paradigm	Redefined paradigm
Strategies in focus areas	**Countries in non-certified regions** • Primarily active, case-based AFP surveillance with multiple facility and community reporting sites, often separate from other IBS systems • Supplemented by ES	**High-risk areas** • 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	**Countries in certified regions** • Mix of AFP, ES, and EVS	**Medium- and low-risk areas** • 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 organization	• Polio-specific laboratories linked in a tiered network with designated capacities	• Maintain the GPLN; polio-specific laboratories continue at global/regional levels, but become integrated virology laboratories at the national level • Potential for improved, faster diagnostics; more stringent containment requirements
Key additional strategies	• Limited iVDPV global registry • Ad hoc surveillance strategies around PEFs	• 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.

Source: WHO, Post-Certification Strategy.

[62] Global Polio Eradication Initiative. Global Polio Surveillance Action Plan. (In preparation).

The redefined polio surveillance paradigm: Five essential strategies

Beyond the minimum capacity to provide early warning of global public health security threats as required for all countries under the 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, ES, and EVS, with supplemental activities for high-risk, hard-to-reach populations or areas**

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 paediatric neurology services, special attention should be paid to include surveillance for conditions that are the main differential diagnoses of poliomyelitis (such as Guillain-Barré 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 non-polio acute flaccid paralysis [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.

Environmental surveillance

Since 2015, 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.[63] Because the benefits of ES will increase as the detectable paralysis-to-infection ratio of polio decreases,[64] the GPEI is preparing a revised long-term strategy to reflect increased reliance on this method.[65]

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

- To track the elimination of Sabin viruses after bOPV cessation or use of mOPV
- To support the early detection of poliovirus circulation
- To monitor the geographic extent of transmission
- To 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 a comprehensive risk analysis, with consideration given to the surveillance and laboratory capacity required to sustain quality. However, ES has potential limitations in terms of the geographic locations where it can be applied, the interpretation of findings, and technical implementation.[66]

Enterovirus surveillance

EVS is primarily a passive, laboratory-based system that collects stool, respiratory specimens, or cerebral spinal fluid from a range of patients showing clinical symptoms of enterovirus infection, including AFP.

[63] World Health Organization. Polio Environmental Surveillance Expansion Plan. Geneva: WHO; 2015 (http://polioeradication.org/wp-content/uploads/2016/07/GPLN_ExpansionPlanES.pdf).
[64] Hovi T, Shulman LM, van der Avoort H, Deshpande J, Roivainen M, de Gourville EM. Role of environmental poliovirus surveillance in global polio eradication and beyond. Epidemiol Infect. 2012;140(1):1–13. doi:10.1017/S095026881000316X.
[65] Global Polio Eradication Initiative. Long-term Strategy for Poliovirus Environmental Surveillance. (In preparation).
[66] Asghar A, Diop OM, Weldegebriel G, Malik F, Shetty S, El Bassioni L et al. Environmental Surveillance for Polioviruses in the Global Polio Eradication Initiative. J Infect Dis. 2014;210(S1): S294–303.

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.[67] 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 that either cannot or chose not to access health services.[68] 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 levels.[69] 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 towards coordination, communication, and outreach tactics for intensified surveillance in high-risk intercountry areas (such as Lake Chad) or conflict zones.

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

   EBS is the organized collection, monitoring, assessment, and interpretation of mainly unstructured ad hoc information regarding health events that may represent an acute risk to human health.[70]

   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, nongovernmental organizations, informal community healthcare providers, or other sources of information, such as social media or a national hotline.[71]

   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.[72] 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 patients with primary immunodeficiency diseases (PIDs) to detect and treat poliovirus excretors**

   Countering iVDPV risks requires the 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 the potential for community spread of iVDPV exists, no occurrences have been documented 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.[73] (*See also **Activity 3.2.1.***)

[67] World Health Organization Regional Office for Europe and Centers for Disease Control and Prevention. Enterovirus surveillance guidelines: Guidelines for enterovirus surveillance in support of the Polio Eradication Initiative. Copenhagen: WHO; 2015.

[68] 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.

[69] World Health Organization. Outbreak surveillance and response in humanitarian emergencies: WHO guidelines for EWARN implementation. Geneva: WHO; 2012 (http://whqlibdoc.who.int/hq/2012/WHO_HSE_GAR_DCE_2012_1_eng.pdf); Hamisu AW, Johnson TM, Craig K, Mkanda P, Banda R, Tegegne SG et al. Strategies for Improving Polio Surveillance Performance in the Security-Challenged Nigerian States of Adamwawa, Borno, and Yobe During 2009–2014. J Infect Dis. 2016;213(S3):S136–9; Global Polio Surveillance Action Plan. (In preparation).

[70] 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; 2014.

[71] WHO Western Pacific Region. A Guide to Establishing Event-based Surveillance. Geneva: WHO; 2008 (http://www.wpro.who.int/emerging_diseases/documents/docs/eventbasedsurv.pdf).

[72] World Health Organization. International Health Regulations (2005), Third Edition. Geneva: WHO; 2016, Part II, Article 9.

[73] Duintjer Tebbens RJ, Pallansch MA, Thompson KM. Modeling the prevalence of immunodeficiency-associated long-term vaccine-derived poliovirus excretors and the potential benefit of antiviral drugs. BMC Infect Dis. 2015;15:379.

The identification of iVDPV excretors without paralysis shows that AFP surveillance alone is insufficient. Other options currently being piloted include: (1) identifying excretors among patients with PIDs (particularly B-cell deficiencies or combined immunodeficiencies) through immunology networks;[74] and (2) conducting clinical screening and then immunologic testing for those who meet the definition of possible PID in all children with or without paralysis aged under 15 years and attending a health facility within an AFP-reporting network.[75]

Better understanding of the risk, including the 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 the tolerance towards undetected iVDPV excretion. Enhanced surveillance (e.g., frequent active surveillance, an increased number of target facilities, expanded age groups) may be required during Years 6–9 post-certification when iVDPVs 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 the Global Action Plan to minimize poliovirus facility-associated risk (Third Edition) (GAPIII), all poliovirus-essential facilities (PEFs) must develop a risk assessment plan to detect any breach within their facility that may 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 ES as well as 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, although 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 the **Research activities** section*). Even in locations without ES, containment requirements will necessitate some new approaches (*see **Goal One, 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 that 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.[76]

[74] Aghamohammadi A, Abolhassani H, Kutukculer N, Wassilak, SG, Pallansch MA, Kluglein S et al. Patients with Primary Immunodeficiencies Are a Reservoir of Poliovirus and a Risk to Polio Eradication. Front. Immunol., 13 June 2017;8:685 (https://doi.org/10.3389/fimmu.2017.00685).

[75] El-Sayed ZA, Mach O, Hossny EM, Galal NM, El-Sawy I, Elmarsafy A 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.

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

Activity 3.1.2 – Sustain adequate and technically qualified laboratory and surveillance infrastructure (including human capacities) and 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 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 to sustain poliovirus surveillance.[77] 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 ministry of health to ministry of health-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.

Primary responsibility for poliovirus surveillance lies at the national level. In the post-certification era, surveillance capacity required beyond this core level will depend on individual country risk and may include conducting environmental surveillance.

World Health Organization

[77] Wassilak SG, Williams CL, Murrill CS, Dahl BA, Ohuabunwo C, Tangermann RH. Using Acute Flaccid Paralysis Surveillance as a Platform for Vaccine-Preventable Disease Surveillance. J Infect Dis. 2017;216(S1):S293–8.

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 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.[78]

Information management

Access to reliable, quality, and timely AFP, laboratory, and ES data, currently provided by the web-based polio information system (POLIS), will continue to be a strategic priority. High-quality data are critical not only to detect infections, but also to help monitor 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 the full utilization of new technologies in mobile health ("mHealth"), and innovations such as Auto-Visual AFP Detection and Reporting (AVADAR), is recommended.[79]

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. Maintaining a global repository of poliovirus nucleotide sequences to facilitate tracking any detected poliovirus will also be needed.

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 offices 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.

Objective 3.2: Adequate response capacity

A. Context

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.[80] The IHR requires WHO to assist country capacity and provide support if local resources are insufficient.

[78] Diop OM, Kew OM, de Gourville EM, Pallansch MA. The Global Polio Laboratory Network as a Platform for the Viral Vaccine-Preventable and Emerging Diseases Laboratory Networks. J Infect Dis. 2017;216(S1):S299–307; Mulders MN, Serhan F, Goodson JL, Icenogle J, Johnson BW, Rota PA. Expansion of Surveillance for Vaccine-preventable Diseases: Building on the Global Polio Laboratory Network and the Global Measles and Rubella Laboratory Network Platforms. J Infect Dis. 2017;216(S1):S324–30.

[79] World Health Organization. mHealth: New horizons for health through mobile technologies. Geneva: WHO; 2011 (http://www.who.int/goe/publications/goe_mhealth_web.pdf).

[80] World Health Organization. Protocol for Assessing National Surveillance and Response Capacities for the International Health Regulations (2005). Geneva:WHO; 2010 (http://www.who.int/ihr/publications/who_hse_ihr_201007_en.pdf); also see Global Health Security Agenda [website] (https://www.ghsagenda.org).

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	• 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	• Comprehensive risk models have been developed, but their predictive value remains to be determined.[81]
Failure to prevent transmission due to inadequate response strategies or capacity	• Develop a global protocol for polio outbreak response specific to the 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 the IHR plus polio-specific expertise to mount an aggressive response	• Capacity to plan and implement an SIA in response to an outbreak may rapidly diminish as experienced staff retire or move to other programmes.
Failure to prevent transmission due to ineffective or insufficient vaccine or antiviral supply	• Create and manage adequate stockpiles of mOPV and IPV • Develop an adequate supply of safe, effective PAVDs • Develop alternative poliovirus vaccines and/or delivery systems that can increase effectiveness and/or supply • Ensure visibility into vaccine supply and demand and healthy IPV market conditions to ensure timely investment of vaccine manufacturers in industrial capacities and production lines	• IPV is highly effective in protecting individual recipients through humoral immunity, but its role in stopping faecal-oral transmission is more limited; the duration of protection of a two-dose schedule is unknown.[82] • 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.[83] • See the ***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	• Develop alternative (preferably oral) polio vaccines that prevent poliovirus transmission without the risks of current Sabin vaccines • Maximize SIA quality and consider a "ring" strategy with IPV around an outbreak	• mOPV can present a risk for VAPP and VDPVs in a low-immunity setting.[84] • See the ***Research activities*** section for details on new poliovirus vaccines.

IHR= International Health Regulations; iVDPV= immunodeficiency-associated vaccine-derived poliovirus; SIA= supplementary immunization activity; 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.

Source: WHO, Post-Certification Strategy.

[81] O'Reilly KM, Lamoureux C, Molodecky NA, Lyons H, Grassly NC, Tallis G. An assessment of the geographical risks of wild and vaccine-derived poliomyelitis outbreaks in Africa and Asia. BMC Infect Dis. 2017;17:367. doi:10.1186/s12879-017-2443-4.

[82] Bandyopadhyay AS, Garon J, Seib K, Orenstein WA. Polio vaccination: past, present and future. Future Microbiol. 2015;10(5):791–808. doi: 10.2217/fmb.15.19.

[83] McKinlay MA, Collett MS, Hincks JR, Oberste MS, Pallansch MA, Okayasu H. Progress in the development of poliovirus antiviral agents and their essential role in reducing risks that threaten eradication. J Infect Dis. 2014;210(S1):S447–53. doi:10.1093/infdis/jiu043.

[84] Estivariz CF, Molnar Z, Venczel L, Kapusinszky B, Zingeser JA, Lipskaya GY. Paralytic Poliomyelitis Associated With Sabin Monovalent and Bivalent Oral Polio Vaccines in Hungary. Am J Epidemiol. 2011;174(3):316–25.

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 the presence of humanitarian emergencies) should help identify countries or areas at risk of either immediate or long-term possible poliovirus re-emergence. Further analysis, including type-specific risks, trends, and the 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 polio-specific outbreak response guidelines. All countries should include the 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.[85]

Country-level response strategies should follow global and regional guidelines. Existing standard operating procedures that provide guidance on risk assessment, control measures, and monitoring specific to responding to the 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.[86]

Vaccine response strategies

Vaccine response strategies required after bOPV cessation should be proposed now in order to determine vaccine stockpile requirements (*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 faecal-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 cVDPVs outside the outbreak zone.[87] Adding IPV preemptively as a ring around an initial SIA target population is a potential strategy to reduce this risk, which needs further research.[88]

Given the risks of mOPV use and the limitations of IPV in areas with poor sanitation, developing alternative vaccines, such as new oral poliovirus vaccine (nOPV), is critical to sustain eradication. (*See the* ***Research activities*** *section.*)

[85] World Health Organization. Emergency Response Framework, Second Edition. Geneva: WHO; 2017 (http://apps.who.int/iris/bitstream/10665/258604/1/9789241512299-eng.pdf); World Health Organization. Rapid Risk Assessment of Acute Public Health Events. Geneva: WHO; 2012; and Inter-Agency Standing Committee. IASC Reference Module for the Implementation of the Humanitarian Programme Cycle (Version 2.0). Geneva: IASC; 2015.

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

[87] Famulare M, Selinger C, McCarthy KA, Eckhoff PA, Chabot-Couture G. Assessing the stability of polio eradication after the withdrawal of oral polio vaccine. 2016 (http://dx.doi.org/10.1101/084012). bioRxiv preprint first posted online 27 October 2016.

[88] Duintjer Tebbens RJ, Thompson KM. Costs and Benefits of Including Inactivated in Addition to Oral Poliovirus Vaccine in Outbreak Response After Cessation of Oral Poliovirus Vaccine Use. MDM Policy & Practice. 2017;2:1–13. doi:10.1177/2381468317697002.

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.[89]

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

The majority of OPV-infected PID patients spontaneously stop excreting any poliovirus in less than six months. A minority of PID patients excrete iVDPVs for more than six months, and even fewer excrete chronically (for over five years).[90] 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 the* ***Research activities*** *section*). Further information on the specific types of PID most prone to excretion and the risk of iVDPV transmissibility will guide the 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. The detection of an iVDPV excretor should prompt the vaccination of close contacts with IPV. If laboratory methods permit the 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

All countries should include poliovirus detection as a possible scenario in their communicable disease outbreak preparedness response plans.

The Bill & Melinda Gates Foundation (Mozambique)

[89] See World Health Organization. Vaccination in Humanitarian Emergencies: Implementation Guide. Geneva: WHO; 2017 (http://www.who.int/immunization/documents/general/who_ivb_17.13/en).

[90] Duintjer Tebbens RJ, Pallansch MA, Thompson KM. Modeling the prevalence of immunodeficiency-associated long-term vaccine-derived poliovirus excretors and the potential benefit of antiviral drugs. BMC Infect Dis. 2015;15:379.

about iVDPV transmissibility is available, the decision to initiate a community vaccination response will depend on a risk analysis of the poliovirus's source (e.g., human vs environment) and on the risk of further spread based on the 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 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 One***).

Activity 3.2.2 – Sustain trained human capacity and create, maintain, and manage adequate stockpiles of polio vaccine and antivirals to appropriately respond

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 heath security threat.[91] 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 depend on individual country situations. Especially 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.[92]

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. Modelling based on an analysis of type 2 outbreaks following tOPV withdrawal will be informative, but decisions on required stockpile size ultimately will depend on the risk tolerance for responding to outbreaks and avoiding stockouts. 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.

[91] World Health Organization. Emergency Response Framework, Second Edition. Geneva: WHO; 2017.
[92] World Health Organization. Joint external evaluation tool: International Health Regulations (2005). Geneva: WHO; 2016 (http://apps.who.int/iris/bitstream/10665/204368/1/9789241510172_eng.pdf).

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.[93] 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.

[93] Duintjer Tebbens RJ, Pallansch MA, Thompson KM. Modeling the prevalence of immunodeficiency-associated long-term vaccine-derived poliovirus excretors and the potential benefits of antiviral drugs. BMC Infect Dis. 2015;15:379.

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 to mitigate future risks.

UNICEF / Phil Hatcher-Moore

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.

Partners of the Global Polio Eradication Initiative (GPEI) maintain independent but highly collaborative polio research programmes. The Polio Research Committee (PRC), which includes the GPEI partners and ex officio representatives from the National Institutes of Health (United States), the U.S. Food and Drug Administration, PATH, and WHO regional offices, serves as a forum to identify research needs, review current research activities, and support a competitive extramural research programme. 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 modellers.

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 Post-Certification Strategy (PCS) goals, recognizing there may be broad applicability across goals, for example with modelling, 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 the 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 One: Contain polioviruses

Poliovirus-essential facilities (PEFs) include vaccine manufacturers, public health testing facilities, and academic laboratories that 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.

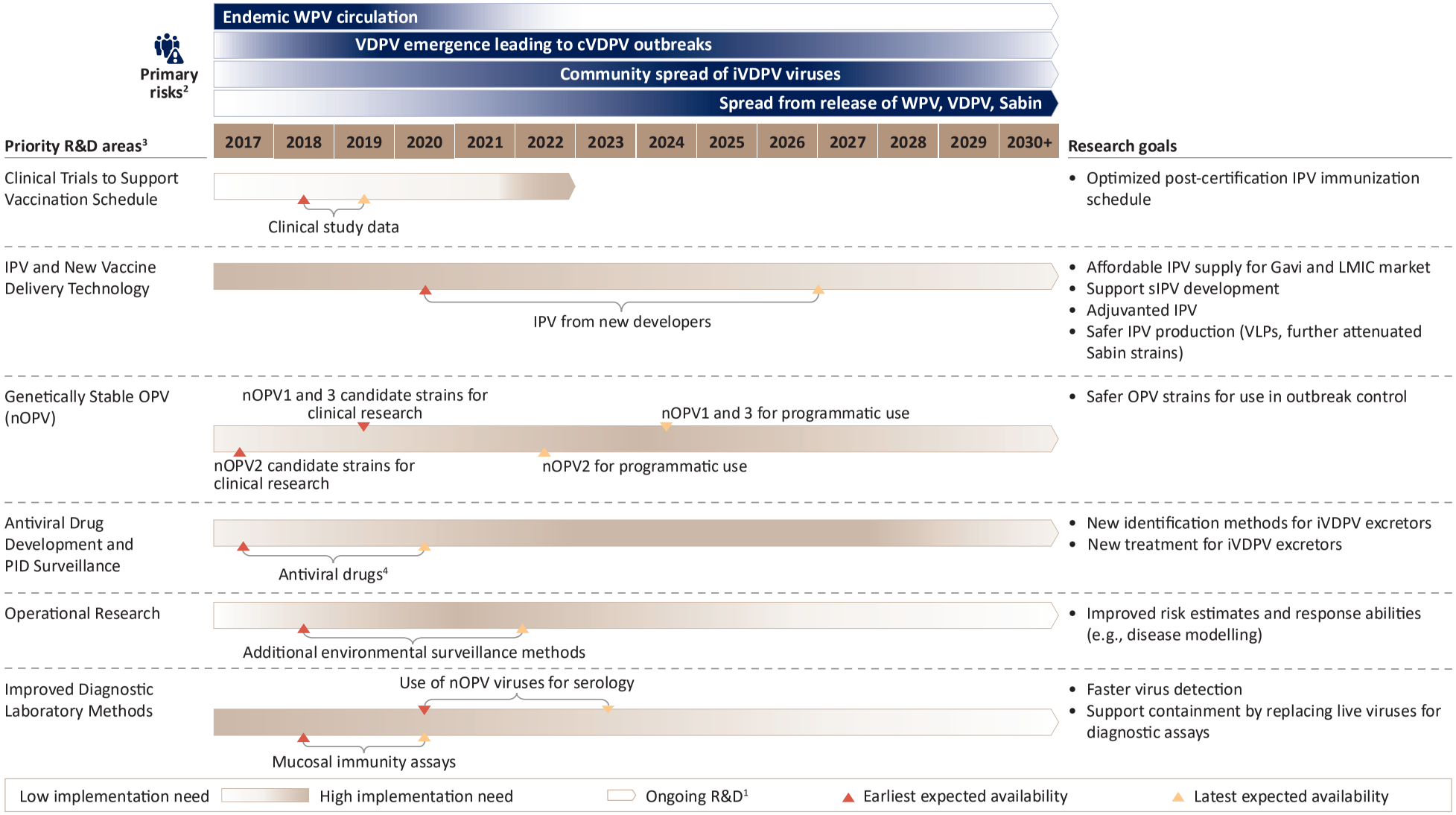
Restrictions on the use of all wild and Sabin polioviruses in clinical research will seriously limit the use of tests essential to assess population immunity as well as the immunogenicity and efficacy of vaccines and antivirals. New assays for the determination of serum antibodies and for the assessment of mucosal immunity are in development.[94] Also, if alternative poliovirus strains prove to be safe to 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 the efficacy of an antiviral drug.

Goal Two: Protect populations

Protecting the global population against a re-emergence of poliomyelitis will require the optimization of individual protection with marketed vaccines, and the development of new vaccines designed to reduce

[94] Wright PF, Connor RI, Wieland-Alter WF, Hoen AG, Boesch AW, Ackerman ME 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;16:1377–84 (http://dx.doi.org/10.1016/S1473-3099(16)30169-4); Wright PF, Wieland-Alter W, Ilyushina NA, Hoen AG, Arita M, Boesch AW et al. Intestinal immunity is a determinant of clearance of poliovirus after oral vaccination. J Infect Dis. 2014;209(10):1628–34. doi:10.1093/infdis/jit671.

Figure 5. Polio research and development, 2017–2030 and beyond



[1] R&D to introduce new products may not always be completed before the need to implement 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. [4] Earliest availability is for compassionate use.

IPV= inactivated poliovirus vaccine; iVDPV= immunodeficiency-associated vaccine-derived poliovirus; LMIC= low and middle-income countries; nOPV= new oral poliovirus vaccine; OPV= oral poliovirus vaccine; PID= primary immunodeficiency disease; R&D= research and development; sIPV= Sabin strain inactivated poliovirus vaccine; VDPV= vaccine-derived poliovirus; VLPs= virus-like particles; WPV= wild poliovirus.

Source: WHO, Post-Certification Strategy.

costs to Gavi, the Vaccine Alliance, and low- and middle-income markets, improve coverage, and reduce the transmission of live polioviruses through induction of mucosal immunity. In addition, advances in vaccine delivery technology may facilitate vaccine administration and enhance coverage.

Optimization of individual protection with currently marketed IPV vaccines – The Strategic Advisory Group of Experts on Immunization (SAGE) recommended a two-dose IPV schedule for the post-certification period and suggested that two fractional doses of inactivated poliovirus vaccine (fIPV) delivered intradermally are equivalent to one full IPV dose delivered intramuscularly for routine immunization (RI), when fIPV is given at the appropriate age. However, additional clinical research is necessary to have confidence in this recommendation. Studies are under way that will provide more information on the optimal full-dose and fractional-dose IPV schedules for primary immunization by early 2019. These studies are complemented by operational research on the 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 programmes that deploy different strategies to reduce costs (enhanced production technology, improved viral yield, antigen-sparing) are in progress. Other manufacturers have started Sabin strain inactivated poliovirus vaccine (sIPV) development programmes designed to enable developing country vaccine production.[95] Several programmes have recently initiated clinical trials that will extend well into the post-certification period, and new IPV vaccine supplies are projected to come to market between 2019 and 2024.

Discovery and translational-phase IPV projects also exist, 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, toll-like receptor (TLR) agonists, and E. coli double-mutant labile toxin (dmLT) that may also induce mucosal immunity.[96] 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.[97] 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 and have the potential to reduce vaccine costs by dose sparing and reduce shipping, storage, and cold-chain costs. MAP availability could facilitate IPV delivery for RI and during campaigns for cessation or outbreak control. To date, MAPs suitable for clinical study have not been produced by any of the developers, and thus the future of MAP technology for polio immunization is uncertain.

[95] Okayasu H, Sein C, Hamidi A, Bakker WA, Sutter RW. Development of inactivated poliovirus vaccine from Sabin strains: A progress report. Biologicals. 2016;44(6):581–7; Sutter RW, Okayasu H, Kieny MP. Next Generation Inactivated Poliovirus Vaccine: The Future Has Arrived. Clin Infect Dis. 2017;64(10):1326–7. doi:10.1093/cid/cix116.

[96] 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(16):1909–15. doi:10.1016/j.vaccine.2015.02.069; Hawken J, Troy SB. Adjuvants and inactivated polio vaccine: a systematic review. Vaccine. 2012;30(49):6971–9. doi:10.1016/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. 2010;29(4):644–9. doi:10.1016/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 (https://doi.org/10.1371/journal.ppat.1006117).

[97] Resik S, Tejeda A, Mach O, Fonseca M, Diaz M, Alemany N 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(2):307–13. doi:10.1016/j.vaccine.2014.11.025; Clarke E, Saidu Y, Adetifa JU, Adigweme I, Hydara MB, Bashorun AO 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(8):e534–47. doi:10.1016/S2214-109X(16)30075-4; Anand A, Zaman K, Estivariz CF, Yunus M, Gary HE, Weldon WC 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(48):6816–22. doi:10.1016/j.vaccine.2015.09.039.

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 Three: Detect and respond

Continued research and development will be required to support post-certification surveillance and outbreak response planning, including ongoing risk assessment and modelling, operational research, innovations in environmental surveillance (ES), and rapid diagnostics to identify and characterize polioviruses in the field and in the laboratory. Additional research on new poliovirus vaccines for outbreak response and the development of antiviral drugs to clear infection in long-term, immunodeficiency-associated vaccine-derived poliovirus (iVDPV) excretors will also be critical to sustain a polio-free world.

Risk assessment and modelling – The forecasting of short- and long-term risks will require the development of models to predict the absolute and relative risks from WPV, circulating vaccine-derived poliovirus (cVDPV), and iVDPV in all regions and over time until all credible threats to eradication are removed.[98] Post-certification, it will be critically important to continuously re-evaluate assumptions and update models based on past and current experience.

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

Gavi, the Vaccine Alliance

[98] 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;15:389; O'Reilly KM, Lamoureux C, Molodecky NA, Lyons H, Grassly NC, Tallis G. An assessment of the geographical risks of wild and vaccine-derived poliomyelitis outbreaks in Africa and Asia. BMC Infect Dis. 2017;17:367; Famulare M, Selinger C, McCarthy KA, Eckhoff PA, Chabot-Couture G. Assessing the stability of polio eradication after the withdrawal of oral polio vaccine. 2016 (http://dx.doi.org/10.1101/084012).

Periodic, targeted serological surveys in high-risk countries may be needed to better inform the models and improve risk assessment. The 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 the development and deployment of new tools, such as geographic information system (GIS) mapping to improve microplans and smartphone 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 withdrawal of bOPV or mOPV use.[99] Improvements to ES will require research on the optimization of site selection through modelling, demography, and the use of GIS technology, as well as continued innovations in specimen collection, sample concentration, and molecular detection methods to distinguish and characterize poliovirus isolates from individual excretors in the sample population.

Rapid diagnostic tests – The development of rapid diagnostic tests that can be applied in the field for quick, point-of-care testing could enhance both acute flaccid paralysis (AFP) surveillance and ES 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 oral poliovirus vaccine type 2 (nOPV2) candidate strains have been manufactured for clinical study, and human trials are now under way. 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 the development of at least two antiviral drugs to reduce the risk of outbreaks from 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.[100,101] Assuming successful completion of clinical trials, ViroD7000 (a combination of pocapavir and V-7404) will be available for distribution under a 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.

[99] Hovi T, Shulman LM, van der Avoort H, Deshpande J, Roivainen M, de Gourville EM. Role of environmental poliovirus surveillance in global polio eradication and beyond. Epidemiol Infect. 2012;140(1):1–13. doi:10.1017/S095026881000316X.

[100] McKinlay MA, Collett MS, Hincks JR, Oberste MS, Pallansch MA, Okayasu H. Progress in the development of poliovirus antiviral agents and their essential role in reducing risks that threaten eradication. J Infect Dis. 2014;210(S1):S447–53. doi:10.1093/infdis/jiu043.

[101] Collett MS, Hincks JR, Benschop K, Duizer E, van der Avoort H, et al. Antiviral Activity of Pocapavir in a Randomized, Blinded, Placebo-Controlled Human Oral Poliovirus Vaccine Challenge Model. J Infect Dis. 2017;215(3)335–43. doi:10.1093/infdis/jiw542.

UNICEF / Al-Issa (Syria)

Annex A

Post-Certification Strategy engagement list

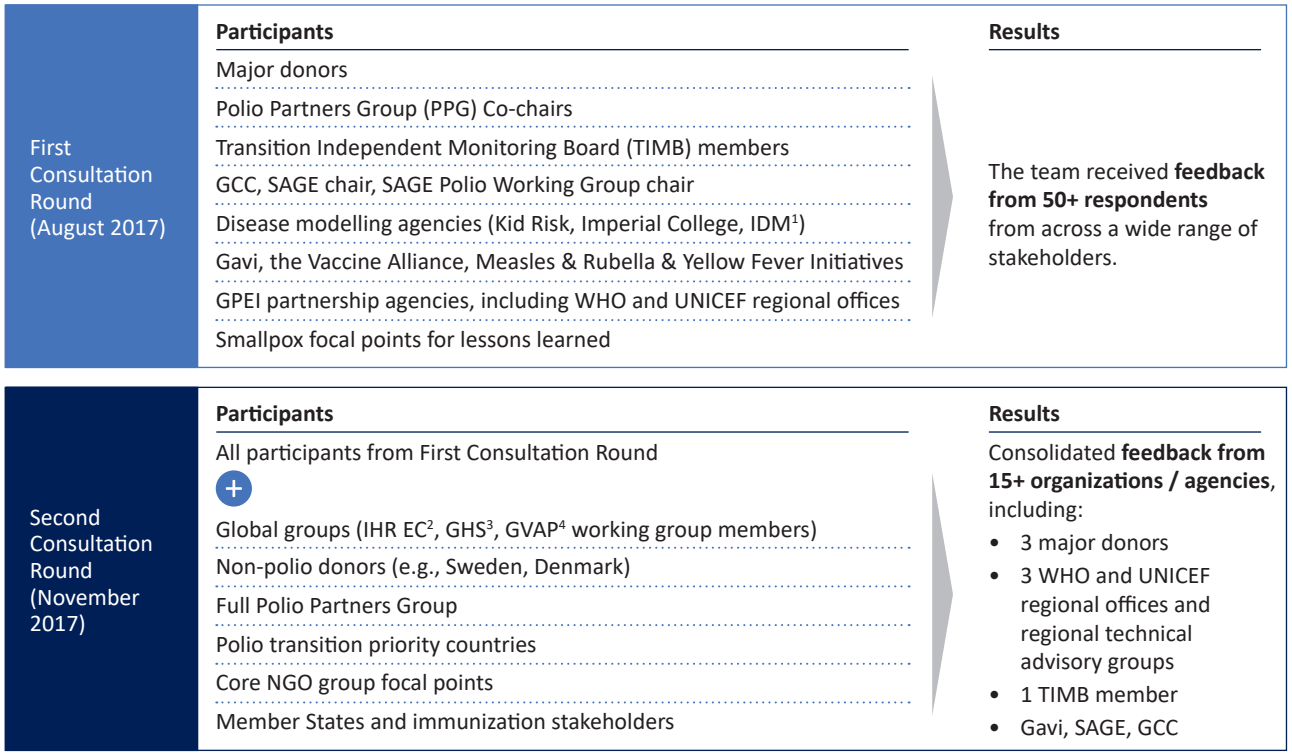
The Global Polio Eradication Initiative (GPEI) engaged a broad set of stakeholders as an opportunity to gather input and begin reviewing the critical functions that will be needed to continue after certification to maintain a polio-free world. These stakeholders and organizations include:[102]

- WHO Member States and Executive Board
- WHO and the United Nations Children's Fund (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 (TAGs)
  - 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 (PPG) 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, Inc. (modelling group)
- Imperial College modelling group
- Institute for Disease Modeling polio team
- Gavi, the Vaccine Alliance
- CORE (Coalition of nongovernmental organizations)
- GPEI Partners (Polio and Immunization teams at the global and regional levels)
- GPEI Management Groups and Task Teams
- Polio Oversight Board (POB)
- Global Polio Laboratory Network (GPLN)
- WHO Health Emergencies Programme

[102] A full list by organization and focal point is available upon request.

The Post-Certification Strategy (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.[103]

Figure 6. Consultation summary provided to the Polio Oversight Board



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

Source: WHO, Post-Certification Strategy.

[103] 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

Risk analysis

This annex provides additional technical explanation and analysis on the risk categories identified in the Post-Certification Strategy.

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, and 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.[104]

Future outbreak risks

Risk category 1: Risks due to continued OPV use

The risk of vaccine-associated paralytic poliomyelitis (VAPP) following exposure to trivalent oral poliovirus vaccine (tOPV) has been well documented, but the risk from monovalent oral poliovirus vaccine (mOPV) in countries with high faecal-oral transmission of poliovirus is unknown.[105] Evidence shows that mOPV use can be associated with VAPP, particularly mOPV type 3, so the risk is expected to continue as long as any OPV is used in outbreak response.[106] However, vaccination with IPV as proposed for routine immunization use after certification could protect against VAPP.[107]

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 faecal-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***).

[104] For a detailed review, see Fine PEM, Ritchie S. Perspective: Determinants of the Severity of Poliovirus Outbreaks in the Post Eradication Era. Risk Anal. 2006;26(6): 1533–40.

[105] Bandyopadhyay AS, Garon J, Seib K, Orenstein WA. Polio vaccination: past, present and future. Future Microbiol. 2015;10(5):791–808. doi: 10.2217/fmb.15.19.

[106] Estivariz CF, Molnar Z, Venczel L, Kapusinszky B, Zingeser JA, Lipskaya GY. Paralytic Poliomyelitis Associated With Sabin Monovalent and Bivalent Oral Polio Vaccines in Hungary. Am J Epidemiol. 2011;174(3):316–25.

[107] Bandyopadhyay AS, Garon J, Seib K, Orenstein WA. Polio vaccination: past, present and future. Future Microbiol. 2015;10(5):791–808. doi:10.2217/fmb.15.19.

The number of type 2 emergences in the first year post-tOPV withdrawal have been at the high end of what models predicted.[108] The number and geographic distribution have highlighted the importance of high-quality surveillance and pre-cessation supplementary immunization activities (SIAs); they also demonstrate the continued susceptibility of populations in insecure or inaccessible areas. Nevertheless, the risk for type 2 circulating vaccine-derived polioviruses (cVDPV2) 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 cVDPV2 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 differences in virulence, reversion patterns, transmissibility, and secondary immunity benefits of OPV must 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.[109] (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 cVDPV2 may be attributed to several factors: (1) differences in OPV reversion rates (OPV2>OPV1>OPV3); (2) improved cVDPV surveillance accompanied by the change to a more sensitive case definition of cVDPV2 than types 1 and 3; and (3) the lack of competition for susceptible individuals given the global eradication of WPV2 in 1999.

While specifics surrounding future outbreaks are unknown, the risk of cVDPV types 1 and 3 post-bOPV cessation should be similar to, or even smaller than, the risk for type 2 after tOPV withdrawal.[110] 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.[111]

Immunodeficiency-associated vaccine-derived poliovirus

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 of iVDPV have been recently been identified from these countries. Although OPV use 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.[112] 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 after six months.[113] Among the 101 iVDPV cases in the World Health Organization's global registry of iVDPV cases detected between 1962 and 2016, average excretion duration has been approximately one year; only seven (7%) were chronic (e.g., after five years) excretors. Only eight excretors (one chronic excretor) are alive and excreting at last specimen.[114]

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.

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

[109] Compiled from the WHO database of poliovirus cases, 17 October 2017.

[110] Lyons H et al. OPV1, 3 cessation and SIA planning. Presentation to Polio SAGE Working Group, Geneva, September 2017.

[111] Duintjer Tebbens RJ, Hampton LM, Wassilak SGF, Pallansch MA, Cochi SL, Thompson KM. Maintenance and Intensification of Bivalent Oral Poliovirus Vaccine Use Prior to its Coordinated Global Cessation. J Vaccines Vaccin. 2016;7(5):340.

[112] Aghamohammadi A, Abolhassani H, Kutukculer N, Wassilak, SG, Pallansch MA, Kluglein S et al. Patients with Primary Immunodeficiencies Are a Reservoir of Poliovirus and a Risk to Polio Eradication. Front Immunol. 2017;8:685.

[113] Duintjer Tebbens RJ, Pallansch MA, Thompson KM. Modeling the prevalence of immunodeficiency-associated long-term vaccine-derived poliovirus excretors and the potential benefits of antiviral drugs. BMC Infect Dis. 2015;15:379.

[114] Macklin G, Liao Y, Takane M, Dooling K, Gilmour S, Mach O et al. Prolonged Excretion of Poliovirus among Individuals with Primary Immunodeficiency Disorder: An Analysis of the World Health Organization Registry. Front Immunol. 2017;8:1103 (https://doi.org/10.3389/fimmu.2017.01103).

Evidence of iVDPV transmission among family contacts or into the community is very rare and no poliomyelitis outbreaks have been attributed to iVDPV.[115,116]

Experience gained from tracking cVDPV2 and iVDPV2 in the pre-certification period will be critically important in estimating the risks of emergence 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-harbouring 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.[117,118]

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 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.[119] Deliberate release of wild, vaccine- or genetically-engineered polioviruses is also possible.[120] 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 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.[121] Between 2000 and 2003, a type 2 poliovirus used exclusively for IPV manufacture and quality control (MEF-1) was isolated from nine children with acute flaccid paralysis (AFP) in India. The same type was found in vials of a single batch of tOPV.[122] In 2014, a vaccine production plant in Belgium accidentally released into the sewage system 45 litres 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.[123] Finally in 2016, a worker was infected following an accidental spillage in a Dutch vaccine manufacturing plant.[124]

A modelling 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.[125] 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.

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[115] Avellon A, Cabrerizo M, de Miguel T, Perez-Brena P, Tenorio A, Perez JL et al. Paralysis Case and Contact Spread of Recombinant Vaccine–derived Poliovirus, Spain. Emerg Infect Dis. 2008;14(11):1807–9.

[116] Alexander JP, Ehresmann K, Seward J, Wax G, Harriman K, Fuller S et al. Transmission of Imported Vaccine-Derived Poliovirus in an Undervaccinated Community in Minnesota. J Infect Dis. 2009;199(3):391–7 (https://academic.oup.com/jid/article/199/3/391/823479).

[117] Dowdle W, van der Avoort H, de Gourville E, Delpeyroux F, Desphande J, Hovi T et al. Containment of polioviruses after eradication and OPV cessation: characterizing risks to improve management. Risk Anal. 2006;26(6):1449–69.

[118] Fine PEM, Ritchie S. Perspective: Determinants of the Severity of Poliovirus Outbreaks in the Post Eradication Era. Risk Anal. 2006;26(6):1533–40.

[119] See Dowdle W, van der Avoort H, de Gourville E, et al.

[120] 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.

[121] Mulders MN, van Loon AM, van der Avoort HG, Reimerink JH, Ras A, Bestebroer TM 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.

[122] 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.

[123] 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.

[124] 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).

[125] 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.

Risk category 3: Risks 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 WPV2 has been globally eradicated. In July 2017, the GCC noted that modelling suggests that, in the presence of high-quality AFP surveillance and high population immunity, a period of three years without detection of both WPV types 1 and 3 provides high confidence (95%) to conclude the eradication of both types.[126]

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 type 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%.[127]

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[126] Global Commission for the Certification of Poliomyelitis Eradication. Report from the Sixteenth Meeting, Paris, France, 4-5 July 2017. For modelling to support their assessment, see Eichner M, Dietz K. Eradication of poliomyelitis: when can one be sure that polio virus transmission has been terminated? Am J Epidemiol. 1996;143(8):816–22, and Kalkowska DA, Duintjer Tebbens RJ, Pallansch MA, Cochi SL, Wassilak SG, Thompson KM. Modeling undetected live poliovirus circulation after apparent interruption of transmission: implications for surveillance and vaccination. BMC Infect Dis. 2015;15:66. doi:10.1186/s12879-015-0791-5; McCarthy KA, Chabot-Couture G, Shuaib F. A spatial model of Wild Poliovirus Type 1 in Kano State, Nigeria: calibration and assessment of elimination probability. BMC Infect Dis. 2016;16:521; Famulare M. Has Wild Poliovirus Been Eliminated from Nigeria? PLoS ONE. 2015 (https://doi.org/10.1371/journal.pone.0135765).

[127] Eichner M, Dietz K. Eradication of poliomyelitis: when can one be sure that polio virus transmission has been terminated? Am J Epidemiol. 1996;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. The 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.

The 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, the 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 (aVDPVs) 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 circulating vaccine-derived poliovirus (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 differences in OPV use.
    - Emergence of cVDPV type 1 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 trivalent oral poliovirus vaccine (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 the 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 poliovirus (WPVs, VDPVs, Sabin) were not distinguished because the 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. Modelling results of cVDPV2 suggests extinction occurs if it has not been detected within three years of the last detection even in the presence of poor surveillance.[128] The time periods used for each risk group reflects a cautious interpretation of modelling results including extrapolation to cVDPV types 1 and 3.

Final determination of country risk classification

The categories and criteria for risk classification for poliovirus reintroduction are summarized in Table C1. 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 the continuity of surveillance activities across high-risk border areas (e.g., Lake Chad).

Surveillance strategies

Countries should adopt a mix of strategies appropriate to their corresponding finalized country risk classification and 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 high-risk countries will immediately lead to the reclassification of the country as high-risk, which will require changes to its long-term surveillance strategies and activities. WHO regional office consultation will also be needed to determine if the reclassification of neighbouring countries will be required. 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 the 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 reintroduction of poliovirus using the most current version of the PCS. After certification, the document will be updated prior to each post-certification stage (*see* ***Annex E, Table E1***). This presents an opportunity to reassess and retool 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. As this is expected, countries need to ensure their surveillance strategies are appropriate to their new risk classification.

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

[128] Kalkowska DA, Duintjer Tebbens RJ, Pallansch MA, Cochi SL, Wassilak SG, Thompson KM. Modelling undetected live poliovirus circulation after apparent interruption of transmission: implications for surveillance and vaccination. BMC Infect Dis. 2015;15:66.

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 RI	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 Expanded Programme on Immunization RI 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.

bOPV= bivalent oral poliovirus vaccine; cVDPV= circulating vaccine-derived poliovirus; IPV= inactivated poliovirus vaccine; OPV= oral poliovirus vaccine; mOPV= monovalent oral poliovirus vaccine; PEF= poliovirus-essential facility; RI= routine immunization.

Source: WHO, Post-Certification Strategy.

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 global[129] and regional levels (e.g., Integrated Disease Surveillance and Response in Africa[130]) 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 the Global Polio Eradication Initiative (GPEI).

Several other "vertical" surveillance systems 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 that 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 has 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, which relies on a comprehensive global diagnostic laboratory network similar to the Global Polio Laboratory Network (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 environmental surveillance (ES).

High-threat pathogens – Surveillance for high-threat pathogens (i.e., highly infectious agents that produce severe diseases, such as viral haemorrhagic fevers, meningitis, cholera, Zika, etc.) utilizes a mix of surveillance strategies based on risk level in order to achieve programme 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.

[129] World Health Organization. WHO Recommended Surveillance Standards, Second Edition. Geneva: WHO; 1999.
[130] World Health Organization.Technical Guidelines for Integrated Disease Surveillance and Response in the African Region, Second Edition. Brazzaville, Atlanta: WHO Regional Office for Africa, CDC; 2010.

Enteroviruses – Enterovirus surveillance (EVS) has been used as a supplementary or alternative surveillance system to AFP, especially in countries that either never developed more targeted poliovirus surveillance or found it difficult to sustain the expected AFP quality indicators over time. EVS 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.[131] 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 enterovirus cases, such as acute flaccid myelitis, may prompt more active case investigation and enhanced surveillance.[132]

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 Red Cross and Red Crescent Societies (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.[133] 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.

[131] World Health Organization Regional Office for Europe and Centers for Disease Control and Prevention. Enterovirus surveillance guidelines: Guidelines for enterovirus surveillance in support of the Polio Eradication Initiative. Copenhagen: WHO; 2015.

[132] Sejvar JJ, Lopez AS, Cortese MM, Leshem E, Pastula DM, Miller L et al. Acute Flaccid Myelitis in the United States, August–December 2014: Results of Nationwide Surveillance. Clin Infect Dis. 2016;63(6):737–45 (https://doi.org/10.1093/cid/ciw372).

[133] International Federation of Red Cross and Red Crescent Societies (IFRC). Community-Based Surveillance: guiding principles. Geneva: IFRC; 2017.

Annex E

Additional Goal Three tables

These tables 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 and operational strategies by post-certification stage and country risk

	Stage I	Stage II	Stage III	Stage IV
	Certification to bOPV Cessation (0-1 yr post-certification)	**Immediate post-cessation (2-5 yrs. post-certification)**	**Intermediate post-cessation (6-9 yrs. post-certification)**	**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	***Years 2–3 post-certification*** Active AFP surveillance Enhanced efforts among high-risk populations ***Years 4–5 post-certification*** Passive AFP + active sentinel site surveillance in specific areas ***All Years 2–5 post-certification*** ES CBS EBS	Passive AFP surveillance ES CBS EBS	
Minimum standards	NPAFP rate ≥2/100k <15 years + stool adequacy ≥80% at **first admin level**	NPAFP rate ≥2/100k <15 years + stool adequacy ≥80% at **national level and for selected sentinel sites**	NPAFP rate ≥2/100k <15 years + stool adequacy ≥80% at **national level**	
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	***Years 2–3 post-certification*** 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 ***Years 4–5 post-certification*** Passive AFP surveillance ES as required EBS	Passive AFP surveillance ES as required EBS	
Minimum standards	NPAFP rate ≥2/100k <15 years + stool adequacy ≥80% at **national level**	NPAFP rate ≥1/100k <15 years + stool adequacy ≥80% at **national level**		
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.			
Polio low-risk countries				
Strategies	Mix of passive AFP, ES, EVS, and EBS			
Minimum standards	NPAFP rate ≥1/100k <15 years + stool adequacy ≥80% at **national level**			
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; bOPV= bivalent oral poliovirus vaccine; CBS= community-based surveillance; cVDPV= circulating vaccine-derived poliovirus; EBS= event-based surveillance; ES= environmental surveillance; EVS= enterovirus surveillance; ITD= intratypic differentiation; iVDPV= immunodeficiency-associated vaccine-derived poliovirus; 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. Surveillance standards for ES and PID surveillance remain to be determined. For 12 months post any outbreak, the NPAFP rate should be ≥ 3/100k <15 years per year.

Source: WHO, Post-Certification Strategy.

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

	Surveillance-detection	Laboratory
Global	• Generic capacity to implement EBS w/ signals for AFP • Maintain core staff of polio expertise with capacity to: – Provide TA/training – Develop updated guidance on poliovirus 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 and periodically evaluate national systems – Conduct research to guide operational and policy changes	• Maintain global specialized laboratories plus polio virologists with capacity to: – Provide TA/training – Prepare and 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	• Maintain staff with general epidemiologic capacity to: – Assist with TA, training, updating surveillance guidance, risk forecasting, data analysis and information management, and monitoring • In regions with high-risk areas, maintain polio-specific technical expertise at the regional and/or subregional level through Year 9 with capacity to: – 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	• Maintain regional reference laboratories and polio virologists with capacity to: – 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
National — The expected scope and intensity of surveillance will depend on the assessed risk; however, regardless of risk, all countries should maintain a core capacity to detect poliovirus with reliable access to a WHO-accredited laboratory to test for polioviruses.		
High risk	• Integrate scope and management of polio surveillance with VPD or communicable disease surveillance but maintain polio-specific technical expertise at the national level at least through Year 5 with capacity to: – 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 the 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	• Integrate scope and management of polio surveillance with VPD or communicable disease surveillance but maintain polio-specific technical expertise at the national level through Year 3 with capacity to: – Implement an appropriate mix of strategies depending on the stage – Conduct polio-specific data analysis from AFP, ES, or EBS, including monitoring performance indicators • After Year 1, possibility to rely on global or regional support to conduct AFP case or event investigations	• 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	• Integrate scope and management of polio surveillance with VPD or communicable disease surveillance with capacity to: – Implement an appropriate mix of strategies depending on the stage – Identify potential polio outbreaks based on surveillance or EBS data • Possibility to rely on regional support for AFP case or event investigations if necessary	• For countries (especially with small populations), possibility to rely on neighbouring country laboratories to process stool samples; for countries with laboratories, maintain VI and ITD diagnostics

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.

Source: WHO, Post-Certification Strategy.

Table E3. Functional capacities for preparedness and response required at the 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	
• **Leadership** (incident management, security, external relations, EOC management)	• Technical input to incident management system and EOC • Decision-making on stockpile release of vaccines and PAVDs
• **Partner coordination/liaison** (GOARN, etc.)	• Mobilization of a global roster for surge capacity
• **Information & planning** (generic preparedness tools, global communication, and planning in response situations)	• Technical guideline development or revisions
• **Health operations & technical expertise** (risk communication, technical guidance, training)	• Training, communication, social mobilization
• **Operational & logistic support** (including vaccine and antiviral stockpile management; syringe deployment)	• Technical assistance to determine future polio vaccine stockpile requirements
• **Finance & administration** (budget, procurement, HR for immediate response)	• Vaccine and antiviral procurement as required; identification of a pool of funds to support outbreak operational costs
• **IHR monitoring and administration**	• Monitoring of outbreak response
Regional – depends on risk	
Mirror of global level	Mirror of global level based on a 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 the IHR. All countries should have Rapid Response Teams. The global or regional level should provide surge capacity as required for all countries, but particularly medium-risk countries in stages III-IV and low-risk countries for all stages.	
High risk	
• **Leadership** (activation of EOC, etc.)	• Technical input to incident management system and EOC
• **Partner coordination/liaison**	• Identification of in-country polio-specific expertise that could be mobilized if required
• **Information & planning**	• Preparedness planning and periodic simulation exercises; enactment of rapid assessment
• **Health operations & technical expertise**	• Planning, organization, and implementation of outbreak response
• **Operational & logistic support**	• Polio vaccine management, including collection/destruction of residual mOPV doses
• **Finance & administration**	• Processing and release of funds • Identification of national resources that could be mobilized for outbreak response activities at lower administrative levels
• **IHR monitoring and administration** (monitoring of the development of minimum core capacity; notification to WHO of verified poliovirus detection)	• Monitoring of outbreak response as part of the JEE, guarantee of adequate polio-specific capacity
Medium risk	
At a minimum, development of the IHR minimum expected capacities, including notification to WHO if poliovirus is detected	Mirror of high-risk capacity for stage I-II; use of global and/or regional surge capacity if required for outbreak support in stages III-IV
Low risk	
At a minimum, development of the IHR minimum expected capacities, including notification to WHO if poliovirus is detected	Use of global and/or regional surge capacity if required for outbreak support

* Based on WHO, Emergency Response Framework, Second Edition, 2017.

EOC= Emergency Operations Center; GOARN= Global Outbreak Alert and Response Network; HR= human resources; IHR= International Health Regulations (2005); JEE= Joint External Evaluation; PAVD= polio antiviral drug.

Source: WHO, Post-Certification Strategy.

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