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## **WHO global action plan to minimize poliovirus facility-associated risk in the post-eradication/post-OPV era**

*The goal is to minimize the risk for poliovirus reintroduction by reducing the number of poliovirus facilities to an absolute minimum (<20) worldwide serving essential international vaccine, reference, and research functions and meeting the primary safeguards of facility containment and secondary safeguards of location in areas of lowest population risks.*

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## Introduction

Launched in 1988, the Global Polio Eradication Initiative has been the largest international public health effort ever undertaken, involving billions of dollars (US) donated through Global Polio Eradication Initiative partners, dedicated efforts of governments at all levels, countless hours of volunteer services, and immunization of billions of children with oral polio vaccine (OPV). When wild poliovirus (WPV) transmission is interrupted worldwide, safe handling and containment of WPV infectious and potential infectious materials in laboratory and vaccine production facilities is crucial to minimize the risk of reintroducing the virus into the population. Global routine use of OPV is proposed to stop [1] sometime after interruption of WPV transmission to prevent vaccine-associated paralytic poliomyelitis, eliminate risk for chronic infection of immunodeficient persons, and prevent outbreaks associated with circulating vaccine-derived polioviruses (cVDPV) [2]. Global consensus to stop OPV will rest on international assurances that eradication has been achieved, potential outbreaks from residual VDPV can be controlled, and that the risk from unintentional facility-associated reintroduction of wild or OPV/Sabin polioviruses will not outweigh the benefits of OPV cessation.

This 3<sup>rd</sup> edition of the *Global action plan* replaces the previous *WHO global action plan for laboratory containment of wild polioviruses* (2<sup>nd</sup> edition). The 3<sup>rd</sup> edition

- Includes containment of OPV/Sabin strains as well as WPV in accord with proposed OPV post cessation policy [1];
- Integrates post eradication projections of programmatic needs for polioviruses, risk assessment findings [3], risk consequence models [4], and risk management strategies (Annex 4);
- Incorporates lessons learned from surveys of >200,000 biomedical laboratory facilities in all six WHO Regions [5] and from development of guidelines for safe production and quality control of inactivated poliomyelitis vaccine (IPV) [6];
- Establishes the goal of minimizing the risk of facility-associated poliovirus in the post-eradication/post-OPV era by reducing to an absolute minimum (<20) the number of facilities retaining polioviruses worldwide that serve essential functions and meet primary and secondary safeguards against transmission; and
- Describes the rationale, strategy, and implementation steps for achieving this goal.

## Rationale

When WPV circulation is interrupted, susceptible populations will increase in many parts of the world as interest declines in immunization against a

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nonexistent infectious agent. The reintroduction of WPV in any population will be an event of international concern. The reintroduction of WPV in poorly immunized or unimmunized populations who live in tropical climates under conditions of high density and poor hygiene would cause widespread outbreaks of paralytic poliomyelitis and pose major challenges to preventing transmission to other unimmunized populations [4].

When routine use of OPV stops, some countries will continue high population coverage with inactivated polio vaccine (IPV), other countries will likely have sub-optimal IPV coverage, and still others may elect to discontinue all national polio immunization. Although OPV/Sabin strains are less virulent, less infectious, and generally less transmissible than WPV, under conditions of low population immunity some OPV-derived polioviruses may continue to circulate and acquire characteristics of WPV (i.e., cVDPV) [7]. When OPV use stops, a facility-associated reintroduction of an OPV/Sabin virus into increasingly susceptible populations carries the risk for initial unrecognized transmission, potential reversion to cVDPV, and reestablishment of poliomyelitis [4].

Facility-associated risk can be eliminated in most countries through destruction of all WPV and OPV/Sabin infectious and potential infectious materials. However, retention of a minimum number of poliovirus facilities in a few countries will be essential for vaccine production, stockpiles, and quality assurance; diagnostic reagent production; virus reference; and critical international research for the years after OPV cessation. Every poliovirus facility that remains constitutes a potential biohazard; maintaining the number of such facilities at a minimum (<20) worldwide reduces the magnitude of risk, facilitates national and international oversight, and ensures that global containment standards can be met.

### **Strategy**

The global strategy for minimizing poliovirus facility-associated risks consists of *risk elimination* by destruction of poliovirus materials in all but a few essential facilities and *risk management* of essential facilities by strict adherence to primary and secondary safeguards.

#### ***Risk Elimination***

Risk elimination comprises two components: 1) worldwide destruction of infectious and potential infectious WPV materials within 18 months after WPV transmission is interrupted and 2) OPV/Sabin materials (Annex 1) when OPV use stops. Destruction also extends to other non-essential virus materials where the potential for poliovirus contamination is high and the presence of poliovirus has not been ruled out, particularly stocks in facilities that work with clinical materials and virus-isolation systems common to poliovirus [8]. OPV production and multiple basic research facilities will not be needed in the post-eradication/post-OPV era. Peripheral-level national surveillance and diagnostic functions will continue through the use of nonviable poliovirus reagents. Successful elimination of risk worldwide requires each country to establish a poliovirus policy and promulgate enforceable legislation or regulations prohibiting retention of

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poliovirus materials (Annex 2), except for the few countries with designated essential facilities (Annex 3).

### **Risk Management**

Risk management of essential facilities comprises establishment of international standards for *primary safeguards* of facility containment, *secondary safeguards* of facility location, and *national and international oversight* to assure such standards are met.

*Primary safeguards* minimize the risk for poliovirus release from an essential facility and are specified in the *Biorisk Management standard for essential poliovirus facilities* (Annex 4) and *Guidelines for the safe production and quality control of Inactivated poliomyelitis vaccine manufactured from wild polioviruses* [6]. Key elements include

- The containment facility, which incorporates appropriate biosafety design, construction, and operation principles,
- Facility management, which practices continuous risk assessment and strict observance of biosafety procedures,
- Immunization of facility personnel, which can reduce the risk of infection in the facility and intra- or extra-household transmission, if infection should occur [3],
- Reduction in the use of WPV and substitution of Sabin strains where possible [3], which reduces risk for infection at the community level if a breach of containment occurs and the consequences of such a breach if transmission were recognized in time [9].
- Contingency plans for potential virus release or exposure, which specify actions and assigns responsibilities for the facility, the institution, the ministry of health (MOH), and other concerned government agencies (Annex 4).

*Secondary safeguards* minimize the risk for poliovirus circulation in the unlikely event of poliovirus release from an essential containment facility. Crucial safeguards include location of facilities in countries with

- Low seasonal enterovirus transmission rates, which are surrogates for environmental factors, sanitary conditions, and hygienic practices likely to reduce the risk for poliovirus spread [10].
- High quality closed sewage systems with secondary or greater effluent treatment, which provides backup for facility effluent treatment and further reduces the risk for community exposure [3].

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- High (>90%) routine national population coverage with IPV, which greatly reduces the risk for post-OPV poliovirus spread if a break in facility containment should occur [11] in countries meeting the above criteria.

*National and international oversight.* Continuous oversight by the institution housing the poliovirus facility ensures compliance with rules of operation and facilitates and strengthens staff management. Annual onsite assessment by a national accrediting body ensures the facility meets national biosafety standards, which must be at least as high as international standards. Biannual onsite assessment by an international accreditation body ensures the facility meets international biosafety and all applicable poliovirus standards (Annex 5).

### Implementation

The Global Action Plan is implemented in four phases: the first two linked to national milestones in polio eradication and the final two linked to international milestones in the global polio eradication initiative (Figure 1).

#### ***Phase I: National survey and wild poliovirus inventory***

This phase informs governments, institutions, and facilities about the upcoming need for containment; initiates efforts to reduce WPV materials and the number of facilities holding such materials; and provides a database of facilities on which subsequent steps towards minimizing risks for facility-associated poliovirus can be based.

During Phase I, when WPV transmission is decreasing worldwide, countries must

- *Survey all biomedical facilities to identify those with infectious or potential infectious WPV materials and encourage destruction of all unneeded materials.* As of 2006, a total of 128 countries reported completing the survey, including all 52 countries in the WHO European Region and all but two in the WHO Western Pacific Region [12]. For OPV-using countries where Sabin materials are ubiquitous, any action on Sabin materials (except to rule out WPV contamination) is premature until Phase IV.
- *Develop a national inventory of facilities that retain WPV materials, and report to the Regional Certification Commission.* The national inventory serves as a current record of poliovirus facilities. National inventories are assembled into regional inventories maintained by WHO regional offices and incorporated into the global inventory maintained by WHO Headquarters.
- *Request facilities that retain infectious or potential infectious WPV materials to institute enhanced biosafety measures (BSL-2/polio) for safe handling.* BSL-2/polio conditions (*WHO global action plan for laboratory containment of wild polioviruses*, 2<sup>nd</sup> edition) reduce the risk for reintroducing WPV into the community while poliovirus circulation is decreasing or no longer occurring in many areas of the world.

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- *Submit documentation to the Regional Certification Commission that Phase I requirements have been met.* The MOH submits the complete report of Phase I activities, the inventory, and supporting documents to the National Certification Committee for review and endorsement before submission to the Regional Certification Commission (*WHO Guidelines for documenting the quality of Phase I wild poliovirus laboratory containment activities: laboratory survey, national inventory*). Countries submit inventory status reports annually to the Regional Certification Commission.

### **Phase II: National long-term poliovirus policy and regulations**

During Phase II, which begins at completion of national surveys and inventories, countries establish long-term national goals and policies for the post-eradication/post-OPV cessation era (Annexes 2 and 3). This phase informs scientific communities and vaccine producers about such policies and establishes national regulatory structures that will take effect immediately after global declaration of Phase III.

All countries should

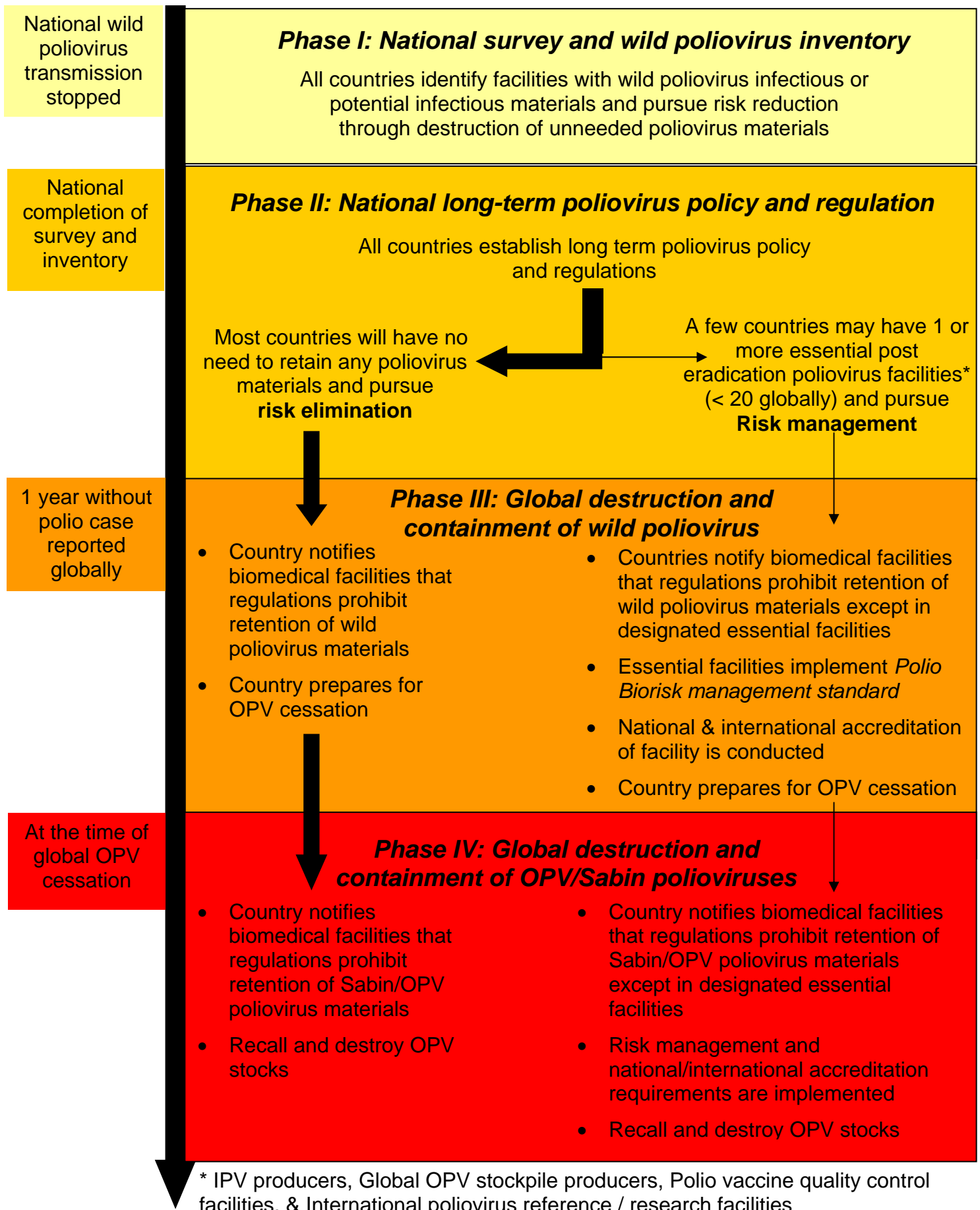
- *Establish long-term poliovirus policy consistent with international goals for destruction or containment of WPV after interruption of transmission worldwide and of OPV/Sabin materials after OPV cessation.* The policy will be to either
  - Prohibit retention of all specified poliovirus materials by any facility after achievement of each milestone (Annex 2), or
  - Prohibit retention of all specified poliovirus materials except in designated essential poliovirus containment facilities (Annex 3).

Countries considering the need for essential poliovirus containment facilities should weigh the risks and benefits of such facilities in consultation with all relevant ministries (e.g., health, education, defense, environment) and the responsibilities inherent in complying with the crucial primary and secondary facility safeguards.

- *Establish national poliovirus regulations.* Annex 2 (prohibition of poliovirus materials) and Annex 3 (prohibition except in essential facilities) provide regulatory frameworks designed to ensure global consistency among countries in content and enforcement of national policy. In many countries, regulations currently governing possession and handling of infectious agents may be modified to ensure compliance with poliovirus policy. Other countries may require new regulatory or legal structures.

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Figure 1: Phased implementation of poliovirus containment



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- *Alert biomedical facilities to national policies and consequent regulations pertaining to retention of WPV materials and eventually OPV/Sabin materials to permit orderly planning for compliance.* Public health facilities should continue to perform crucial poliovirus diagnostic, environmental testing, and surveillance activities using procedures that do not involve WPV strains. If WPV is isolated after declaration of Phase III, the facility must immediately notify the MOH and transfer the isolate to an approved poliovirus facility (Annexes 2 and 3).
- *Instruct facilities that work or have worked with poliovirus, enteroviruses, or rhinovirus to confirm the identity of all virus stocks, reference strains, and derivatives of such viruses grown in poliovirus-permissive cell cultures to rule out the presence of poliovirus [3].* Virus stocks of uncertain histories or multiple passages must be replaced with stocks of documented authenticity from an international culture collection or from other investigators using appropriate reference techniques. Sabin poliovirus stocks (if needed) should be replaced with authenticated Sabin strains. Laboratories wishing to retain historic collections of clinical materials potentially infectious for WPV should explore options with designated essential poliovirus research and reference containment facilities for storage and working arrangements.
- *Request facilities on the national inventory to submit plans for compliance with poliovirus regulations, including status of materials and action timelines.*

Countries *with* essential WPV facilities should

- *Request designated facilities to submit plans outlining activities and timelines for compliance with appropriate management standards (Annex 4 or ref 6).*
- *Prepare for international accreditation of containment facilities.* Countries may arrange with WHO for provisional international accreditation in advance of Phase III (Annex 5) to ensure rapid accreditation and uninterrupted facility operations.
- *Establish contingency plans for responding to potential release of or exposure to WPV (Annex 4).*

### **Phase III: Global destruction and containment of WPV**

This phase specifies the simultaneous global implementation of national regulatory and enforcement actions required for immediate destruction or containment of WPV. Countries will take action when the Director General of WHO declares that 1 year has passed without isolation of naturally occurring WPV anywhere in the world,

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### Countries *without* designated essential WPV facilities must

- *Notify the general biomedical laboratory community that national regulations now in force prohibit retention of WPV materials.* Facilities are fully responsible for compliance with national regulations, including destruction of WPV infectious and potential infectious materials and any non-authenticated OPV/Sabin materials or the transfer of such materials to a designated essential facility. Facilities on the national database that perform activities placing them at risk of having potential infectious WPV materials or contaminated stocks must respond to the MOH confirming the absence of such materials.

### Countries *with* essential WPV facilities must

- *Notify the general biomedical laboratory community that national regulations now in force prohibit retention of WPV materials except in designated essential facilities.* Facilities are fully responsible for compliance through penalties for noncompliance. Facilities on the national database that perform activities placing them at risk from potential infectious WPV must be requested to respond to the MOH confirming the absence of such materials.
- *Notify designated essential facilities to immediately implement management standards for containment of WPV materials (Annex 4).* Written notice to the designated senior management official should request a reply within 10 days signifying receipt of the notice and acknowledgement that documentation of compliance will be submitted to the MOH within 3 months.
- *Implement national and international accreditation procedures to assess facility compliance with requirements for containment of WPV.* All nationally accredited essential facilities also must be accredited internationally through WHO (Annex 5). Facilities should be accredited no later than 6 months after official WHO notification of the Minister of Health of the last-identified WPV case. Facilities failing international accreditation must discontinue WPV activities until deficiencies are verified as corrected.

### All countries must

- *Submit documentation within 6 months to the relevant WHO Regional Certification Commission that requirements for destruction or containment of WPV (Phase III) have been met.* The WHO Global Certification Commission will communicate detailed guidelines for assessing and documenting containment through WHO Regional offices.
- *Prepare for Phase IV.* It is anticipated that several years before OPV cessation would occur, an amendment to the International Health Regulations (IHR) would be established prior to effective date of implementation. The amendment or accompanying documents will provide specific dates for implementing each step leading to OPV cessation,

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including recall of unused OPV and containment of OPV/Sabin polioviruses. Advance planning in response to specific dates established by the IHR permits an orderly stepwise process towards OPV cessation.

- *OPV-using countries should respond to the amendment with detailed plans for compliance.*
- *All countries should review or expand the Phase I institution or facility database to include new or other biomedical laboratories that might have infectious or potential infectious poliovirus materials of any origin (wild or OPV/Sabin). (Physicians' offices, pharmacies, and health facilities that may have OPV vials will be notified through other government channels as described in the amended IHR).*
- *All countries should notify the general laboratory community of pending requirements for OPV/Sabin poliovirus materials. The general laboratory community already is, or should be, aware of pending actions linked to OPV cessation. Facilities should be reminded in writing of the planned date for OPV cessation and that national policies and regulations pertaining to OPV/Sabin poliovirus destruction or containment will be in force at that time. Communications from the MOH to all biomedical laboratory facilities should further encourage destruction of unneeded Sabin materials. Laboratories wishing to retain historic collections of clinical materials potentially infectious for OPV/Sabin polioviruses should explore options with designated essential poliovirus research and reference containment facilities for storage and working arrangements.*
- *Countries with essential facilities that handle only OPV/Sabin materials should instruct these laboratories to submit a plan for compliance with risk management requirements (Annex 4) and prepare for national and international accreditation.*

### **Phase IV: Global destruction and containment of OPV/Sabin polioviruses**

This phase specifies the sequential implementation of actions worldwide ensuring effective OPV recall from the field, destruction of OPV/Sabin poliovirus materials, and containment of Sabin polioviruses in designated essential facilities.

At the effective date established by the World Health Assembly for cessation of global OPV administration for routine immunization, countries without designated essential facilities must

- *Notify the general biomedical laboratory community that national regulations now in force prohibit retention of OPV/Sabin materials. All infectious and potential infectious OPV/Sabin materials must be destroyed. Virology laboratories in recent OPV-using countries are likely to isolate Sabin-like viruses from fecal and respiratory clinical samples for up to 6 months after OPV cessation until limited transmission and normal*

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virus shedding stops. Such isolates must be immediately reported to the MOH and submitted to the designated poliovirus reference laboratory. Similarly, diagnostic microbiology laboratories in recent OPV-using countries should assume fecal and respiratory clinical materials will be potentially infectious for Sabin viruses for up to 6 months after use of OPV stops. The issue of retaining potential infectious Sabin poliovirus materials will self-resolve in facilities that retain diagnostic samples for only a few weeks. Facilities performing activities placing them at risk of retaining OPV/Sabin strain materials must respond to the MOH confirming the absence of such materials.

At the effective date, countries *with* designated essential facilities must

- *Notify the general biomedical facilities that national regulations now in force prohibit retention of OPV/Sabin materials except in designated essential facilities.* Nonessential facilities must destroy or transfer all such infectious or potential infectious materials to approved facilities.
- *Notify essential facilities to immediately implement appropriate management standards required to contain or control OPV/Sabin materials (Annex 4).* Designated facilities must meet the same biosafety requirements for OPV/ Sabin infectious and potential infectious materials as required for retention of WPV materials (Annex 4 or ref 6). Facilities finalizing and then housing OPV stockpiles in sealed containers must meet international requirements for control, safety, and security as described in the WHO *Standard operating procedures for the stockpile of monovalent oral poliovirus vaccines (mOPV) for the post-eradication/post-OPV era* and amended IHR documents.
- *Implement national or international accreditation procedures to assess facility compliance with post OPV cessation containment requirements.* Accreditation must be completed no more than 6 months after OPV cessation (Annex 5). Facilities failing to be accredited must discontinue all poliovirus activities until designated authorities verify that deficiencies have been corrected.

At the effective date, *all* countries must

- *Recall and destroy OPV stocks.* WHO and UNICEF will provide specific implementation guidelines at the time of the IHR amendment for collection and destruction of OPV from designated collection points, health facilities or private practitioners, and national and sub-national storage facilities.
- *Submit documentation within 6 months to the Regional Certification Commission that requirements for global containment of OPV/Sabin polioviruses (Phase IV) have been met.* The Global Certification Commission will communicate detailed guidelines for assessing and documenting containment through WHO Regional offices.

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## ANNEX 1

### Definitions

**Accredit:** To certify as meeting and maintaining defined biorisk standards.

**Containment:** Protection of personnel and the immediate laboratory environment from exposure to infectious agents through the use of appropriate laboratory technique and safety equipment and protection of the environment external to the facility through facility design and operational practices.

**Diagnosis:** The analysis of samples for the purpose of identifying or confirming the presence of a specific agent.

**Facility:** Any laboratory or vaccine production unit owned or operated by any level of government, academic institution, corporation, company, partnership, society, association, firm, sole proprietorship, or other legal entity.

**Facility, essential:** A facility designated by the Ministry of Health as serving critical national or international functions that involve storage or handling poliovirus infectious materials or potential infectious materials

**Facility, accreditable:** A facility approved by Ministry of Health as a qualified applicant for international accreditation.

**Legislation:** The process of making laws.

**Policy:** The course or principle of action adopted or proposed by the responsible government entity.

**Poliovirus:** A picornavirus consisting of three serotypes: 1, 2, and 3. Poliovirus serotypes are further sub-divided into wild (circulating in nature) and Sabin strains (attenuated strains of oral polio vaccines [OPV]).

Wild poliovirus are naturally occurring isolates known or believed to have circulated persistently in the community, attenuated strains not approved for vaccines (Cox/Lederle and Koprowski/Wistar series), and vaccine-derived polioviruses [VDPV] (isolates consistent with an extensive period of virus excretion or transmission in the community, demonstrating 1–15% differences from parent OPV strains by full VP1 sequence homology). Wild poliovirus materials may be infectious (a) or potential infectious (b).

(a) *Wild poliovirus infectious materials* include:

- Clinical materials from confirmed wild poliovirus (including VDPV) infections

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- Environmental sewage or water samples in which wild polioviruses are present
- Cell culture isolates, and reference strains of wild poliovirus
- Seed stocks and infectious materials from IPV production
- Infected animals or samples from such animals, including PVR transgenic mice
- Derivatives produced in the laboratory that have capsid sequences from wild polioviruses
- Full-length RNA or cDNA that include capsid sequences derived from wild poliovirus
- Cells persistently infected with poliovirus strains whose capsid sequences are derived from wild poliovirus

(b) *Wild poliovirus potential infectious materials* include:

- Fecal or respiratory secretion samples collected for any purpose in a time and geographic area of wild poliovirus (including VDPV) circulation
- Products of such materials in poliovirus permissive cells or animals
- Uncharacterized enterovirus-like cell culture isolates
- Respiratory and enteric virus stocks handled under conditions where poliovirus contamination or replication is possible

OPV/Sabin strains are attenuated poliovirus strains (approved for use in oral polio vaccines by national regulatory authorities, principally Sabin strains) and OPV-like polioviruses (isolates consistent with a limited period of virus excretion or person-to-person transmission, demonstrating less than 1% difference from parent OPV strains by full VP1 sequence homology). OPV/Sabin materials may be infectious (a) or potential infectious (b).

(a) *OPV/Sabin infectious materials* include:

- Cell culture isolates and reference OPV/Sabin strains
- Seed stocks and live virus materials from OPV production
- Environmental sewage or water samples in which OPV/Sabin strains are present
- Fecal or respiratory secretion samples from recent OPV recipients
- Infected animals or samples from such animals, including PVR transgenic mice
- Derivatives produced in the laboratory that have capsid sequences from OPV/Sabin strains

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- Full-length RNA or cDNA that include capsid sequences derived from OPV/Sabin strains
- Cells persistently infected with poliovirus strains whose capsid sequences are derived from OPV/Sabin strains

(b) *OPV/Sabin potential infectious materials* include:

- Fecal or respiratory secretion samples collected for any purpose in a time and geographic area of OPV use
- Products of such materials from poliovirus permissive cells or animals
- Respiratory and enteric virus stocks handled under conditions where OPV/Sabin strain contamination or replication is possible

**Regulation:** Government action to control by rule or subject to restrictions.

**Risk:** A chance or possibility of an adverse event.

**Safeguards, primary:** The containment precautions and stipulations designed to minimize the facility-associated poliovirus risks of exposing and/or infecting populations.

**Safeguards, secondary:** The environmental conditions consistent with reducing the facility-associated risk of infecting populations and minimizing the risk of subsequent transmission in the event of a poliovirus release.

**Senior Manager (SM):** The official representative of the institution who has overall authority and accountability for ensuring responsive biosafety management of the facility.

**WHO Global Certification Commission (GCC):** The term commonly used to refer to the *WHO Global Commission for the Certification of the Eradication of Poliomyelitis*, which has responsibility to define the parameters and processes by which polio eradication will be certified, receive and review reports of the Regional Commissions, and issue a final report to the Director-General, WHO certifying that global polio eradication has been achieved.

**WHO Regional Certification Commission (RCC):** The term commonly used to refer to the *WHO Regional Commission for the Certification of the Eradication of Poliomyelitis*, which has been established in each of the six WHO regions with responsibility to certify to GCC that eradication has been achieved throughout all member states.

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## ANNEX 2

(Draft concept document)

### Example of draft legislative or regulatory text for countries with no planned essential poliovirus facilities

1. Definitions
2. Purpose
3. Applicability
4. General prohibition
5. Exemptions from requirements under this part
6. Civil or Criminal penalties

#### 1. Definitions

See Annex 1

#### 2. Purpose

This draft legislative/regulatory text is provided to assist countries with no planned essential poliovirus facilities to establish national policies consistent with the international goals and strategies described in the *Global Action Plan to minimize poliovirus facility-associated risk in the post-eradication/post-OPV era, 3<sup>rd</sup> edition*. Each country is anticipated to adapt the basic elements of the framework to its own situation.

#### 3. Applicability

(a) On and after the Director General, World Health Organization (WHO), declares that one-year has passed without isolation of naturally occurring wild poliovirus (*Global Action Plan, 3<sup>rd</sup> edition, Phase III*), provisions of this enactment automatically go into effect for facilities that have such wild poliovirus infectious and potential infectious materials as described in Section 2, above.

(b) On and after the date announced by the Director General, WHO that global routine use of oral polio vaccine (OPV) will stop (*Global Action Plan, 3<sup>rd</sup> edition, Phase IV*), the provisions of this enactment automatically go into effect for facilities that have such OPV/Sabin infectious and potential infectious materials as described in Section 2, above.

#### 4. General prohibitions

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(a) Following the declaration in Section 3(a) that one year has passed without the isolation of wild poliovirus (Phase III), a facility or its representative may not possess, use, or receive wild poliovirus materials.

(b) On and after the date announced by the Director General, WHO in Section 3(b) that global routine use of oral polio vaccine (OPV) will stop (Phase IV), a facility or its representative may not possess, use, or receive OPV/Sabin materials.

### 5. Exemptions from Requirements

(a) *Diagnostic exemption.* A facility is exempt from the provisions of this part provided that **all** of the following apply:

1. The only poliovirus activities conducted by the facility pertain to isolation of polioviruses in current samples or identification of isolates from current samples submitted for diagnosis or identification;
2. Upon identification of a isolate as poliovirus, the facility reports to the Minister of Health within 24 hours by email or fax (the MOH immediately notifies WHO) and submits the isolate to the designated poliovirus reference laboratory;
3. The facility submits to the MOH within 7 days of virus identification all records pertaining to laboratory manipulation of clinical materials and the isolate, safety precautions taken, and documentation of transfer of all materials to the designated reference laboratory.

(b) *Emergency public health exemption.* The Minister may temporarily exempt a facility from the requirements of this part, in whole or in part, based on the determination that the exemption is necessary to provide for timely participation of the facility in response to a domestic or international public health emergency.

### 6. Civil or Criminal penalties

The Minister of Health or other designated authorities have the authority under these laws/regulations to conduct an investigation and to impose civil or criminal penalties against any individual or entity found to be in violation of these provisions.

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## ANNEX 3

(Draft concept document)

### Example of draft legislative or regulatory text for countries with planned essential poliovirus facilities

1. Definitions
2. Purpose
3. Applicability
4. General prohibition
5. Exemptions from requirements under this part
6. National Registration and Approval
7. Denials, Withdrawal, or Limitation of Certificate of Registration
8. Facility Safeguards
9. International Accreditation
10. Inspections
11. Notification of a Poliovirus Release or Loss
12. Civil or Criminal penalties

#### 1. Definitions

See Annex 1

#### 2. Purpose

This draft legislative/regulatory text is provided to assist countries with planned essential poliovirus facilities to establish national policies consistent with the international goals and strategies described in the *Global Action Plan to minimize poliovirus facility-associated risk in the post-eradication/post-OPV era, 3<sup>rd</sup> edition*. Each country is anticipated to adapt the basic elements of the framework to its own situation.

#### 3. Applicability

(a) On and after the Director General, World Health Organization (WHO), declares that one-year has passed without isolation of naturally occurring wild poliovirus (*Global Action, 3<sup>rd</sup> edition, Phase III*), provisions of this enactment automatically go into effect for facilities that have such wild poliovirus infectious and potential infectious materials as described in Section 2, above.

(b) On and after the date announced by the Director General, WHO that global routine use of oral polio vaccine (OPV) will stop (*Global Action Plan, 3<sup>rd</sup> edition, Phase IV*), the provisions of this enactment automatically go into effect for facilities that have such OPV/Sabin infectious and potential infectious materials as described in Section 2, above.

#### 4. General prohibitions

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(a) Following the declaration in Section 3(a) that one year has passed without the isolation of wild poliovirus (Phase III), a facility or its representative may not possess, use, or receive wild poliovirus materials unless the facility is registered and approved by designated national authorities and accredited by WHO.

(b) On and after the date announced by the Director General, WHO in Section 3(b) that global routine use of oral polio vaccine (OPV) will stop (Phase IV), a facility or its representative may not possess, use, or receive OPV/Sabin materials, unless the facility is registered and approved by designated national authorities and accredited by WHO.

### 5. Exemptions from requirements

(a) *Diagnostic exemption.* A facility is exempt from the provisions of this part provided that **all** of the following apply:

1. The only poliovirus activities conducted by the facility pertain to isolation of polioviruses in current samples or identification of isolates from current samples submitted for diagnosis or identification;
2. Upon identification of a isolate as poliovirus, the facility reports to the Minister of Health within 24 hours by email or fax (the MOH immediately notifies WHO) and submits the isolate to the designated poliovirus reference laboratory;
3. The facility submits to the MOH within 7 days of virus identification all records pertaining to laboratory manipulation of clinical materials and the isolate, safety precautions taken, and documentation of transfer of all materials to the designated reference laboratory.

(b) *Emergency public health exemption.* The Minister may temporarily exempt a facility from the requirements of this part, in whole or in part, based on the determination that the exemption is necessary to provide for timely participation of the facility in response to a domestic or international public health emergency.

### 6. National Registration and Approval

(a) To apply to the designated national authorities for a certificate of registration as a essential poliovirus facility (as defined in Section 2), the Senior Manager of the institution/facility must:

- (1) Submit information to the designated national authority as specified in the registration package, which should include:
  - (i) Identification information (e.g., name, address, contact numbers)
  - (ii) Characterization information on poliovirus materials and quantities being held

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- (iii) The location, including building and room number and floor plans for each building and room where materials will be stored and used.
- (iv) Supporting documents addressing safety, security, emergency response plans, and training appropriate for the materials being held.
- (v) The name, position, and information regarding the Senior Manager.
- (vi) The names and positions of all persons who will have access to poliovirus materials.
- (vii) A certification statement signed by the Senior Manager attesting to the accuracy of the information submitted.
- (viii) The types and frequency of procedures that may be conducted with the poliovirus materials being held.

(b) The certificate of registration and approval is valid only for the specified facility and the specified activities, and specified locations. The Senior Manager must promptly notify the Minister of Health or designated national authorities in writing if a change occurs in any information submitted in the initial application or amendments.

### **7. Denials, Withdrawal, or Limitation of Certificate of Registration.**

Upon good cause, the Ministry of Health shall have the power to deny an application for registration, withdraw an existing registration certificate, or limit the conditions of a continuing registration certificate of a facility operating under these provisions.

### **8. Facility Safeguards**

(a) Facilities must meet all required primary and secondary safeguards as described in the *Global Action Plan, 3<sup>d</sup> ed. (Annex 4 and reference 6)*.

(b) *Annual Facility Inspections*: Facilities must undergo an annual onsite review or accreditation process by a national expert group to ensure all procedures and practices meet at a minimum the specifications of the *Global Action Plan, 3<sup>rd</sup> ed. (Annex 4 or reference 6)*. The results of these inspections must be documented and any deficiencies identified during inspections must be corrected, with documentation submitted to the Minister of Health or designated national authority.

### **9. International Accreditation**

(a) All nationally approved wild poliovirus facilities must be accredited internationally no later than six months after the Director General, WHO officially informs the Minister of Health that one-year has passed without isolation of naturally occurring wild poliovirus (*WHO Global Action Plan, Annex 5: International accreditation of essential poliovirus facilities in the post-eradication/post-OPV era*). The Minister of Health or the designated national

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authority submits requests for accreditation through the WHO Regional Office, with separate applications for each facility.

(b) International accreditation is granted for a 2-year period, contingent upon favourable annual national reviews and approval.

### **10. Inspections**

The designated national authority has the authority, without prior notification to conduct random, or for cause, inspections of facilities possessing, or registered to possess, poliovirus materials. Inspections may include review of safety, security, working records, risks analyses, mechanisms to track transfers within the facility, emergency and disposal procedures, and other items as defined by the scope of the inspection. Access to storage areas and relevant forms and records must be provided upon request to authorized personnel conducting these inspections.

### **11. Notification of a Poliovirus Release, or Loss.**

(a) Upon discovery of an unauthorized or accidental release or loss of poliovirus materials, the facility shall immediately notify the Minister of Health or responsible health officials, who shall notify responsible WHO officials.

(b) When reporting such a release, the facility shall include the time and location of the event, the poliovirus category (ies) involved, number of individuals potential exposed, and actions taken. Reports of loss shall include estimated quantities along with the foregoing relevant information.

### **12. Civil or Criminal penalties**

The Minister of Health or other designated authorities have the authority under these laws/regulations to conduct an investigation and to impose civil or criminal penalties against any individual or entity found to be in violation of these provisions.

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# Annex 4

## **Biorisk management standard for essential poliovirus facilities**

1. Introduction
2. Poliovirus facility-associated risks
3. Table of contents
4. Definitions

### **I. Introduction**

A facility-associated poliovirus infection or release into the environment following eradication and cessation of oral polio vaccine (OPV) use will be a public health event of international proportions. The *WHO global action plan* addresses that risk by establishing a post eradication/post OPV cessation goal of retaining poliovirus in less than 20 essential facilities worldwide. The *WHO action plan* further reduces the risk posed by these facilities by establishing international standards for primary safeguards of facility containment and secondary safeguards of facility location and assurance through national and international oversight that such standards are met.

Primary safeguards minimize the risk of facility-associated poliovirus release and include design and operation of the containment facility; facility management, practices and procedures; vaccination of facility personnel; reduction in the use of wild polioviruses; and contingency plans for potential virus release or exposure. Secondary safeguards minimize the risk for poliovirus circulation in the event of poliovirus release from an essential containment facility and include facility location at sites with low rates of seasonal enterovirus transmission, access to a high quality closed sewage system with secondary or greater effluent treatment, and high (>90%) routine population coverage with IPV.

This *Biorisk Management Standard* (annex 4 of the *WHO action plan*) is the international benchmark for primary safeguards established for the essential poliovirus facility. The *Standard* is based on the principles of the *WHO Laboratory Biosafety Manual* (3rd Edition, 2004) and the extensive poliovirus scientific literature spanning nearly 7 decades and compiled in the publication *Containment of polioviruses after eradication and OPV cessation: Characterizing risks to improve management* (Dowdle W, van der Avoort H, de Gourville E, Delpreyroux F, Desphande J, Hovi T, Martin J, Pallansch M, Kew O, Wolff C 2006 *Risk Analysis* 26: 1449-1469). The *Standard* serves as the framework for national and international accreditation (Annex 5: *International accreditation of poliovirus facilities in the post-eradication/post-OPV era*). It consists of 16 elements and sub elements based on the principles of a quality management system. It assumes that the organization is best placed to understand the risks associated with its work and can manage those risks in a number of ways acceptable to the national and international bodies responsible for facility oversight. The *Standard* further

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assumes that essential facility personnel and management at all levels fully appreciate the enormity of the consequences of poliovirus release in the post eradication/post OPV era and are prepared to demonstrate that the appropriate systems and controls are in place to manage that risk.

Standards specific for vaccine production are published in *Containment of polio vaccine production and quality control facilities: BSL-3/IPV containment requirements following the cessation of immunization with oral polio vaccine (OPV)*, WHO, Geneva, 2007.

## II. Poliovirus facility-associated risks

Polioviruses are defined in Annex 1 of this document as picornaviruses consisting of three serotypes: 1, 2, and 3, sub-divided into wild (circulating in nature) and Sabin strains (attenuated strains of oral polio vaccines [OPV]). Polioviruses under moist conditions in clinical or environmental samples can survive indefinitely in the laboratory freezer (<-20C), for many months in the refrigerator, and for weeks on the bench top at ambient temperatures. Infectivity is inactivated by dehydration, heat (>50C), or treatment with dilute solutions of formaldehyde or bleach (0.5%).

The most common routes of exposure to infectious agents in the facility environment are: 1) ingestion, 2) inhalation, 3) injection, and 4) contaminated skin and mucous membranes. The infectious dose is a factor of virus virulence, route of presentation, and virus particles in sufficient number to overcome mechanical loss and natural and immune host defenses. In the poliovirus facility, poliovirus content of common materials ranges from a mean of  $10^{3.7}$  CCID<sub>50</sub>/gm (Sabin) -  $10^{4.3}$  CCID<sub>50</sub>/gm (wild) in stool samples, to  $10^8$  CCID<sub>50</sub> in cell culture harvests, and  $10^{11}$  CCID<sub>50</sub>/ml in concentrates in vaccine production facilities. Sabin strains are less pathogenic than wild and have lower secondary infection rates, but all 3 Sabin virus types have been linked to vaccine-derived poliovirus outbreaks.

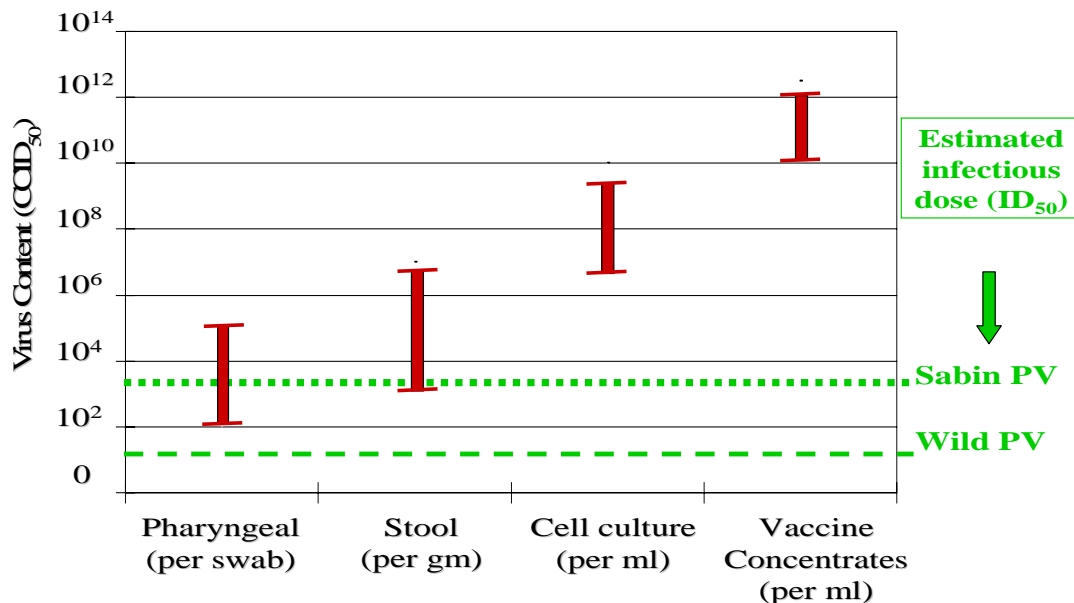
Ingestion presents the highest risk for facility personnel. Immunization with OPV or inactivated polio vaccine (IPV) prevents disease, but neither fully inhibits silent poliovirus infection or re-infection of the gut. Ingestion of poliovirus may result from any laboratory operation, activity, or incident that leads to transfer of infectious particles to the gastrointestinal tract. Estimated infectious doses (ID<sub>50</sub>) by ingestion, based on studies with infants and children, are  $\pm 10^1$  CCID<sub>50</sub> for wild polioviruses and  $\pm 10^3$  CCID<sub>50</sub> for Sabin strains. Immunized adult laboratory workers are likely more resistance than immunologically naïve children, but resistance is dose related and may be overcome by ingestion of sufficient poliovirus particles. Droplets created by sprays, spills, and splash of poliovirus cell cultures ( $10^8$  CCID<sub>50</sub>) and concentrates ( $10^{11}$  CCID<sub>50</sub>) constitute the highest personnel exposure risks (Figure 1).

Inhalation, defined as exposure to small particle aerosols <5  $\mu$  (droplet nuclei) deposited predominately in the lower respiratory tract, has not been identified as a route of infection for poliovirus. The respiratory tract appears not to be a

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significant portal of entry. Unresolved, however, is whether small particle aerosols deposited in the lower respiratory tract may initiate alimentary tract infection through mucociliary transport to the pharyngeal region. Inhalation risks may be further reduced in facility environments maintained at low relative humidity (<50%). Antibodies acquired through immunization greatly reduce infection risks through injection or breaks in skin or mucous membranes.

**Figure 1: Estimated poliovirus content and infectious dose\***



\*Estimated ingestion ID<sub>50s</sub> are based on studies with infants and children. Immunized adult laboratory workers are likely much more resistance than immunologically naïve children, but dose-related resistance may be overcome by ingestion of sufficient poliovirus particles

Community members may be exposed to infectious agents from the laboratory through 1) workers' contaminated skin or clothing or unrecognized infection, 2) contaminated air effluents, 3) contaminated liquid effluents, 4) uncontrolled transport of infectious material, 5) solid waste transported to landfills, 6) contaminated equipment or materials removed from the facility, and 7) escape of infected animals. Exposure risks through the latter four routes (4-7) are low for poliovirus facilities that adhere to International requirements for transportation of infectious substances, Good Laboratory Practice, and Good Manufacturing Practice and likely low for inhalation of contaminated air effluent where facilities maintain low relative humidity environments and exhaust air away from direct human exposure. Exposure risks through ingestion of liquid effluents range between high and low, depending on poliovirus content of facility effluent, sewerage system size and integrity, and potential for human consumption. Risks of community exposure are highest through facility personnel unknowingly contaminated or infected with poliovirus. Routine IPV immunization of facility personnel may greatly reduce the risk of intra- and extra-household transmission.

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Effective poliovirus risk management is achieved by careful assessment of exposure risks, implementation of risk-appropriate personnel protection measures, and the quality operation of a facility designed to minimize the risk of poliovirus contamination and dissemination to the community. The main risk is infection of laboratory workers by ingestion. Airborne transmission is conceivable but not demonstrated and infection through parenteral exposure such as needle stick is unlikely in immunised individuals. The appropriate containment level most closely resembles BSL3, but there will be significant differences of emphasis with the focus on preventing exposures identified through risk assessment as the most hazardous.

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## 1. Management and Organization

**1.1 Biorisk Policy.** There shall be a biorisk policy relating to the management of biosafety and biosecurity (biorisk) of the poliovirus facility, authorized and signed by the organization's top management that

- Establishes the safe and secure operation of the poliovirus facility as a top priority of the organization
- Commits to compliance with this Standard
- Commits to prevent the release of viable poliovirus
- Is effectively communicated to all employees
- Commits to continually improve biorisk management performance

**1.2 Roles, Responsibilities and Authorities.** The roles, responsibilities and authorities for those who manage, perform and verify work associated with the poliovirus facility shall be defined, documented and communicated within the organization.

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**1.2.1 Senior Manager.** A member of top management with decision-making authority shall be appointed with overall responsibility for management of polio biorisk, which includes:

- Providing necessary resources to ensure the safe and secure operation of the facility;
- Instituting review, audit and reporting measures to provide assurance that the Standards are being implemented and maintained effectively.
- Review and sign-off of Biosafety Committee meeting minutes and documented follow-up on action items
- Regular reporting to top management and staff in the poliovirus facility on the performance of the biorisk management system and needs for improvement;

**1.2.2 Biosafety Officer (BSO).** A biosafety expert shall be appointed as the BSO to provide up-to-date advice and guidance to scientific and other personnel on polio biorisk management. The BSO shall be directly accountable to the senior manager and independent from those responsible for implementing the program of work within the poliovirus facility. The BSO shall have delegated authority to stop work as necessary and verify that all biorisk management considerations relevant to the poliovirus facility have been addressed.

**1.2.3 Scientific Manager.** A manager, usually the Principal Investigator (PI), shall be appointed with day to day responsibility for the scientific program and its safe conduct within the poliovirus facility, including:

- Supervision of all personnel authorized to enter and work in the facility;
- Planning and conducting work activities with the required authorizations;
- Ensuring availability of sufficient qualified personnel, time, space and equipment;
- Ensuring risk assessments have been performed, reviewed and approved, and the required control measures are in place.

**1.2.4 Occupational Health Professional.** A qualified medical occupational health professional with specific knowledge of poliovirus and its transmission shall be identified to provide advice and guidance on worker health and related issues, including:

- Input into risk assessment
- Advising on first aid / treatment measures
- Liaising with external healthcare providers
- Coordinating medical examinations and vaccination programs

**1.2.5 Facility Manager.** A facilities manager, normally an engineer or someone with specific knowledge relevant to the poliovirus facility and its engineering controls, shall be appointed with responsibility to manage and coordinate facilities issues including:

- Input into risk assessment
- Coordinating building / maintenance work
- Liaising with contractors for the poliovirus facility

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- Ensuring that the facility and associated equipment are functioning properly
- Monitoring control systems in place and ensuring checks are carried out at the required frequency

**1.2.6 Security Manager.** A manager shall be appointed to provide advice and guidance on security issues including input into risk assessment, overseeing the security controls in place, and liaising with security contractors, police, and other security professionals.

**1.2.7 Biosafety Committee.** A Committee shall be constituted with terms of reference as an independent review group for biorisk issues associated with the poliovirus facility. The Biosafety Committee shall meet regularly (at least once a year or more frequently as needed) and preferably be chaired by a senior individual independent of the poliovirus facility. Committee members shall consist of a cross section of expertise including the scientific manager, additional scientific specialists (e.g. virologists, disinfection experts, epidemiologists), the biosafety officer, the occupational health professional, the facility manager, the security manager, and worker representatives from the facility. Functions of the Committee shall include:

- Oversight and approval of facility policy development, SOPs and codes of practice
- Review and approval of risk assessments and protocols;
- Review and approval of methods for poliovirus inactivation and methods for waste disposal.

**1.3 Records, Documents and Data Control.** The poliovirus facility shall ensure that records are established and maintained to provide evidence of conformity to requirements of this Standard and the effective operation of the biorisk management system. Records shall be maintained for a minimum period of 10 years and be available in English for review during national/international accreditation procedures. The records system shall identify responsibilities to ensure timely review, updating, and approval of procedures for storage, protection, retrieval, and disposal including

- Standard operating procedures (SOPs) and risk assessments;
- Job descriptions and charts of authority;
- Design records and commissioning / test plans, maintenance plans and records and all associated data;
- Accident/incident reports
- Results from validation tests
- Audit and inspection checklists, results and actions required / taken;

**1.4 Analysis of data.** Appropriate data from monitoring, measurement, and other sources shall be identified, collected and analysed to assess the suitability and effectiveness of the biorisk management system and to evaluate where continual improvement of the effectiveness of the system can be made.

**1.5 Change Management.** All changes associated with the design, operation and maintenance of the poliovirus facility shall be reviewed,

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evaluated as to effect on risk assessment, verified, validated, and approved before implementation, including:

- Modifications to the building, its equipment or its operation;
- Altered staffing arrangements (including contractors, visitors and other non-core personnel);
- Changes to the program of work including alterations to work flow or volume;
- Alterations to SOPs, including changes in materials or reagents;
- Modifications to entry / exit protocols;
- Modifications to disinfection and other waste management methodologies;
- Changes associated with PPE provision and usage.
- When actual or potential non-conformance with internal / external rules and regulations is identified (e.g. introduction of new legislation or major accident exposure);
- When considering emergency response and contingency planning requirements.

**1.6 Consultation and Communication.** Pertinent biorisk management information relating to the poliovirus facility shall be regularly communicated to and from employees, management, and other relevant persons and organizations including emergency service providers, health care staff, community representatives, accreditation teams, consultants, and visitors.

**1.7 Program of Work and Standard Operating Procedures (SOPs).** The program of work for the poliovirus facility shall be defined, documented, and supported by formal SOPs and reviewed and approved prior to commencement of activity by at least the scientific manager, BSO, and Biosafety Committee.

**1.8 Work Planning and Capacity.** The organization shall conduct a risk assessment process to identify and ensure that workload demands and deadlines do not exceed capacity to maintain safe and secure working conditions within the poliovirus facility.

**1.9 Legal and Other Requirements.** All national and international requirements relevant to managing poliovirus-associated biorisk shall be identified, assessed and the requirements implemented.

**1.10 Continual Improvement.** Continual improvement in the effectiveness of the biorisk management system shall be ensured through policies, objectives, audit results, analysis of data, risk assessment, corrective and preventive actions and management review.

**1.11 Non-compliance.** Action shall be taken to prevent non-compliance with this Standard by providing all required items and services (e.g. staff, appropriate facilities, mechanical systems, PPE, equipment, training, and vaccinations) and to promptly correct such causes of non-compliance should they occur.

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**1.12 Facility / national inspection and audit.** A program of inspection and audit shall be conducted at planned intervals, no less than every 2 years, by both the facility and national authorities to determine if the biorisk management system conforms to the requirements of this Standard and is functioning properly and that necessary corrective actions are taken and verified without undue delay.

**1.13 International inspection and audit.** Top management shall ensure that information and access necessary for the periodic comprehensive international review of the poliovirus facility is made available in English as requested by the WHO review team and that deficiencies identified by the process, as outlined in the *WHO global action plan to minimize poliovirus facility associated risk in the post-eradication/post-era*, are addressed to the satisfaction of WHO.

**1.14 Management Review.** Top management shall review the biorisk management system at planned intervals (at least annually) to ensure its continuing suitability, adequacy and effectiveness. The review shall include assessing opportunities for improvement and the need for changes to the system, procedures, policies and objectives. Review output shall include decisions and actions and statements of resource needs. Records of the review shall be maintained. The review should include:

- Results of audits and accident / incident investigations.
- Performance of SOPs and work instructions;
- Status of risk assessment activities;
- Status of preventive and corrective actions;
- Follow-up actions from previous management reviews;
- Evaluation of changes that could affect the system;
- Recommendations for improvement;

## 2.0 Risk Assessment

The organization shall ensure that:

- Risk assessment is an ongoing, proactive and clearly defined procedure with respect to scope, nature, and timing that underpins all activities associated with this Standard, including determination of physical requirements, identification of training needs, the development of SOPs and emergency plans. As a minimum, the following shall trigger a risk assessment, either a new or review of an existing one:
  - New construction / modifications to buildings, plant and equipment or its operation;
  - Introduction of altered staffing arrangements (including contractors, visitors and other non-core personnel);
  - Changes to the program of work including alterations to work flow or volume;
  - Alterations to SOPs including changes in materials or reagents;
  - Modifications to entry / exit protocols;

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- Modifications to disinfection and other waste management methodologies;
  - Changes associated with PPE provision and usage;
  - When actual or potential non-conformance with internal / external rules and regulations is identified (e.g. introduction of new legislation or major accident exposure);
  - Review of the incident/accident register
  - When considering emergency response and contingency planning requirements
- Methodologies for identifying and recording work/facility associated hazards (any substance, situation, or activity with potential for causing harm) are identified and implemented as the first step of risk assessment
  - Persons with subject expertise (scientific, operational, management, facilities, occupational health, regulatory) who need to be involved in conducting and reviewing risk assessments are identified and consulted
  - Suitable methodologies for assessing and recording risks and allocation of actions responding to results from risk assessment, including timelines, responsible persons, reporting and approval mechanisms, are identified, implemented, and maintained.

### 3.0 Poliovirus Inventory and Information

**3.1 Poliovirus Inventory.** Poliovirus materials shall be strictly controlled to prevent accidents and security incidents. An accurate and up to date inventory of stored poliovirus materials (isolates, cultures, samples, and other sources of poliovirus) shall be established and maintained, which at a minimum meets the following requirements:

- Poliovirus is preferably stored within the containment perimeter of the poliovirus facility or in a separate secure area as close as possible to the containment perimeter (e.g. same building) meeting the security standards provided in section 14. *Security* and with movement of materials to and from storage meeting the standards of section 4. *Transportation*;
- Access to both stored and working poliovirus materials is restricted to authorized individuals with legitimate need;
- Stored samples of wild and Sabin poliovirus materials are segregated from each other and other isolates, cell lines, cultures or other materials that could be subject to cross-contamination or misidentification
- Storage equipment (freezers, fridges, incubators, liquid nitrogen, and waste containers prior to treatment) is kept locked when not under the direct supervision of approved individuals, and a secure system of access control is enforced;

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- Storage vessels should be break-proof and have adequate seals (e.g. screw capped) to minimize the risk of leakage during transportation, storage, and use
- The surfaces of all storage vessels shall be decontaminated with a validated method for inactivating polioviruses.

**3.2 Information.** All records (both electronic and paper) relating to the inventory shall be current, complete, restricted to designated individuals, and stored securely with adequate backup provision. The inventory information shall include as a minimum:

- The name(s) of the individual responsible for the material;
- The names of personnel with access to the materials;
- The names of personnel with access to the area where the materials are held;
- Accession numbers and other relevant identifiers;
- Amounts (number of containers/vials or applicable equivalent) and exact location of storage
- Origin, including geographical source and date of collection;
- Records of materials removed from storage to conduct work and the fate of those materials and any newly developed stocks following the completion of the work (destroyed, returned to storage in X location)
- Records of materials destroyed or removed from the facility.

**3.3 Monitoring and Control.** Inventories shall be monitored such that materials missing, unaccounted for, or no longer needed are identified, consistent with the goal of reducing amounts of live poliovirus materials to the lowest level. An inventory review shall be conducted at least annually.

## 4.0 Transport

**4.1 Transport Procedures.** Procedures for transport of isolates, cultures, samples and potentially contaminated materials, both inside and outside the facility containment perimeter shall be established and maintained. As a minimum the organization shall ensure that:

- Internal transport of poliovirus (within the facility, but outside the containment perimeter) meets the same biosafety and biosecurity standards required for external transport outside the facility.
- External transport requirements, including relevant legal requirements and codes of practice, are identified, recorded, and adopted by the institution. At a minimum, the facility shall ensure that practices meet ICAO requirements
- Adequate and appropriate packaging systems, materials (e.g. break and leak proof containers), labels, PPE and documentation are available and used in the transportation process;
- External poliovirus transport to and from the facility comply with all national and international transfer and security requirements and have approval from the Ministry of Health
- Transport arrangements are secure and appropriate for risk group 4 organisms

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- Emergency response and contingency plans are in place relevant to poliovirus transport, including adequate precautions to handle and, if needed, quarantine packages presenting a risk;
- Documents relating to poliovirus transport are up-to-date.

### 5.0 Personnel and Competency

**5.1 Recruitment.** The organization shall ensure that qualifications, experience and aptitudes relating to biorisk management are considered explicitly as part of the recruitment process for the poliovirus facility such that

- All personnel in the poliovirus facility are subject to a formal selection process whether or not they are existing employees of the organization (i.e. contractors);
- Employment references are received and verified as legitimate and satisfactory;
- A security check with the police and / or security services is carried out for evidence of a criminal record or association with subversive or terrorist organizations (for further information see section 14. *security*);
- All recruits who will be entering areas with potential for exposure to poliovirus materials accept compliance with the healthcare standards outlined in section 6. *Healthcare*, specifically including immunization with IPV every 3 years and an annual medical examination;
- Applicability of the above procedures for non-core personnel (e.g. contractors, visitors) are assessed and measures implemented to ensure compliance as necessary.

**5.2 Training.** Procedures for training of personnel for safe conduct within the poliovirus facility shall be established and maintained including:

- Definition of training needs, including training specific to characteristics of poliovirus and the procedures for minimizing risk within the facility, for all persons working within the containment perimeter as well as all persons who may have a need to enter the perimeter, including medical support staff, and emergency responders.
- Provision of required training;
- Determination of training effectiveness;
- Provision of periodic refresher training or in the event of a change in duties or introduction of new equipment/methods;
- Restrictions on untrained personnel to ensure they do not perform tasks for which they are not eligible;
- Maintenance of adequate records.
- Emergency Response

**5.3 Competence.** No personnel shall conduct activities within the poliovirus facility until he/she has demonstrated competency to perform the task in a safe and secure manner, including:

- Definition of competency needs and evaluation;
- Successful completion of required training;
- Demonstrated ability to perform tasks with and without supervision;
- Maintenance of adequate performance and training records.

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**5.4 Dismissal.** Measures shall be set in place for the removal (both temporary and permanent) of personnel to be excluded from the poliovirus facility including:

- Removal of passes, retrieval of keys, and changes in locking mechanisms, access codes, and other security devices;
- Removal of access to information relating to the poliovirus facility including documentation, electronic records and data;
- Immediate physical removal of personnel if deemed necessary.

## 6.0 Healthcare

**6.1 Worker Health.** The organization shall determine that the health of personnel does not impact on the ability to work in the poliovirus facility in a safe and effective manner. Personnel are informed of the confidentiality of the information and the nature of any treatments / vaccinations they may receive and their inherent risks and benefits. The determination shall include:

- Annual medical examinations that include an assessment of polio antibody titers as per section 6.2 and an assessment of medical conditions that could present a risk when working with poliovirus materials (e.g. hypogammaglobulinemia, epilepsy, heart attack, impaired vision, physical mobility/ dexterity, mental health, substance abuse)

**6.2 Vaccination of personnel.** The organization shall ensure availability of Inactivated polio vaccine (IPV) for individuals associated with the facility, consistent with the objectives to:

- Restrict containment facility access to individuals who have demonstrable immunity to poliovirus (defined as annual verification of serum neutralizing antibody titers of 1:8 or greater against all three poliovirus types), including:
  - Personnel assigned to work within the containment perimeter;
  - Contractors, auditors, and visitors who have a need to enter the containment perimeter;
  - Support personnel and contractors working immediately outside the containment perimeter (e.g. maintenance personnel, cleaning staff).
- Administer an IPV booster every three years to all personnel mentioned above or in the event of an antibody titer determined to be <1:8 on annual testing.
- Provide effective secondary population safeguards by an established program of education and promotion to encourage acceptance of immunization by:
  - Non-core facility personnel, including contractors
  - Worker's families/companions
  - Other groups in contact with the facility

## 7.0 Human Factors

**7.1 Human Factors.** A program shall be established to address risk associated with human factors, with measures in place to address:

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- Human reliability and behavioral safety, including adherence to procedures;
- Communication, consultation and feedback;
- Conflict management and resolution;
- Empowerment, including authority to stop work if potentially unsafe conditions are identified;
- Avoidance of blame culture, including willingness to report accidents and incidents;
- Management of stress and fatigue;
- Ergonomics, including equipment and work practice design to take account of individual needs;
- Respect for individual privacy and dignity;
- Team building and motivation;
- Access to counseling

### 8.0 General Safety

**8.1 General Safety.** A formal process shall be in place to identify and manage risk associated with specific hazards and their potential implications for biorisk that includes expertise from the Occupational Health and Safety Officer (see section 1.2.4) and related requirements/guidelines including:

- Fire safety;
- Electrical safety;
- Radiation safety;
- Chemical safety;
- Use of compressed gasses;
- Handling of high or low temperature materials
- General housekeeping, including storage requirements and tidiness and control of garbage/general waste.

### 9.0 Good Microbiological Technique

**9.1 Good Microbiological Technique (GMT).** The organization shall ensure:

- All relevant personnel have completed GMT training (WHO Laboratory Biosafety Manual, 3<sup>rd</sup> edition) and are documented as competent (see section 5 *Personnel and Competency*) in safe poliovirus-specific techniques that include but are not limited to:
  - Culture, transfer, disruption, purification, extraction, and storage;
  - Use of class II, III Biological safety cabinets (BSC) or similar site-specific construction offering equivalent protection;
  - Pipetting;
  - Use of needles and sharps;
  - Handling infectious and potential infectious human samples;
  - Minimizing aerosols;
  - Centrifuging;
  - Antibody or virus assays, quality control tests, and any procedure involving manipulation of live virus;

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- Decontaminating work surface daily and after any spill of live virus.
- Use of disinfectants, including hand washing and showering;
- Protocols and procedures are informed by risk assessment and designed to minimize poliovirus exposure including:
  - Provision of appropriate resources (equipment and time);
  - Required use of class II or III BSCs for all procedures using live poliovirus or use of a site-specific construction that minimizes risk of handling poliovirus equivalent to the protections provided by a BSC (localizing work with live poliovirus materials, protects from splashes, spills, and aerosols);
  - Limited manipulation of live poliovirus;
  - Substitution of Sabin strains for wild polioviruses when live virus use is required.

### 10.0 Clothing and Personal Protective Equipment (PPE)

**10.1 General PPE requirements.** PPE shall be correctly used within the poliovirus facility so that:

- Selection and use of PPE (gowning and de-gowning procedures) are explicitly addressed in SOPs and competency assessments;
- All personnel who are required to use PPE (including scientific staff, visitors, and contractors) are supplied with correctly fitting equipment and clothing;
- Routine inspections and maintenance of PPE are defined and carried out;
- The need for and provision of replacement and spare PPE have been adequately identified and addressed;
- The hazards associated with PPE itself are identified and controlled (impaired vision, movement, reduced dexterity);
- Adequate PPE is provided during both normal and emergency working conditions.

**10.2 Poliovirus specific PPE requirements.** Selection and use of PPE in the poliovirus facility shall be guided by risk assessment (see section *II. Poliovirus-facility associated risks*) and include the following minimum provisions:

- Protection from ingestion/inhalation: Ingestion poses the greatest risk of poliovirus infection. PPE shall at a minimum prevent introduction of poliovirus to mouth or nasal passages. Inhalation risk, though remote, must also be addressed whenever high titer poliovirus materials are being handled or aerosol-generating procedures are performed. PPE shall be layered to risk, with protection from ingestion required as a minimum (ex. face shield, particulate filter mask - N95 or equivalent). When high titer materials are being handled or aerosol generating procedures are being performed PPE shall include a HEPA filtered respirator.

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- **Protection from injection and exposure to skin/mucous membranes:**  
Although the risk of infection through these routes is remote in the fully immunized individual, PPE practice shall ensure that:
  - Only clothing dedicated for use within the containment perimeter is worn (no jewelry, watches);
  - Clothing provides a solid front and covers as much skin as possible (feet, hair, ankles, legs, arms are not exposed);
  - SOPs are developed and followed to ensure that dedicated clothing does not leave the containment perimeter without conducting a validated decontamination procedure;
  - Gloves are worn at all times and two pairs are worn while manipulating poliovirus or potentially contaminated materials or equipment.

### 11.0 Facility Physical Requirements

**11.1 Design.** The poliovirus facility shall be the result of a formal planning, design, and redesign process that ensures:

- Incorporation of relevant legislative requirements, together with information from recognized standards, guidelines (WHO Biosafety Manual, 3<sup>rd</sup> ed.), industry good practices and facility-specific risk assessments;
- Consultation with relevant parties associated with the facility and its operation such as scientific personnel, architects / designers, constructors, maintenance engineers, materials and equipment suppliers, commissioning agents, certifiers, regulators, and WHO;
- Signed concurrence by competent professionals, peer reviewed, and approved by a competent independent third party

**11.2 Poliovirus-facility specific features.** The poliovirus facility shall incorporate features that are guided by assessment of the risk of poliovirus reintroduction to the community (see section II *Poliovirus-facility associated risks*) and include the following minimum provisions:

- Poliovirus facilities are either poliovirus dedicated or used on a campaign basis with documented effective decontamination procedures between periods of work with agents other than poliovirus;
- The containment perimeter is a defined working area sealable for gaseous decontamination and with secure penetrations to prevent uncontrolled outward airflow. The containment perimeter is required irrespective of the choice of primary containment (class II or III biological safety cabinets (BSC)).
- Primary containment consists of class II or III BSCs or equivalent site-specific designs for all manipulations with live poliovirus. Facilities using class III BSCs will meet all physical aspects of this Standard with deviation in procedures permitted during normal operation of the BSC (i.e. showering out not required when class III BSC is functioning properly).
- Controlled entry into the containment perimeter is through a double-door personnel airlock; Features include interlocking doors or an

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equivalent system to ensure that more than one door cannot be opened at a time, alarms, and associated operating procedures to ensure the system functions effectively at all times.

- Controlled exit from the containment perimeter is via a walk-through exit shower. Showering is mandatory except for facilities employing fully functional class III BSCs or similar isolators (in such facilities, showering-out is required in the event of an uncontrolled breach of the primary containment equipment).
- Controlled air system maintains directional airflow via a dedicated ventilation system with ductwork sealable for gaseous decontamination, HEPA filtration on exhaust, backflow protection on inlet, and monitors/alarms to ensure directional air flow can be readily validated
- Decontamination of all liquid effluent (including shower water, eye wash, autoclave condensate) from within the containment perimeter is achieved through a validated inactivation procedure. Backflow prevention is implemented on all services / utilities entering the facility (water, gases, cabling) and measures to prevent release through traps, sinks and showers;
- Decontamination of all materials exiting the facility is achieved through a validated sterilization / decontamination procedure consisting of:
  - A dedicated pass-through autoclave with a bioseal, interlocking doors to prevent opening the clean side prior to cycle completion, HEPA filtration of steam discharge, cycle recording mechanisms and alarms, and positioned so that maintenance can be performed from the clean side of the barrier.
  - A material airlock / decontamination chamber sealable for gaseous decontamination;
  - A dunk tank containing sufficient active compound to inactivate poliovirus.

**11.3 Poliovirus animal facility specific features.** The poliovirus animal facility shall incorporate features guided by risk assessment as described in section 11.2 and shall meet all poliovirus containment criteria as described in this document including:

- Compliance with criteria for animal facilities at Biosafety Levels 1,2, and aspects of 3 that are consistent with the controls outlined in other sections of this document (WHO Laboratory Biosafety Manual, 3<sup>rd</sup> edition);
- Special training and supervision of personnel responsible for inoculating, harvesting, sampling, animal autopsies, and any other manipulations with poliovirus infected animals;
- Use of class II or III BSCs or equivalent site specific constructions for all animal manipulations with live poliovirus;
- Housing infected animals separately in a containment area in isolators;
- Maintaining barriers to prevent escape of infected animals;
- Maintaining accurate records and accounting for all infected animals;

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- Meeting international criteria for laboratory animal care (e.g., Association for Assessment and Accreditation of Animal Care, International).

### **12.0 Equipment, Maintenance, Calibration and Certification**

**12.1 Maintenance Management.** Procedures for maintenance of the facility and its equipment shall be established and maintained such that

- The physical integrity of the facility and its fixtures and fittings is adequate and meets the design intent
- Maintenance activities are planned and performed by competent individuals, and that adequate controls are in place to prevent workers being exposed to poliovirus in the course of their work
- Maintenance requirements are identified and recorded at time of purchase / acquisition of equipment;
- A documented and up-to-date maintenance register is created for all applicable equipment;
- Planned maintenance is scheduled and conducted in line with manufacturer's requirements and / or other specified intervals as identified in risk assessments;
- Unplanned (breakdown) maintenance provision ensures integrity of the poliovirus facility is maintained
- Essential spare parts / components / materials are made available at frequencies appropriate to the risk of failure and need for replacement;
- Documentation of maintenance activities is current, up-to-date and secure.

**12.2 Control of Equipment.** Procedures for the control of equipment associated with the poliovirus facility shall be established and maintained, such that

- Equipment is in line with identified work needs and minimization of risk informs the choice of equipment type (ex. - plastic containers in preference over glass containers)
- Risk assessments are complete and approval for acquisition is authorized by competent personnel;
- Controls are specific for movement of equipment to and from the poliovirus facility, including decontamination and airlock requirements;
- An asset register is current

**12.3 Calibration.** Procedures for calibration of equipment shall be established and maintained, such that

- Calibration requirements are identified and recorded at time of purchase / acquisition of equipment;
- Standards / tests are specified to ensure the equipment is correctly calibrated;
- A documented and up-to-date calibration register is created for all applicable equipment;

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- Calibration is scheduled and conducted in line with manufacturer's requirements and / or other specified intervals as identified in risk assessments;
- Documentation relating to calibration activities is up-to-date and secure

**12.4 Certification.** Procedures for all equipment shall be established and maintained such that

- Certification requirements are identified and recorded at time of purchase / acquisition of equipment, including relevant and current standards against which to certify;
- The certification process is performed by competent and independent certifiers
- Certification is scheduled and conducted in line with manufacturer's requirements and / or other specified intervals as identified in risk assessments;
- Documentation relating to certification activities is current, up-to-date and secure.

### 13.0 Disinfection, Decontamination and Sterilization

**13.1 Containment of Viable Poliovirus.** No viable poliovirus shall be released from the facility unless approved by the MOH for transfer to another approved facility under controlled conditions. Potential routes whereby viable poliovirus could unintentionally exit the facility shall be identified and adequate prevention measures set in place.

**13.2 Identification of Waste Streams.** All potential waste streams shall be identified (including those that may occur during an emergency), documented, and subject to risk assessment. Sources of waste and infected materials shall include as a minimum:

- Clothing and PPE;
- Cultures and associated materials;
- Contaminated supernatant and culture media;
- Paper and plastic waste;
- Contaminated needles and sharps;
- Waste water, including that from sinks and showers;
- Contaminated air;
- Filters and air handling systems;
- Discarded equipment used in the facility

For each of these sources, procedures shall be put in place to validate the decontamination regime and records shall demonstrate that no contaminated persons / materials leave the facility and inactivation measures have been implemented effectively.

**13.3 Inactivation of Poliovirus.** Procedures shall be established and maintained to ensure complete inactivation of all poliovirus from all materials and waste streams leaving the containment perimeter such that

- Heat sterilization (autoclaving) shall be the preferred method of inactivation of poliovirus;

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- All disinfectants shall be proven to contain sufficient active compound to address the working conditions under which they will be applied and are prepared and handled to ensure such concentrations are maintained throughout the process;
- SOPs are available to address both routine and non-routine activities (e.g. daily routines vs. major spills);
- SOPs are developed to respond to failure of decontamination procedure or equipment
- SOPs are validated and shown to be effective against poliovirus prior to their use;
- Monitoring measures are implemented to ensure the methods have been effective (e.g. cycle recording and use of biological indicators in autoclaves);
- All materials leaving the containment perimeter (including clothing liquid / solid waste) are heat sterilized or subject to chemical treatment of proven effectiveness prior to removal;
- All material leaving the containment perimeter is accompanied by documentation of its decontamination
- Resources are available to deal with emergencies, accidents, and other incidents;
- In the event that live poliovirus is to be removed from the facility this will be done through use of a dunk tank, decontamination chamber or other mechanism that ensures disinfection of the exterior surfaces of any packaging materials used;
- The facility inactivates all waste and other potentially contaminated material before it is passed to contractors or other third parties for waste disposal.

**13.4 Decontamination of the facility.** Procedures shall be established, validated, and maintained for effective poliovirus decontamination of the facility.

## 14.0 Security

**14.1 Security Plan.** A security plan based upon a threat assessment shall be implemented and maintained such that

- A system is established and procedures documented to ensure that threat assessments are conducted and action taken in line with the findings and recommendations addressing
  - Theft of poliovirus or related equipment, documents or data;
  - Sabotage including vandalism and tampering;
  - Break-in and intrusion;
  - Labor issues and disputes;
  - Kidnapping and extortion;
  - Workplace violence;
  - Natural disasters
  - Picketing, occupation and barricade;
  - Screening and isolation of suspect packages;
  - Acts of terrorism;
  - Civil unrest or war.

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- Breaches of security are reported, recorded and investigated as accidents and incidents.

**14.2 Physical Security.** Procedures for the physical security of poliovirus materials including cultures, specimens, samples and potentially contaminated materials shall be implemented and maintained such that:

- The containment facility shall be located on a secure site with perimeter control to prevent unauthorized access;
- The containment facility shall be located away from uncontrolled traffic flows and entrance shall be via a locked door with double control measures (e.g. requirement for electronic pass with access code);
- During poliovirus manipulations, a second person within the containment perimeter or in close proximity should be aware of the work being conducted and available for contact if needed;
- The perimeter of the facility shall be subject to constant monitoring, e.g. the use of alarms, security personnel and closed circuit TV;
- Measures shall be implemented to identify and record all personnel in the facility at any point in time
- Anti-intrusion alarms and sensors shall be installed, including interfaces with police and other security services;
- Panic buttons and 'silent' emergency alert measures shall be implemented (e.g. key codes to alert security in the event of a hostage situation).

**14.3 Information Security.** Sensitive information shall be identified and securely managed, including:

- Virus inventories;
- Security plans;
- Security inspection reports;
- Design drawings;
- Maintenance plans;
- Electronic data including email correspondence;
- Human Resource information including worker contact details;
- Sensitive documents associated with the facility that are no longer required shall be destroyed under secure conditions;
- IT security protection including computer viruses and unauthorized external access.

**14.4 Personnel Security.** The organization shall ensure that access to poliovirus containment areas are limited to personnel that have been screened for subversive behaviors / associations or criminal records or are accompanied at all times by authorized individuals (as in the case of visitors, contractors, etc). The screening includes:

- Association with organizations that could present a threat to integrity of the facility;
- Medical conditions that could lead to unstable / undesirable behavior;
- Providing assurance that individuals do not work under the influence of drugs or alcohol.

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**14.5 Security Drills and Exercises.** Documented security drills and exercises shall be conducted at regular intervals to test plans, prepare personnel and learn from any deficiencies.

### 15.0 Accident / Incident Investigation

**15.1 Accident / Incident Investigation.** Documented procedures to define, record, analyse, and learn from accidents and incidents shall be established and maintained. As a minimum, the process shall:

- Define what constitutes an accident / incident and what triggers recording and reporting, with emphasis on events that may result in exposure to live poliovirus (e.g. sticks, spills, splashes, sprays, leaks, aerosol generating events);
- Create a culture of self-reporting of incidents, including “near misses” in addition to incidents that may trigger an investigation or emergency response;
- Define what constitutes a significant poliovirus exposure (e.g., ingestion) and thresholds for initiating procedures to determine whether individuals are infected;
- Establish a poliovirus incident evaluation/response team (composed of facility medical, public health, and polio-specific expertise) that determines whether an exposure is significant, reports its findings to the senior manager, and recommends such actions as deemed necessary.
- Establish and publicize 24 hour accident/incident reporting channels, identifying those responsible for maintaining the system;
- Specify required documentation to support the system, frequency and distribution of reports generated, and communicate to relevant personnel;
- Ensure analysis of trends, identify root causes, and provide feedback and action tracking mechanisms to ensure that lessons learned are implemented.

### 16.0 Emergency Plan and Response

**16.1 Emergency scenarios.** All credible and foreseeable emergency scenarios shall be identified, including those associated with:

- The facility (fire, explosions, breach of security, internal flooding, equipment or control system failure, utility failure including electricity, gas, and water supplies);
- Medical events needing possible evacuation from containment (e.g. heart attack, stroke, seizures);
- Natural disasters (e.g. earthquake, floods, extreme weather);
- Poliovirus
  - Infected / potentially infected worker or other contact;
  - Loss of poliovirus through theft or any other reason;
  - Failure of disinfection regime;
  - Major spillage / aerosol release / environmental release.

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**16.2 Emergency Plans.** Emergency plans shall be prepared, implemented, communicated, and tested to demonstrate that emergency situations will be managed effectively, and that control and contingency measures in place are reasonable and proportionate to the scale and nature of the emergency. At a minimum, plans shall address:

- The identification of those responsible for devising, implementing and testing the control measures specified and their communication to all relevant personnel;
- The legality and enforceability of proposed emergency response plans;
- Response to emergencies at all hours and during weekends and holiday periods;
- The need for emergency access / exit, including the ability to override access / exit control systems;
- The need to inform visitors and contractors of emergency response plans and the possible consequences of exposure.

**16.3 External Agencies.** All relevant external agencies with contact details maintained shall be identified and consulted on emergency planning issues, including:

- Police and security services;
- Fire services;
- Ambulance and local hospitals / healthcare providers;
- Transport providers / couriers;
- Local and national government officials
- WHO

**16.4 Emergency Exercises and Simulations.** Structured and realistic emergency exercises and simulations shall be conducted at regular intervals to test plans, prepare personnel, and learn from good practices or deficiencies identified.

**16.5 Response to a significant poliovirus exposure.** A system shall be established to effectively manage incidents determined by the evaluation /response team as significant exposures, including:

- Implementation of full preventive measures by isolating individuals under evaluation, particularly from children and the unimmunised, and securing stool and associated waste;
- Educating the individual under investigation, his/her family, and close contacts on the risk of poliovirus infection to the community, procedures for diagnosis, and precautionary measures necessary to prevent possible transmission;
- Initiating procedures to determine whether individuals are infected by collecting and testing nose, throat, and stool specimens daily for a minimum of 7 days post exposure.

**16.6 Response to a confirmed poliovirus facility-associated infection.** A system shall be established to effectively manage a confirmed facility-associated poliovirus infection until the individual is free of poliovirus in stools for three consecutive days. This includes procedures for:

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- Isolating infected individuals, particularly from children and the unimmunised;
- Securing collection and disinfecting stool and associated waste;
- Educating families and frequent contacts on the risk posed by the poliovirus infection and procedures for isolation;
- Communicating to relevant national and local officials to evaluate needs to implement community immunization response plans;
- Notifying WHO;
- Disinfecting areas potentially contaminated by infected individuals.

### IV. Definitions

**The definitions given below apply to the terms as used in this Standard, and may have different meanings in other contexts.**

**Aerosol:** A dispersion of solid or liquid particles of microscopic size in a gaseous medium.

**Accredit:** To certify as meeting and maintaining defined standards.

**Audit:** An official examination of facility operation relative to this Standard.

**Biological safety cabinets:** Class II cabinets for microbiological work are partially open-fronted enclosures with air drawn around the operator into the front grille and a downward laminar flow of HEPA-filtered air provides product protection by minimizing the chance of cross-contamination along the work surfaces of the cabinet. Class III cabinets are gas-tight enclosures with a non-opening view window, with access for materials into the cabinet through a dunk tank or double-door pass-through box that is decontaminated between uses. Both supply and exhaust air are HEPA filtered or incinerated before discharge. Airflow is maintained under negative pressure.

**Biorisk:** The risk relating to biosafety and biosecurity where the principal hazard is a biological agent (in the case of this Standard, poliovirus).

**Biorisk Management System:** The organizational structure, planning activities, responsibilities, practices, procedures, processes and resources for developing, implementing, achieving, reviewing and maintaining the organization's biorisk policy.

**Biosecurity:** The protection, control, and accountability for valuable biological materials within biological facilities to prevent their unauthorized access, loss, theft, misuse, diversion, or intentional release

**CCID<sub>50</sub>:** Cell culture infectious dose which will infect 50% of the cell monolayers challenged with the defined inoculum

**Calibration:** Correlation of the readings of an instrument with a standard.

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**Certification:** Documentation stating that a system qualification, calibration, validation or revalidation has been performed appropriately and the results are acceptable.

**Containment:** Protection of personnel and the immediate laboratory environment from exposure to infectious agents through the use of appropriate laboratory technique and safety equipment and protection of the environment external to the facility through facility design and operational practices.

**Contingency planning:** Preparing for a future event or circumstances regarded as likely to occur, or as influencing present action.

**Decontamination:** A process by which an object or material is freed of contaminating agents.

**Disinfection:** A physical or chemical means of killing microorganisms, but not necessarily spores.

**Facility:** Any laboratory or vaccine production unit owned or operated by any level of government, academic institution, corporation, company, partnership, society, association, firm, sole proprietorship, or other legal entity.

**Facility, essential:** A facility designated by the Ministry of Health as serving critical national or international functions that involve storage or handling poliovirus infectious materials or potential infectious materials under conditions set out in this Standard

**Fumigation:** The process whereby one or more chemicals are applied in the gaseous state to an enclosed space for the purpose of decontaminating the area and the items therein.

**Good microbiological techniques:** Technical methods designed to avoid or minimize the most common causes of laboratory injuries or work-related infections (See WHO Laboratory Biosafety Manual, 3<sup>rd</sup> edition, 2004).

**Guidelines:** Principles or criteria guiding or directing action.

**Hazard:** Any substance, situation, or activity with potential for causing harm.

**High efficiency particulate air (HEPA) filter:** A filter capable of removing at least 99.97% of all particles with a mean aerodynamic diameter of 0.3 micrometres.

**Inactivation:** Rendering an organism inert by application of heat, or other means.

**Legislation:** The process of making laws.

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**Organization:** The legal entity responsible for management of the poliovirus facility, such as a university, private company, or government agency.

**Penetrations:** Opening through walls, floors, or ceilings to allow for mechanical services.

**Policy:** The course or principle of action adopted or proposed by the responsible government entity.

**Poliovirus:** A picornavirus consisting of three serotypes: 1, 2, and 3. Poliovirus serotypes are further sub-divided into wild (circulating in nature) and Sabin strains (attenuated strains of oral polio vaccines [OPV]).

**Poliovirus, wild:** Wild poliovirus are naturally occurring isolates known or believed to have circulated persistently in the community, attenuated strains not approved for vaccines (Cox/Lederle and Koprowski/Wistar series), and vaccine-derived polioviruses [VDPV] (isolates consistent with an extensive period of virus excretion or transmission in the community, demonstrating 1–15% differences from parent OPV strains by full VP1 sequence homology). Wild poliovirus materials may be infectious (a) or potential infectious (b).

**Poliovirus infectious materials, wild:** Wild poliovirus infectious materials include:

- Clinical materials from confirmed wild poliovirus (including VDPV) infections Environmental sewage or water samples in which wild polioviruses are present;
- Cell culture isolates, and reference strains of wild poliovirus Seed stocks and infectious materials from IPV production;
- Infected animals or samples from such animals, including PVR transgenic mice;
- Derivatives produced in the laboratory that have capsid sequences from wild polioviruses;
- Full-length RNA or cDNA that include capsid sequences derived from wild poliovirus;
- Cells persistently infected with poliovirus strains whose capsid sequences are derived from wild poliovirus.

**Poliovirus potential infectious materials, wild:** Wild poliovirus potential infectious materials include:

- Fecal or respiratory secretion samples collected for any purpose in a time and geographic area of wild poliovirus (including VDPV) circulation
- Products of such materials in poliovirus permissive cells or animals
- Uncharacterized enterovirus-like cell culture isolates
- Respiratory and enteric virus stocks handled under conditions where poliovirus contamination or replication is possible

**Poliovirus Sabin:** OPV/Sabin strains are attenuated poliovirus strains (approved for use in oral polio vaccines by national regulatory authorities,

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principally Sabin strains) and OPV-like polioviruses (isolates consistent with a limited period of virus excretion or person-to-person transmission, demonstrating less than 1% difference from parent OPV strains by full VP1 sequence homology). OPV/Sabin materials may be infectious (a) or potential infectious (b).

***Poliovirus infectious materials, OPV/Sabin:*** OPV/Sabin infectious materials include:

- Cell culture isolates and reference OPV/Sabin strains
- Seed stocks and live virus materials from OPV production
- Environmental sewage or water samples in which OPV/Sabin strains are present
- Fecal or respiratory secretion samples from recent OPV recipients
- Infected animals or samples from such animals, including PVR transgenic mice
- Derivatives produced in the laboratory that have capsid sequences from OPV/Sabin strains
- Full-length RNA or cDNA that include capsid sequences derived from OPV/Sabin strains
- Cells persistently infected with poliovirus strains whose capsid sequences are derived from OPV/Sabin strains

***Poliovirus potential infectious materials, OPV/Sabin:*** OPV/Sabin potential infectious materials include:

- Fecal or respiratory secretion samples collected for any purpose in a time and geographic area of OPV use
- Products of such materials from poliovirus permissive cells or animals
- Respiratory and enteric virus stocks handled under conditions where OPV/Sabin strain contamination or replication is possible.

***Risk:*** A chance or possibility of danger, loss, injury, or other adverse consequences.

***Risk assessment:*** A qualitative or semi-qualitative process undertaken by individuals with expertise in appropriate disciplines and backgrounds in response to an identified hazard.

***Sharps:*** Devices used in the facility that are capable of cutting and/or puncturing skin (e.g. needles, scissors, glass).

***Sterilization:*** A process that destroys and/or removes microorganisms and their spores.

***Standard:*** The basic measure (document) by which performance quality is judged.

***Validation:*** The documented act of proving that a procedure, process, equipment, material activity, or system actually leads to expected results.

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**Verification:** Establish truth or correctness through demonstration (or documentation).

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## Annex 5

(Draft concept document)

### International accreditation of essential poliovirus facilities

1. Definitions
2. Purpose
3. International standards
4. Criteria for accreditation
5. Steps of the procedure
6. Monitoring
7. Reassessments
8. Confidentiality
9. Fees
10. Conflicts of interest

#### 1. Definitions

See Annex 1

#### 2. Purpose

This annex sets forth the procedures for international accreditation of essential poliovirus facilities as described in the *Global Action Plan to minimize poliovirus facility-associated risk in the post-eradication/post-OPV era, 3<sup>rd</sup> edition*.

#### 3. International standards

WHO, Geneva, establishes the standards and requirements for accreditation guided by the following general principles:

- Physical facilities and biosafety practices meet all published national and WHO primary safeguards of containment and secondary safeguards of location (*Global Action Plan, 3<sup>rd</sup> edition, Annex 4 and reference 6*).
- Persons qualified by training and experience direct all laboratory operations.
- Supervisory personnel and staff at all administrative levels are informed of the national, institutional, and laboratory responsibilities inherent to working with polioviruses.

#### 4. Criteria for accreditation

The poliovirus facility and its administrative entity must be nominated by the Minister of Health or designated national authority for WHO accreditation and

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declared to meet all national programmatic and biosafety criteria consistent with international standards.

### 5. Steps of the procedure

(a). Official request: The senior manager of the facility applies to the Ministry of Health or designated authority for international accreditation. Facilities must be fully operational. Applications must provide evidence of meeting requirements defined in the WHO *Global Action Plan, 3<sup>rd</sup> ed. (Annex 4 or reference 6)* and include the following information at a minimum:

1. Contact information
  - 1.1. Country and designated national authority requesting review
  - 1.2. Name and address of institution applying for accreditation
  - 1.3. Name and address of parent organization, if different
  - 1.4. Name and address of responsible institutional officials
2. Overview
  - 2.1. Category of poliovirus facility requesting accreditation
  - 2.2. Name of facility
  - 2.3. Nature and purpose of facility
  - 2.4. Description of organization, including organizational chart
  - 2.5. History of facility
  - 2.6. Summary of facility
3. Description
  - 3.1. Institutional biosafety policies
    - 3.1.1. Biosafety committee and biosafety program
    - 3.1.2. Procedures for and frequency of national or institutional biosafety reviews
  - 3.2. Personnel qualifications and training
    - 3.2.1. Supervisory personnel
    - 3.2.2. Research staff
    - 3.2.3. Technical staff
  - 3.3. Occupational health and safety
    - 3.3.1. Identification and risk assessment of hazardous operations
    - 3.3.2. Description of education programs
    - 3.3.3. Personal protective equipment/laboratory clothing
    - 3.3.4. Biological safety cabinets
    - 3.3.5. Provisions for washing hands, showering, changing clothes
    - 3.3.6. Entry and exit procedures
  - 3.4. Medical evaluation and preventive measures
    - 3.4.1. Immunization policies and records
    - 3.4.2. Infection surveillance procedures

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- 3.5. Waste disposal methods
  - 3.5.1. Policies and procedures
  - 3.5.2. Autoclaves
- 3.6. Physical facilities
  - 3.6.1. Location in relation to other biomedical laboratories in institution
  - 3.6.2. General arrangement of facilities
  - 3.6.3. Storage areas for poliovirus materials
  - 3.6.4. Functional space
    - 3.6.4.1. Exterior windows
    - 3.6.4.2. Floors, walls, ceilings
    - 3.6.4.3. Drainage and plumbing
    - 3.6.4.4. Heating, ventilation, and air conditioning
      - 3.6.4.4.1. Ductwork
      - 3.6.4.4.2. Air flow
      - 3.6.4.4.3. Control sequences and alarms
    - 3.6.4.5. Power, lighting, and provisions for emergency power
- 3.7. Inventory of poliovirus materials
  - 3.7.1. Policies
  - 3.7.2. Records
- 3.8. Shipping and receiving poliovirus materials
  - 3.8.1. Policies and procedures
  - 3.8.2. Records
- 3.9. Security

(b). Evaluation of application: The national authority determines whether the application is in the national interest, whether the facility qualifies as accreditable, and whether the information requirements are met. The national authority nominates the qualifying facility for WHO accreditation and submits an application through the WHO Regional Office to WHO headquarters, Geneva. Separate applications must be submitted for each facility. Detailed instructions for completing the application process are available upon request from Regional Offices.

**(c).** Site visits and reviewers: Facilities are evaluated on-site by a team of at least two reviewers selected by WHO from an international roster of qualified biosafety professionals and are agreed to by the Minister of Health or its designated authority. Site reviewers must be permitted to enter all laboratory and storage facilities related to operation of the facility and have access to all relevant laboratory programmatic information, protocols, and records. Site reviewers must respect and adhere to facility biosafety policies and procedures such as showering and wearing protective clothing.

(d). Reports and outcome: The accreditation office, WHO, Geneva, reviews national applications and site visit reports and recommendations, makes final

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determination on accreditation status of individual facilities, and informs the national authority of its findings.

### **6. Monitoring**

Accreditation is granted contingent upon favourable annual national reviews, reports submitted by the national authority to WHO, and international on-site visits at two year intervals. Additional interim visits may be required to confirm corrections of deficiencies or review modifications or changes in program or facilities. Interim or follow-up on-site visits may require only one reviewer.

### **7. Reassessments**

Once granted, international accreditation may be revoked by either the designated national authority or WHO upon due cause of adverse changes in facility operations or structure. The Ministry of Health must be notified in writing of the decision to withhold or revoke facility accreditation. Depending upon the nature of the infraction, the accredited facility may be given additional time (up to 12 months) to correct deficiencies before final revocation. Appeals to WHO to restore facility accreditation are accepted only from the designated national authority.

### **8. Confidentiality**

Site reviewers must keep all information confidential and disclose findings and recommendations only to WHO. All WHO files and records of accreditation shall be held in confidence.

### **9. Fees**

Facilities applying to national authorities for international accreditation should expect to support WHO administrative cost and actual cost of the on-site review.

### **10. Conflict of interest**

Site reviewers must not be employees of the facility or its parent organization and must have no conflict of interest. Statements must be on file in WHO.