

GAPIV

WHO Global Action Plan for Poliovirus Containment

After type-specific eradication and containment of wild poliovirus and cessation of oral polio vaccination, minimizing the risk of poliovirus reintroduction is critical. To prevent reintroduction, the number of international poliovirus facilities will need to be reduced to the minimum necessary to perform critical functions of vaccine production, diagnosis and research.

NOTE:

This document is the revised version of the WHO Global Action Plan to minimize poliovirus facility-associated risk after type-specific eradication of wild polioviruses and sequential cessation of oral polio vaccine use also known as the WHO Global Action Plan for Poliovirus Containment (3rd edition; 2015) (available at: https://polioeradication.org/wp-content/uploads/2016/12/GAPIII_2014.pdf) and is being shared following the critical review and approval from the Containment Advisory Group for the purpose of inviting comments and feedback on the proposed changes contained therein, which will then be considered by CAG.

Publication of this early draft is to provide information about the proposed document – WHO Global Action Plan for Poliovirus Containment (GAPIV) – to a broad audience and to improve transparency of the consultation process.

Comments and feedback proposing modifications to this document MUST be received by 1 May 2022 using the Comment Form available separately. Electronic submissions are encouraged and should be submitted to the Responsible Officer: Dr Harpal SINGH at email: hsingh@who.int with copy to containment@who.int.

The final agreed formulation of this document will be edited to be in conformity with the "WHO style guide, second edition".

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1 **Acknowledgements**

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3 TO BE WRITTEN FOR FINAL DRAFT



Abbreviations and Acronyms

AFP	Acute flaccid paralysis
AQAS	Auditor Qualification and Audit Support Plan 2021–2023
BSC	Biological safety cabinet
CAG	Containment Advisory Group
CCID ₅₀	Cell culture infectious dose 50%
CCS	Containment Certification Scheme to support the WHO Global Action Plan for Poliovirus Containment
CEN	European Committee for Standardization
CWA	CEN Workshop Agreement
GCC-CWG	Global Certification Commission – Containment Working Group
DTP	Diphtheria–tetanus–pertussis
DTP3	Diphtheria–tetanus–pertussis vaccine third dose
EUL	WHO emergency use listing
GCC	Global Commission for the Certification of the Eradication of Poliomyelitis
GPEI	Global Polio Eradication Initiative
HEPA	High-efficiency particulate arresting
HSSE	Health, safety, security and environment
IHR	International Health Regulations
IPV	Inactivated polio vaccine
Sabin-IPV	Sabin-inactivated polio vaccine
Salk-IPV	WPV-inactivated polio vaccine
µm	Micrometre
MoH	Ministry of Health
NAC	National Authority for Containment
NCC	National Certification Committee for the Eradication of Poliomyelitis
nOPV	Novel oral polio vaccine
NPCC	National poliovirus containment coordinator
NTFC	National task force for containment
OPV	Sabin oral poliomyelitis vaccine
bOPV	Sabin bivalent oral poliomyelitis vaccine serotypes 1 and 3
mOPV2	Sabin monovalent oral poliomyelitis vaccine serotype 2
nOPV2	Novel oral poliomyelitis vaccine serotype 2
OPV1	Sabin oral poliomyelitis vaccine serotype 1
OPV2	Sabin oral poliomyelitis vaccine serotype 2
OPV3	Sabin oral poliomyelitis vaccine serotype 3
tOPV	Sabin trivalent oral poliomyelitis vaccine serotypes 1, 2 and 3
PEF	Poliovirus-essential facility
PHEIC	Public health emergency of international concern
PIM	Potentially infectious material, poliovirus

1	PIM Guidance	Guidance to minimize risks for facilities collecting, handling or storing materials
2		potentially infectious for polioviruses – 2nd edition
3	PPE	Personal protective equipment
4	PV	Poliovirus
5	PVSRIP0	Neuro-attenuated recombinant poliovirus; live attenuated Sabin serotype 1 poliovirus with
6		heterologous internal ribosomal entry site (IRES) of human rhinovirus type 2.
7	RCC	Regional Commission for the Certification of the Eradication of Poliomyelitis
8	R ₀	Basic reproductive rate
9	S19	S19 with the structural (capsid) protein encoding P1-region (of WPV or Sabin
10		polioviruses; of serotypes 1, 2 or 3)
11	S19/N18S	S19 with the structural (capsid) protein encoding P1-region (of WPV or Sabin
12		polioviruses; of serotypes 1, 2 or 3) with a mutation (substitution) of asparagine (N) by
13		serine (S) at amino acid 18 of the non-structural protein 2A to allow better growth in
14		Vero cells
15		
16	SAGE	Strategic Advisory Group of Experts on Immunization
17	SIA	Supplementary immunization activity
18	SOP	Standard operating procedure
19	VAPP	Vaccine-associated paralytic poliomyelitis
20	VDPV	Vaccine-derived poliovirus
21	VDPV2	Vaccine-derived poliovirus serotype 2
22	aVDPV	Ambiguous vaccine-derived poliovirus
23	aVDPV2	Ambiguous vaccine-derived poliovirus serotype 2
24	cVDPV	Circulating vaccine-derived poliovirus
25	cVDPV2	Circulating vaccine-derived poliovirus serotype 2
26	iVDPV	Immunodeficiency-associated vaccine-derived poliovirus
27	iVDPV2	Immunodeficiency-associated vaccine-derived poliovirus serotype 2
28	VLP	Virus-like particle
29	WHA	World Health Assembly
30	WHO	World Health Organization
31	WPV	Wild poliovirus
32	WPV1	Wild poliovirus serotype 1
33	WPV2	Wild poliovirus serotype 2
34	WPV3	Wild poliovirus serotype 3

Definitions

These definitions apply to the terms as used in this standard; the words may have different meanings in other contexts.

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

Audit: The systematic, independent, and documented process for obtaining audit evidence and evaluating it objectively to determine the extent to which audit criteria are fulfilled.

Biological safety cabinets: Class II and Class III cabinets that are designed to protect the operator, the laboratory environment, and work materials from exposure to infectious aerosols and splashes that may be generated when manipulating materials containing infectious agents, such as primary cultures, stocks, and diagnostic specimens. Class II cabinets for microbiological work are partially open-fronted enclosures with air drawn around the operator into the front grille and feature a downward laminar flow of HEPA-filtered air that 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, allowing access into the cabinet through a dunk tank, rapid transfer port, or double-door pass-through chamber that is decontaminated between uses. Work is conducted using arm-length gloves. Supply and exhaust air pass through single and double HEPA filters, respectively, before discharge. The cabinet is maintained under negative pressure.

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

Biorisk management committee: An independent review group for biorisk issues associated with the poliovirus facility.

Biorisk management system: The organizational structure, planning activities, responsibilities, practices, procedures, processes, and resources for developing, implementing, achieving, reviewing, and maintaining an organization's biorisk policy and its objectives.

Biosafety, laboratory: The containment principles, technologies, and practices that are implemented to prevent unintentional exposure to pathogens and toxins, or their accidental release.

Biosecurity, laboratory: The protection, control, and accountability for biological agents and toxins within biological facilities to prevent their unauthorized access, loss, theft, misuse, and diversion, or their intentional unauthorized release.

CCID₅₀: A cell culture infectious dose that will infect 50% of the cell monolayers challenged with the defined inoculum.

Calibration: The correlation of the readings of an instrument with a standard.

Certification: The systematic, documented process to ensure systems perform in accordance with available certification standards or applicable validation guidance. National certification to this standard is expected to be performed once a year through responsible national oversight bodies.

Containment: A system for confining microorganisms, organisms, or other entities within a defined space.

Contingency planning: The preparation for a future event or circumstance regarded as likely to occur, or as influencing present action.

Decontamination: A procedure that eliminates or reduces biological agents and toxins to a safe level with respect to the transmission of infection or other adverse effects.

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

Disinfection: The process to reduce the number of microorganisms, but not usually of bacterial spores, without necessarily killing or removing all organisms.

Facility: Any laboratory, repository, 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, certifiable: A facility approved by the ministry of health or another designated national body or authority as a qualified applicant for national containment certification.

Facility, poliovirus-essential: A facility designated by the ministry of health or another designated national body or authority as serving critical national or international functions that involve the handling and storage of needed poliovirus infectious materials or potentially infectious materials under conditions set out in this standard.

Formal design process: A structured and documented approach where the needs of the facility are determined through risk assessment.

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

Global Certification Commission (GCC): The term commonly used to refer to the Global Commission for the Certification of the Eradication of Poliomyelitis, which has the 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 of WHO certifying that global polio eradication has been achieved.

Good microbiological practices and procedures: Technical methods designed to avoid or minimize the most common causes of laboratory injuries or work-related infections (See WHO *Laboratory biosafety manual, Fourth edition*, 2020).

Guidelines: Principles or criteria guiding or directing action.

Hazard: Any source, situation or act with potential for causing harm.

High-efficiency particulate arresting or 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 the application of heat or other means.

Inspection: A conformity evaluation by observation and judgement accompanied as appropriate by measurement, testing, or gauging.

Legislation: The process of making laws; a law or a set of laws passed by a country's government.

National Certification Committee: The term commonly used to refer to a country's *National Committee for the Certification of the Eradication of Poliomyelitis*, which is responsible for certifying to the Regional Certification Commission that eradication has been achieved throughout the country.

Needed poliovirus materials: Poliovirus materials deemed needed and worth storing to ensure the continuation of critical international and national functions, including Salk-IPV and Sabin-IPV production, the development and storage of oral polio vaccine stockpiles, vaccine quality assurance, diagnostic reagent production, virus diagnostic and reference functions, and crucial research, as determined by the respective NAC or other designated national authority.

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

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

Policy: Intentions and direction of an organization as formally expressed by its top management.

Poliovirus: A picornavirus consisting of three serotypes: 1, 2, and 3. Poliovirus serotypes are further subdivided into wild (circulating in nature) and Sabin strains (attenuated strains used for oral polio vaccines). Polioviruses use CD155 as the primary cellular receptor.

Poliovirus, wild:

- Wild polioviruses are naturally occurring isolates known or believed to have circulated persistently in the community.
- Vaccine-Derived polioviruses (VDPs) are classified with polioviruses. Vaccine-derived polioviruses (VDPV) are rare strains of poliovirus that have genetically mutated from the strain contained in the oral polio vaccine. They usually demonstrate 1–15%¹ sequence differences from the parental oral polio vaccine (OPV) strain; they may have circulated in the community (cVDPV) or have replicated for prolonged periods in immunodeficient subjects (iVDPV) or be ambiguous and of unknown origin (aVDPV).
- Attenuated strains not licensed for use as live vaccines (Cox/Lederle and Koprowski/Wistar series) are classified with wild polioviruses as their clinical properties are unproven.

Wild poliovirus materials may be (a) infectious or (b) potentially infectious.

(a) Poliovirus infectious materials, wild: These include:

- clinical materials from confirmed wild poliovirus (including VDPV) infections;
- environmental sewage or water samples that have tested positive for the presence of wild polioviruses;
- 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 human poliovirus receptor transgenic mice;
- derivatives produced in the laboratory that have capsid sequences from wild polioviruses, unless demonstrably proven to be safer than Sabin strains. The safety of new derivatives containing wild poliovirus capsid sequences will be assessed by an expert panel, on the basis of comparison to reference Sabin strains for (i) degree and stability of attenuation; (ii) potential for person-to-person transmission; and (iii) neurovirulence in animal models;
- full-length RNA or cDNA of viruses proven to be safer than Sabin strains, but that includes wild poliovirus capsid sequences. The safety of these full-length RNA or cDNA and their containment requirements will be assessed by an expert panel convened by WHO, on the basis of comparison to reference Sabin strains for (i) degree and stability of attenuation; (ii) potential for person-to-person transmission; and (iii) neurovirulence in animal models;
- cells persistently infected with poliovirus strains whose capsid sequences are derived from OPV/Sabin strains.

(b) Poliovirus potentially infectious materials, wild: These include:

- faecal or respiratory secretion samples and their derivatives (e.g., stool suspensions, extracted nucleic acids, etc.) collected for any purpose in a time and geographic area of wild poliovirus (including VDPV) circulation;
- products of such materials from poliovirus permissive cells or animals;
- uncharacterized enterovirus-like cell culture isolates from countries known or suspected to have circulating wild poliovirus or VDPV at the time of collection;
- respiratory and enteric virus stocks handled under conditions where poliovirus contamination or replication is possible;
- environmental samples (i.e., concentrated sewage, wastewater) collected from areas known or suspected to have circulating WPV or VDPV at the time of collection.

Poliovirus nucleic acid: Poliovirus RNA, cDNA, and total nucleic acid extracted from poliovirus infectious materials (e.g., a virus isolate) or potentially infectious materials (e.g., stool, respiratory

¹ Some isolates display >15% sequence diversity but are phylogenetically related to parental Sabin strains.

specimen, sewage) using methods demonstrated to inactivate poliovirus, or synthesized RNA/cDNA (e.g., cDNA clone, synthetic transcript). Poliovirus nucleic acid can be handled outside poliovirus containment under the condition that these materials will not be introduced into polio-permissive cells or animals (as defined in GAPIV and the “Guidance for non-poliovirus facilities to minimize risk of sample collections potentially infectious for polioviruses”) with or without transfection reagent; except under appropriate containment conditions as described in the Annex 1.

Poliovirus, Sabin (OPV/Sabin strains): Attenuated poliovirus strains (approved for use in oral polio vaccines by national regulatory authorities, principally Sabin strains).

Poliovirus, OPV-like: For the laboratory network not involved in manufacture, isolates consistent with a limited period of virus excretion or person-to-person transmission, demonstrating less than 1% difference from parent OPV strains for poliovirus types 1 and 3, and less than 0.6% difference from the type 2 parent OPV strain by full Viral Protein 1 sequence homology. The phenotype of clinical and environmental OPV-like isolates need not be determined as the great majority are assumed to be of low virulence.

Sabin materials may be (a) infectious or (b) potentially infectious. The attenuated phenotype of viruses resulting from manufacture based on the OPV/Sabin seeds must be assured and cannot rely on the lack of sequence drift alone.

(a) **Poliovirus infectious materials, OPV/Sabin:** These include:

- cell culture isolates and reference OPV/Sabin strains;
- seed stocks and live virus materials from OPV production;
- environmental sewage or water samples that have tested positive for the presence of OPV/Sabin strains;
- faecal or respiratory secretion samples from recent OPV recipients;
- infected animals or samples from such animals, including poliovirus receptor transgenic mice;
- derivatives produced in the laboratory that have capsid sequences from OPV/Sabin strains;
- full-length RNA or cDNA of viruses proven to be safer than Sabin strains, but that include OPV/Sabin poliovirus capsid sequences. The safety of these full-length RNA or cDNA and their containment requirements will be assessed by an expert panel convened by WHO, on the basis of comparison to reference Sabin strains for (i) degree and stability of attenuation; (ii) potential for person-to-person transmission; and (iii) neurovirulence in animal models;
- cells persistently infected with poliovirus strains whose capsid sequences are derived from OPV/Sabin strains.

(b) **Poliovirus potentially infectious materials, OPV/Sabin:** These include:

- faecal 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;
- environmental samples (i.e., concentrated sewage, wastewater) collected from areas known or suspected to have circulating OPV/Sabin at the time of collection.

PVSRIPPO: Neuro-attenuated recombinant poliovirus; live attenuated Sabin serotype 1 poliovirus with heterologous internal ribosomal entry site (IRES) of human rhinovirus type 2.

Regional Certification Commission (RCC): The term commonly used to refer to the 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 the GCC that eradication has been achieved throughout all Member States of their region.

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

Reproductive rate (R_0): A measure of the transmissibility of a pathogen that captures community vulnerability and virus characteristics, calculated as the number of secondary infections caused by a single index case in an entirely susceptible population.

Risk: A combination of the probability of the occurrence of harm and the severity of that harm.

Risk assessment: A systematic process involving a team of personnel who have the knowledge, training and competence to identify, assess, control, and evaluate risks.

S19: A hyperattenuated, genetically stable poliovirus type 2 strain.

Safeguards, Facility: Containment precautions and stipulations designed to minimize the facility-associated poliovirus risks of exposing and/or infecting populations.

Safeguards, Immunization Coverage: The population immunization coverage consistent with minimizing the consequence of a poliovirus release from a poliovirus-essential containment facility.

Safeguards, Environmental: The environmental, sanitation and hygiene conditions (good personal, domestic, and environmental hygiene standards; closed sewage systems with secondary or greater effluent treatment; low population density in surrounding areas) that minimize the risk of re-establishing the circulation of highly transmissible wild poliovirus in the event of reintroduction.

Senior Manager (SM): The official representative of an institution with overall authority and accountability for ensuring the biosafety management of the facility.

Sharps: Devices used in a facility that can cut and/or puncture skin (e.g., needles, scissors, glass).

Standard: A document that provides requirements, specifications, guidelines, or characteristics that can be used consistently to ensure that materials, products, processes, and services are fit for their purpose.

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

Top management: Person or group of people who directs and controls an organization at the highest level.

Validation: Confirmation, through the provision of objective evidence, that the requirements for a specific intended use or application have been fulfilled.

Verification: Confirmation, through the provision of objective evidence, that specified requirements have been fulfilled.

- WHO verification of compliance with this standard may be requested for certified poliovirus-essential facilities [1].

Virus-like particles (VLPs): Self-assembling multiprotein structures that resemble viruses but contain no genetic material and are therefore non-replicative and non-infectious. VLP-based poliovirus vaccines have been proposed as potential safe next-generation vaccines, as their production avoids the need for growing large quantities of infectious virus.

Introduction

Launched in 1988, the Global Polio Eradication Initiative (GPEI) is the largest international public health effort ever undertaken, involving billions of United States (US) dollars donated through GPEI partners, the dedicated efforts of governments at all levels, countless hours of volunteer services, and the immunization of billions of children with oral polio vaccine (OPV). The requirements and guidance on poliovirus containment outlined in GAPIV have been developed to ensure that this monumental achievement in global health is not undermined by an incident in a laboratory that handles poliovirus prior to and/or post-eradication.

Global Eradication Status

The *Polio Eradication Strategy 2022-2026: Delivering on a Promise* set the goal of a polio-free world by 2026 [2]. Achieving this goal requires: (i) permanently interrupting all poliovirus transmission in endemic countries; and (ii) stopping circulating vaccine derived poliovirus (cVDPV) transmission and preventing outbreaks of cVDPV in polio-free regions.

The Global Commission for the Certification of Poliomyelitis Eradication (GCC) declared wild poliovirus type 2 (WPV2) eradicated in 2015 and type 3 (WPV3) eradicated in 2019. World-wide WPV type 1 (WPV1) cases have dropped considerably, and international spread of WPV has not been detected since 2014. Despite these achievements, the continuing circulation of WPV1 and outbreaks of cVDPV present significant obstacles to overcome before total eradication can be reached.

The first step towards eliminating cVDPV occurred in 2016 when 155 OPV-using countries successfully switched from using trivalent OPV (tOPV) to bivalent OPV (bOPV for types 1 & 3) as a part of their immunization programs. The switch, combined with delays in IPV availability, led to a decline in immunity to poliovirus type 2. As a result, outbreaks of cVDPV2 have occurred in at-risk regions across the globe, with cVDPV2 cases tripling between 2019 and 2020. Currently, cVDPV2 presents as great a public health threat as the ongoing circulation of WPV1 in endemic countries. Outbreaks of cVDPV1 and cVDPV3 remain low, and their instance can be traced to poor OPV coverage.

To better respond to ongoing and future cVDPV2 outbreaks, novel OPV type 2 (nOPV2) was developed as a more genetically stable version of monovalent OPV type 2 (mOPV2). Clinical trials of nOPV2 show that it provides comparable safety and immunogenicity to mOPV2 against poliovirus while being significantly less likely to seed new cVDPV2 outbreaks [3-5]. In November 2020, WHO's Prequalification program issued an Emergency Use Listing (EUL) recommendation for nOPV2 to enable its rapid availability for responding to cVDPV2 outbreaks [6]. The Strategic Advisory Group of Experts (SAGE) on Immunization has further endorsed, in principle, that nOPV2 become the vaccine of choice in response to cVDPV2 outbreaks after a review of the initial use period for the vaccine's safety, immunogenicity, and genetic stability is complete [7]. Additionally, based on available safety data, the Containment Advisory Group (CAG) granted an interim exception for nOPV2 to be manufactured and used outside of GAPIII containment conditions, although it is currently still subject to the requirements outlined in the second edition of the *Guidance to Minimize Risk for Facilities Collecting, Handling or Storing Materials Potentially Infectious for Poliovirus* (the Potentially Infectious Materials Guidance, or "PIM Guidance"), including inventory reporting [8-10].

Currently, bOPV is the vaccine of choice to respond to any WPV1 and WPV3 outbreaks, while mOPV2 or nOPV2 is the choice for responding to type 2 outbreaks. Clinical trials for nOPV for types 1 and 3 (nOPV1 and nOPV3) are expected to begin in 2021, but there is currently no plan to replace bOPV in routine immunization programmes [11]. After OPV cessation, a combination of type-specific mOPV/nOPV and IPV will be used to respond to any WPV or vaccine-derived poliovirus (VDPV) outbreak.

Achieving global consensus to stop using bOPV will require international assurance that the transmission of wild and vaccine-derived poliovirus has been interrupted, affordable, safe and effective inactivated polio vaccines (IPVs) are available, potential outbreaks from undetected or newly emerged cVDPV can be controlled, and the risk from facility-associated reintroduction of wild or OPV/Sabin polioviruses can be minimized.

Purpose of GAPIV

After certification of eradication and OPV cessation, facilities that store and/or work with poliovirus or poliovirus potentially infectious materials (PIM) represent the most significant threat to maintaining global eradication. This document describes the safe handling requirements for facilities that intend to retain WPV and/or OPV/Sabin materials. This edition of the Global Action Plan (GAP) aligns the safe handling and containment of poliovirus infectious and potentially infectious materials with the Polio Eradication Strategy 2022-2026 and replaces the 2014 third edition (GAPIII). This document should be used in conjunction with the *Containment Certification Scheme to support the WHO Global Action Plan for Poliovirus Containment (CCS)*; *Auditor Qualification and Audit Support Plan*; *Guidance to minimize risks for facilities collecting, handling or storing materials potentially infectious for polioviruses (PIM Guidance) – 2nd edition*; and *Reports of the Meetings of the CAG*.

While GAPIV addresses the requirements for facilities that intend to continue storing and/or working with poliovirus infectious materials, inventorying, destroying, and/or containing PIM is also critical for maintaining containment. PIM can include historical sample collections from areas where circulating WPV/VPV was occurring, samples from facilities that research enteric viruses and use poliovirus-permissive cell lines, and/or any samples, products, or isolates that may contain poliovirus in addition to their main purported use. Detailed guidance on the requirements regarding PIM identification, inventory, and handling can be found in the second edition of the PIM Guidance.

The GAP is an evolving document, subject to revisions as new information emerges relevant to achieving the appropriate balance between community risk and the systems and controls to manage that risk. The poliovirus “Biorisk Management Standard” provides the framework for facility certification based on the principles of a biorisk management system. This standard requires the institution/facility to understand the risks associated with its activities and to manage those risks in ways acceptable to the national and international bodies responsible for the oversight of poliovirus containment. As such, risk assessment and control are a critical component for adequate application of this standard; additional guidance on biological risk assessment can be found in the WHO Laboratory Biosafety Manual 4th Edition Monograph: Risk Assessment [12]. Ultimately, national authorities are responsible for ensuring the application of these risk management standards and principles in local circumstances and ensuring they are adequately applied.

Summary of Changes

Developments in polio eradication strategy, risk characterization, and vaccine technology have necessitated the revision of the third iteration of the WHO Global Action Plan and its annexes, published in 2015. Extensive efforts were undertaken to solicit feedback on GAPIII from a range of global poliovirus containment stakeholders and subject matter experts. The newly revised GAPIV incorporates updated guidance documents, clarifies the basis of facility requirements, and emphasizes utilizing risk-based approaches for risk control that can be applied across the range of PEFs, which vary by location, size, and purpose. Significant changes were made to both the structure and the contents of the standard, including the following:

- The organization has been restructured for clarity and concision: Annex 2 and 3 of GAPIII have been combined into a single annex that designates strain-specific requirements, as needed; Annex 4 was superseded by the CCS and so has been removed; Annex 5 was removed in favour of reference to the LBM4; and Annex 6 was superseded by the PIM Guidance, 2nd edition and so has been removed.
- Within the revised Annex 1 of GAPIV, the management system elements have been reorganized and collapsed from sixteen to fourteen total elements.
- The entire standard has been amended in accordance with all decisions and recommendations made by the CAG since the publication of GAPIII, including guidance for non-dedicated laboratories and containment requirements for novel poliovirus strains.
- Guidance referencing CWA 15793 has been further aligned and harmonized with current containment requirements outlined in other international risk management documents.
- In accordance with the shift to a risk-based approach, prescriptive titre and vaccination requirements have been replaced with risk-based language.
- Exit shower requirements have been replaced with performance-based language that more generally applies to the range of PEFs.
- To improve understanding and implementation, primary, secondary and tertiary safeguards have been reclassified as facility, immunization coverage, and environmental safeguards.
- The requirement that PEFs must be located in areas with closed sewage systems with secondary or greater treatment of effluents has been removed, but facility locations must maximize the use of environmental features that reduce risk of onward transmission with approval by their national authorities.
- Language on gaseous decontamination, backflow prevention, and HEPA filtration of exhaust has been modified.
- Guidance on inactivation and validation techniques as well as equipment decontamination has been bolstered.
- Requirements for BSC certification and labelling stored materials have been added, though volume of poliovirus materials need not be maintained in the inventory documentation.
- Facility specific requirements have been expanded to include considerations for retrofitting existing spaces.
- Language defining the containment perimeter, organizational responsibilities, animal care, storage conditions, and non-dedicated spaces has been updated.
- Emergency planning has been expanded to encourage the involvement of external agencies, implement surveillance following an incident, and report public health events the IHR 2005 framework.

New material has also been added to GAPIV. The activities of key poliovirus stakeholders are outlined to clarify their roles and interdependencies with other bodies for containment activities. Additional requirements describing primary containment needs as well as additional specific mitigation measures applicable to all PEFs, such as the requirement of a hands-free hand washing sink and updated BSC certification requirements, have been included. The phased implementation of containment as described in GAPIII has been replaced by the inventory/destruction and containment requirements. All strains, WPV and Sabin, are subject to the described inventory and destruction requirements. Containment requirements are determined by strain, and the implementation of containment requirements is determined by WHO on an individual basis to allow for adaptability to the

- 1 current status of eradication. The overarching strategy of risk elimination wherever possible and
- 2 appropriate biorisk management where elimination is not possible is retained.
- 3
- 4 These revisions make GAPIV better suited to minimize the poliovirus facility-associated risk with
- 5 PEFs, a critical element towards ensuring the safety of PEFs and global public health following
- 6 eradication.
- 7

Rationale

When WPV circulation is interrupted, interest in immunization against polio is expected to decline as the cost of immunization may no longer be justified by its public health benefit. As a result, population susceptibility will increase in many parts of the world. When the use of OPV stops, some countries will maintain high population coverage with IPV, other countries will have suboptimal IPV coverage, and still others may discontinue all national polio immunization activities. Given this decline in immunization activities, any facility-associated reintroduction of poliovirus risks re-establishing poliovirus transmission and undermining one of the most stunning achievements in global health in the last 50 years: polio eradication [13].

Given these substantial risks, all regions should seek both to minimize the number of poliovirus-essential facilities and to destroy all infectious and potentially infectious poliovirus materials unless facilities must perform critical functions. Most countries will have no need to retain live polioviruses after eradication because polio will pose a lesser threat to public health. Those that forgo retaining poliovirus materials are helping the global community achieve and safeguard eradication. Facility-associated risks in these countries can be eliminated by a thorough nationwide search for and destruction of all infectious and potentially infectious poliovirus materials.

Some countries will host a limited number of PEFs that serve critical functions in global health, including Salk-IPV and Sabin-IPV production, production and storage of mOPV stockpiles, vaccine quality assurance, diagnostic reagent production, virus diagnostic and reference functions, and crucial research, as determined by the respective NAC or other designated national authority.. Given the risk of reintroduction from these facilities, any facility that will retain poliovirus for any reason post-eradication must adhere to the biorisk management principles outlined in this document to ensure that one careless mistake does not undermine decades of effort in global health.

The progression of poliovirus eradication and containment is a dynamic process that continues to face numerous challenges as the world moves towards becoming polio-free. Despite these challenges, immense progress has been made and continues to be made in advancing the Polio Eradication Strategy 2022-2026 [2]. National authorities and facilities should not slow, postpone, or halt containment and destruction efforts—inventory, destruction, containment, and certification can and should occur in advance of eradication for all strains of polio whenever and wherever possible. Not only does a continued focus on containment help ensure the globe is ready to transition to a post-eradication world when the time comes, pre-eradication containment may also prevent facility-associated releases that could delay and undermine eradication.

Facilities that continue to retain live poliovirus material must ensure that the risks of accidental exposure and release are extremely low and develop appropriate mechanisms to recognize and adequately deal with such incidents. These conditions can be met by developing and implementing a robust biorisk management system based on the requirements outlined in Annex 1. This system should adopt a risk-based approach to assessing PEFs that considers the specific facility, location, and work being performed, ensuring that controls put in place are both appropriate and effective. This adaptive approach to risk control allows for the application of appropriate safeguards, and, by incorporating site-specific considerations, decreases the risk of exposure or release. Independent review of the risks and benefits of retaining live poliovirus material should occur at the national level based on international guidelines, and countries should favour destruction of poliovirus materials wherever possible.

Destroying unnecessary poliovirus materials, minimizing the number of PEFs, and implementing strong biorisk management programs at PEFs are each critical steps to ensuring global containment standards can be met and successfully maintained. Ensuring eradication requires that all countries, with national, regional, and international oversight, commit to these critical efforts.

Roles and Activities

To achieve global polio eradication and sustain a polio-free world, collaboration is key among global, regional, national, and subnational levels. Stakeholder groups must fully understand their roles in the global polio partnership so that they may fulfil their independent duties and coordinate key activities. This section outlines the activities expected of each containment stakeholder group for minimizing poliovirus facility-associated risks; Figure 1 shows the interdependencies between stakeholders for activities reliant on multiple groups. This content will serve as a guide but not an exhaustive list of responsibilities for compliance with GAPIV. Governance and the designation of specific activities will vary among countries, and so, the roles defined herein are generalized to be compatible with all existing national frameworks.

Poliovirus-Essential Facility (PEF)

A poliovirus-essential facility (PEF) is designated as serving critical national or international functions that involve the handling and storage of needed poliovirus materials post-eradication under conditions set out in this GAP.

To fulfil their role in the safe handling and containment of poliovirus materials, designated PEFs shall:

- Establish, implement, and maintain a biorisk management system aligned with the requirements set forth in Annex 1.
- Handle and store all poliovirus materials according to the provisions of this document.
- Achieve and maintain containment certification and operate within the terms of the certificate throughout the certification cycle.
- Provide relevant parties, including the National Authority for Containment (NAC), audit team members, and the GCC with access to all information and physical spaces relevant to containment certification activities.
- Undergo annual reassessment against the GAPIV implementation provisions, including facility, immunization coverage and environmental safeguards, by the respective NAC.
- Report any event, process change, or other issue that could jeopardize the status of a certificate under the Containment Certification Scheme (CCS) to the NAC and other relevant parties.
- Consider accepting poliovirus material from facilities that are not designated as PEFs.
- Notify and consult the National Poliovirus Containment Coordinator (NPCC) before initiating any intra- or inter-country transfer.
- Coordinate with the NAC and appropriate public health entities to establish a facility-specific emergency response plan for responding to a potential poliovirus exposure, release or outbreak.
- Declare poliovirus infectious materials, including nOPV and new attenuated strains (e.g., S19), and potentially infectious materials to the NPCC in the national poliovirus survey and maintain an accurate inventory of holdings in their possession.

Non-Poliovirus-Essential Facility

A non-poliovirus-essential facility is a facility that may investigate new PV cases or samples from countries that have recently used OPV but has not been designated as serving critical national or international functions that involve the handling and storage of needed poliovirus materials post-eradication.

To fulfil their role in the safe handling and containment of poliovirus materials, these facilities shall:

- Implement the PIM Guidance and a non-retention policy.
- Declare poliovirus infectious materials, including nOPV and new attenuated strains (e.g., S19), and potentially infectious materials to the NPCC in the national poliovirus survey and maintain an accurate inventory of holdings in their possession.
- Destroy, inactivate or transfer poliovirus materials to a PEF.

National Authority for Containment (NAC)

For countries hosting one or more poliovirus-essential facilities, the role of the National Authority for Containment (NAC) is ensuring the requirements established in this document are effectively implemented and maintained in such facilities.

To fulfil this role, NACs shall:

- Determine the critical national or international functions that justify the retention of poliovirus or potentially infectious materials post-eradication.
- Designate the facilities serving these critical functions that involve the handling and storage of needed poliovirus materials and solicit their formal engagement in the CCS.
- Ensure that the required facility, immunization coverage, and environmental safeguards are met and demonstrated in applications for containment certification.
- Establish national mechanisms, including a regular inspection and audit programme aligned with the CCS, to ensure PEFs are appropriately assessed and comply with GAPIV requirements.
- Ensure effective procedures are established and maintained to address relevant aspects of the containment certification cycle and to verify that internal processes function appropriately within the NAC, per the CCS.
- Review and process applications for containment certification in consultation with the GCC, ensuring only designated facilities serving critical functions enter the containment certification process.
- Issue, suspend or revoke certificates of containment, in consultation with the GCC.
- Submit issues requiring technical guidance to the CAG for consideration. NACs are encouraged to coordinate with PEFs and submit issues to the CAG on behalf of PEFs.
- Communicate with the NPCC as they oversee transfer between facilities.
- Coordinate with the Ministry of Health (MoH) and the PEFs to establish a national emergency response plan(s) for responding to a potential poliovirus exposure, release, or outbreak.
- Facilitate the consultation between all pertinent ministries (e.g., health, education, defence, environment, etc.) to weigh the risks and benefits of retaining poliovirus in-country and the responsibilities inherent in complying with the crucial facility, immunization coverage, and environmental safeguards.

Ministry of Health (MoH)

The role of the Ministry of Health for countries retaining poliovirus materials and potentially infectious materials is to support progress towards global polio eradication and provide all relevant country-specific information to the WHO.

To fulfil their role in support of containment, the MoH in-country shall:

- Nominate the country's NAC.
- Encourage the destruction of poliovirus materials not supporting critical functions.
- Continually reassess the necessity for retention of poliovirus or potentially infectious material.
- Request non-poliovirus-essential facilities that will investigate new PV cases or samples from countries recently using OPV implement the PIM guidance and a non-retention policy.
- Provide relevant documentation on poliovirus containment, immunization coverage, surveillance, risk assessment, outbreak preparedness, and eradication status annually to the NCC.
- Establish a national emergency response plan(s) in coordination with the NAC for responding to a potential poliovirus exposure, release, or outbreak, which specifies actions and assign responsibilities for the facility, the institution, and local public health entities and provide this plan to the NCC for review.
- Assess any potential public health emergency of international concern (PHEIC) involving polioviruses and report qualifying events to the WHO within 24 hours, per the International Health Regulations (IHR) 2005 framework [14].

Containment Advisory Group (CAG)

The Containment Advisory Group (CAG) acts as an advisory body to the Director-General of the WHO and makes recommendations on technical issues related to poliovirus containment after evaluating the available scientific evidence and risk assessments.

To fulfil this role, the CAG shall:

- Provide recommendations to the WHO Director-General on technical issues arising from implementation of GAPIV.
- Issue guidance on the handling of poliovirus-related materials, new strains, and new processes for diagnosis, research, vaccine production and production-associated quality.
- Provide guidance on the identification and categorization of poliovirus potentially infectious materials, their destruction, or handling and storage.
- Provide guidance on the identification of acceptable alternative containment solutions in the interim period before full eradication.

National Poliovirus Containment Coordinator (NPCC)

The role of the National Poliovirus Containment Coordinator (NPCC), also referred to as the National Task Force for Containment (NTFC), is to facilitate all survey activities to ensure completeness of the national inventory.

To fulfil their role in support of containment, the NPCCs/NTFC shall:

- Collate the list of facilities across all sectors that may handle or store biomedical material and therefore could possess samples containing poliovirus.
- Facilitate a survey of the abovementioned facilities and analyse the data to identify all facilities that may retain poliovirus and potentially infectious materials, thereby ensuring the completeness of the national inventory.
- Review and update the inventory of facilities in the country that hold poliovirus or potentially infectious materials and the holdings in their possession annually.
- Submit an annual report on poliovirus containment progress, including an update on the national inventory, to the NCC.
- Provide guidance to stakeholders on the materials considered to be infectious and potentially infectious and their safe storage, handling, and disposition.
- Supervise the process of transfer and destruction of poliovirus materials and ensure appropriate documentation.
- Confer with the relevant NPCCs and Regional Certification Commissions (RCCs) before approving any intra- or inter-country transfer between facilities.
- Notify the NAC before approving any transfer between facilities.

National Certification Committee for the Eradication of Poliomyelitis (NCC)

The role of the National Certification Committee for Poliomyelitis Eradication (NCC) is to collect and validate information demonstrating progress towards poliovirus eradication within their country.

To fulfil their role in support of containment, the NCCs shall:

- Compile annual reports and supporting documentation to assess country-level progress on poliovirus containment, population immunization coverage, surveillance, risk assessment, outbreak preparedness, and eradication status, where applicable.
- Submit the national report and supporting documentation, including an update on the national inventory of facilities that handle and store poliovirus or potentially infectious materials, to the RCC on an annual basis.
- Coordinate with the NAC and MoH on the implementation of RCC recommendations for risk control measures necessary to achieve containment goals within their country.
- Review and approve the national emergency response plan(s) for a potential poliovirus exposure, release, or outbreak.
- Assess the fulfilment of polio eradication certification requirements in their country, as defined by the RCC.

Regional Certification Commission for the Eradication of Poliomyelitis (RCC)

The role of the Regional Commissions for the Certification of the Eradication of Poliomyelitis (RCC) is to independently guide progress towards eradication and, ultimately, certify eradication to the GCC for all Member States of their region.

To fulfil this role in support of containment, the RCCs shall:

- Evaluate national reports and supporting documentation annually to assess regional progress on poliovirus containment, population immunization coverage, surveillance, risk assessment, outbreak preparedness, and eradication status, where applicable.
- Submit annual reports to the GCC and bring unresolved issues to their attention.
- Recommend risk control measures necessary to achieve containment goals within their region to the respective NCCs.
- Consult with the relevant NPCCs and respective RCCs on inter-country transfer between facilities.
- Assess the fulfilment of polio eradication certification requirements in their region, as defined by the GCC.

Global Commission for the Certification of the Eradication of Poliomyelitis (GCC)

The role of the Global Commission for the Certification of the Eradication of Poliomyelitis (GCC) is to define the parameters and processes by which polio eradication will be certified, receive and review reports of the regional commissions, review and set global containment requirements, and certify when global polio eradication has been achieved.

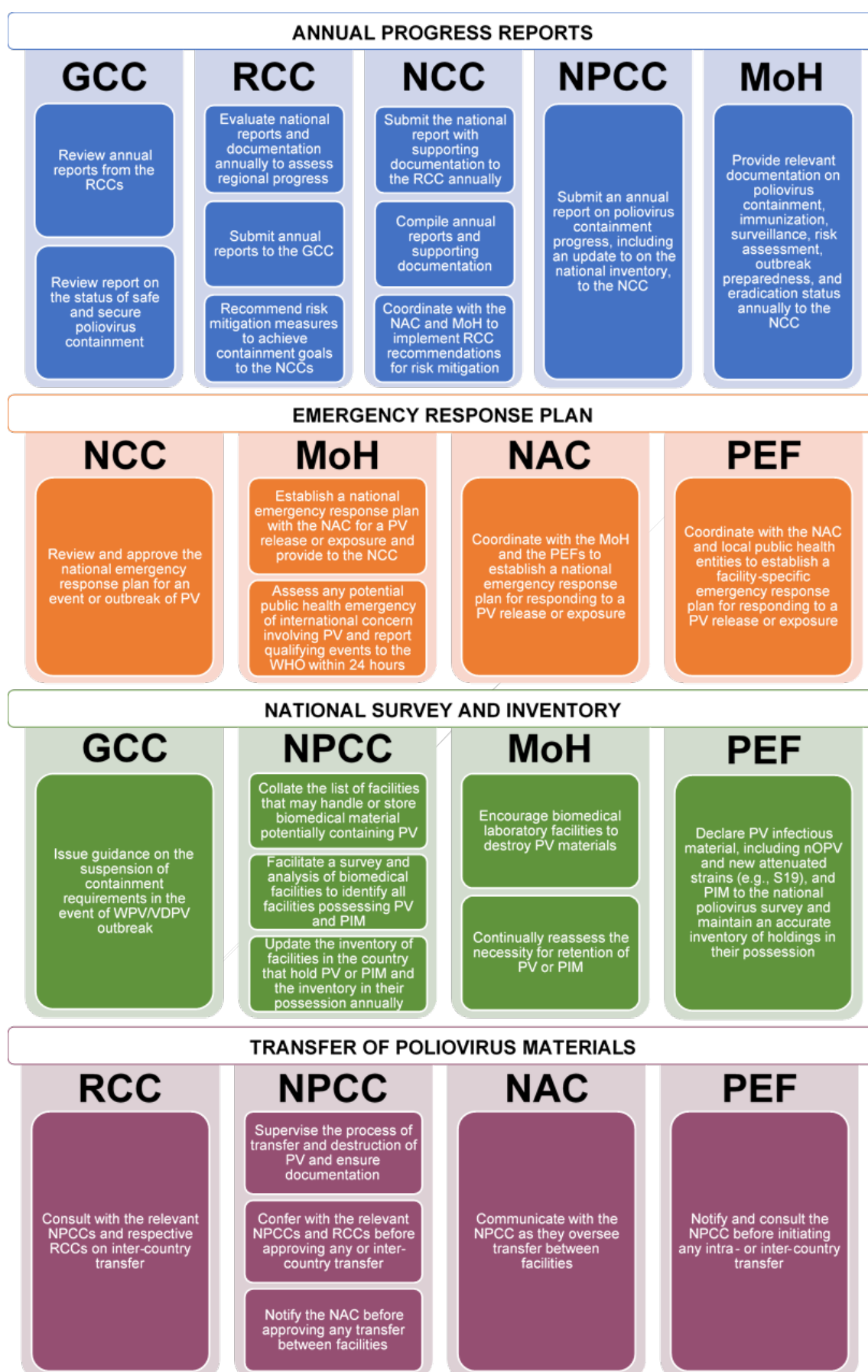
To fulfil this role, the GCC shall:

- Endorse facility containment certification following GCC-Containment Working Group (CWG) recommendations as part of the CCS.
- Receive and review the following information sources for certification of eradication as outlined in the Polio Eradication Strategy 2022-2026:
 - o annual reports from the RCCs, with particular consideration of poliovirus containment, population immunization coverage, surveillance, risk assessment, outbreak preparedness, and eradication status updates; and
 - o a report on the status of safe and secure poliovirus containment from the CWG.
- Review annual progress towards global containment for all PV strains and, when appropriate, update the containment requirement status as described in this standard.
- Issue guidance on the suspension of containment requirements for a given poliovirus strain in the event of WPV/VPV circulation.
- Confirm the global containment of polioviruses is met.

The Containment Working Group (CWG), under the GCC, reviews national containment certification activities and makes recommendations to the GCC. Its role is to provide the required level of assurance that the controls established in this document are appropriately identified, implemented, and monitored.

The GCC-CWG shall:

- Review audits and reports from the NACs on the national containment certification activities of PEFs.
- Make recommendations for the approval of facility certification to the GCC as part of the CCS.
- Report on the global status of safe and secure poliovirus containment to the GCC.

1 **Figure 1. Stakeholder Roles in Activities with Interdependencies**

Strategy

Risk Elimination in Poliovirus-non-essential Facilities

Risk elimination in non-poliovirus-essential facilities starts with the identification of:

1. infectious and potentially infectious WPV materials;
2. infectious and potentially infectious OPV/Sabin materials, as described below.

Once these materials are identified, risk is controlled if these materials are destroyed or transferred to a PEF. PEFs will minimize the amount of poliovirus samples they retain and destroy any poliovirus samples that are no longer needed to eliminate the risk that these samples present.

Destruction applies to all materials potentially containing any type or strain of WPV or OPV/Sabin poliovirus, particularly untested virus stocks in (a) facilities that previously worked with polioviruses [15] or (b) in non-polio facilities retaining clinical materials potentially infected with polio or OPV/Sabin viruses. Poliovirus PIM exists in non-poliovirus facilities worldwide, including clinical facilities, repositories, enteric disease research facilities, and a variety of other locations. Successful identification and destruction or containment of PIM is critical to ensuring that the risk of facility-associated infection or release is minimized. The PIM Guidance outlines the steps required for identifying PIM. To control risk of a facility-associated infection or release, PIM should be destroyed whenever possible, and the use of PIM substituted with other non-poliovirus materials. Facilities handling PIM must meet the requirements outlined in the PIM guidance.

Successful global risk control requires each country to robustly prohibit retention and subsequent acquisition of poliovirus materials in all non-poliovirus-essential facilities according to global recommendations [2].

Risk Control and Biorisk Management in Poliovirus-essential Facilities

A robust biorisk management system is critical for maintaining containment in facilities that store and/or work with polioviruses. A loss of containment at a PEF can lead to a local outbreak of poliovirus, which could then threaten global eradication. The primary way to prevent such a scenario is effective biorisk management at PEFs, which minimizes the likelihood of a loss of containment and quickly recognizes one if it occurs. If a loss of containment does occur, immunization coverage and environmental safeguards mitigate the likelihood of re-establishing poliovirus transmission in a region, which would threaten eradication.

Biorisk management in designated PEFs (Annex 1) is achieved through the implementation of international biorisk management standards that:

1. include polio-specific containment requirements to reduce the likelihood of release of polioviruses from poliovirus-essential facilities (facility safeguards);
2. describe requirements for population immunization coverage to safeguard against re-establishing community spread in the event of a release of polioviruses from poliovirus-essential facilities (immunization coverage safeguards);
3. describe requirements for environmental control measures to minimize the likelihood of community exposures in the event of a release from poliovirus-essential facilities (environmental safeguards);

A sustainable biorisk management system will utilize control strategies that are commensurate with the facility-associated risks, including both the degree of risk and the specific risks generated by the work undertaken. The risk assessment process is clearly described for all stakeholders and utilizes the strategies for risk reduction in choosing suitable control measures [16]. Controls implemented must consider local conditions to ensure their efficacy. A variety of controls measures may be utilized, but the expected outcome is clearly defined and standardized according to the requirements outlined in this document. Risks and threats, including security risks, vary across the regions of the world and must be assessed based on local circumstances. The local risk assessment will include population immunization status to evaluate vulnerability to loss of containment incidents and threat analysis to assess biosecurity risks, among many other factors [12].

Facility safeguards for containment reduce the likelihood of accidental or intentional poliovirus release from a poliovirus-essential facility and are specified in the *Biorisk Management Standard for Poliovirus-essential Facilities Holding Wild and/or OPV/Sabin Poliovirus Materials* (Annex 1). Key elements include:

- Management at the facility who practise continuous risk assessment and strict observance of biosafety and laboratory biosecurity procedures.
- The containment facility, which incorporates appropriate design, construction, and operation principles, thereby addressing identified biorisk.
- A worker health programme, which can reduce the risk of infection in the facility and intra- or extra-household transmission should infection occur [17, 18].
- Contingency plans for potential virus release or exposure, which specify actions in alignment with the “Public health management of facility related exposure to live poliovirus guidance” [19].

Immunization coverage safeguards minimize the consequences of a poliovirus release into the community from a poliovirus-essential facility retaining WPV and/or Sabin/OPV and consist of:

- Implementing a routine immunization schedule with a minimum of two IPV doses (IPV2; full or fractional, standalone, or in combination vaccines), with the first dose administered at four months and the second dose administered at least four months after the first dose [20].
- Maintaining high immunization coverage with $\geq 90\%$ IPV2 coverage in infants in the area surrounding the PEF and maintaining the Global Vaccine Action Plan target coverage in that area [21].
 - The geographic size of the area surrounding the PEF that must be covered by these vaccination data will be determined through risk assessment by the respective NAC. Immunization coverage can be presented as multinational, national, or subnational data, as appropriate for the geographic area and demonstrated in the application for containment certification.
 - Prior to all OPV cessation, immunization coverage data can be presented as $\geq 90\%$ coverage of IPV2 or diphtheria–tetanus–pertussis vaccine third dose (DTP3) to meet this criterion. After all OPV cessation, only IPV2 coverage will be accepted to meet this criterion.
- Have an outbreak plan specifying response to containment breach and conduct outbreak simulation exercises.

Environmental safeguards will maximize the use of environmental features that reduce risk of onward transmission (e.g., areas with closed sewage systems with a minimum of secondary treatment of effluents, with low population density, with demonstrated low faecal-oral disease transmission). In coordination with the NAC, additional environmental safeguards can be implemented (e.g., frequent environmental testing for poliovirus to detect silent outbreaks in vaccinated communities).

Facility, immunization coverage and environmental safeguards are required for poliovirus-essential facilities that handle and store either WPV or OPV/Sabin, with additional community safeguards required for PEFs that handle WPV specifically (Table 1). Additional safeguards are required for WPV because the potential for spread is much greater for WPV than for Sabin/OPV strains. The nature of these safeguards are determined by the PEF in coordination with the NAC based on the site-specific risk assessment and be outlined in the facility’s application for certification under the CCS. Wherever possible, PEFs should destroy poliovirus samples that no longer need to be retained and substitute Sabin/OPV or other non-infectious strains for wild poliovirus strains. These actions reduce the risk for infection at the community level if a breach of containment occurs and minimize the consequences of such a breach if transmission was recognized in time [18].

National certification and regular annual recertification thereafter are required for all poliovirus-essential facilities. Compliance with GAPIV may be requested on a regular (triennial) basis. National certification provides assurance that the required safeguards are met.

1 **Table 1. Facility, Immunization Coverage, and Environmental Safeguards**

	Poliovirus-Essential Facility Holding:	
	OPV/Sabin	WPV/VPV
Facility Safeguards		
Operator protection	Yes	Yes
Decontamination of materials/equipment	Yes	Yes
Dedicated effluent treatment plant	No ¹	Yes ¹
Air/exhaust treatment	No	Yes
Immunization Coverage Safeguards		
IPV2 coverage pre-OPV cessation	= DTP3 coverage or ≥90%	= DTP3 coverage or ≥90%
IPV2 coverage post-OPV cessation	≥90%	≥90%
Environmental Safeguards		
Environmental controls in place to minimize onward transmission risk	Yes	Yes
Additional environmental safeguards determined by risk assessment	No	Yes, in coordination with the NAC

¹All waste from facilities potentially containing live poliovirus will be inactivated prior to release through adequate and validated inactivation procedures. In facilities without a dedicated effluent treatment plant, in most cases an effluent decontamination system, this would normally be achieved by applying heat or chemicals as part of a validated treatment process. Under no circumstances should raw poliovirus containing effluents be discharged to drains, unless the effluent treatment plant has been designed and validated to handle such effluents, effectively acting as part of the primary containment system.

9 **Containment Requirements for Novel Poliovirus Strains**

11 The CAG provides recommendations on the risks posed by novel strains of poliovirus, which includes
 12 recommendations for the evaluation of improved safety of these strains to determine the containment
 13 requirements for their storage and handling. Several specific poliovirus strains have been identified as
 14 presenting a lower risk profile than WPV and OPV/Sabin. The handling of these strains outside the
 15 containment requirements of this standard may be permitted either temporarily or completely on the
 16 CAG's recommendation, but they are still subject to national inventory requirements and the PIM
 17 Guidance. The CAG's assessment of these strains—including nOPV, S19, and PVSRIPO—and their
 18 containment requirements can be found on the GPEI website.

21 Entities may submit to CAG requests for review of specific strains for additional exemptions. On the
 22 recommendation of the CAG, the criteria for the evaluation of improved safety of novel poliovirus
 23 strains to determine containment requirements for their storage and handling will include but are not
 24 limited to the following:

A. Novel poliovirus strain properties

1. Genetic stability to loss of attenuation – conditions
 - a. Theoretical
 - b. Cell culture (e.g., serial passage)
 - c. Animal studies (e.g., single, multiple passage)
 - d. Characterization (phenotype, genotype)

2. Neurovirulence – degree of attenuation
 - a. Theoretical
 - b. Cell culture
 - c. Animal studies
 - i. TgPVR mice
 - ii. Non-human primates
3. Replicative fitness – proxy for infectiousness
 - a. Cell culture yield (single cycle; infectivity measure)
 - b. Animal studies (e.g., shedding)
4. Transmissibility – a proxy of which is 'duration and amount of shedding'
5. * Data from human studies (if available) should be included when performing the risk assessments of such strains.

B. Proposed use of the novel poliovirus strain

1. The impact of proposed use of these novel and related poliovirus strains on the containment requirements must be considered - any risk assessment of novel poliovirus strains must include an assessment of the risk associated with the intended use of the strains.

Inventory, Destruction, and Containment

The previous iteration of the Global Action Plan outlined a progression of containment in line with WPV2-specific eradication as it was projected to develop. Since that time, WPV3 has also been declared eradicated by the GCC, another landmark achievement in the progression towards global eradication. However, the emergence of multiple cVDPV2 outbreaks worldwide after tOPV withdrawal has greatly complicated the envisioned progression towards type-specific containment. Outbreaks of cVDPV2 that necessitate the use of mOPV2 for supplementary immunization activities (SIAs) generate new poliovirus type 2 infectious and potentially infectious materials in samples collected from these regions. This dynamic nature of eradication demands a similarly flexible and adaptable approach to containment progression.

This Global Action Plan comprises two main lines of effort that should be progressing concurrently:

- **Inventory and destruction** of poliovirus infectious and potentially infectious materials
- **Containment** of poliovirus infectious and potentially infectious materials that are not destroyed

Inventory and destruction are dynamic and ongoing processes that apply to all regions for all strains and types. Facilities are encouraged to destroy any identified poliovirus infectious or potentially infectious materials whenever possible to minimize potential sources of facility-associated reintroduction. Containment applies to all nations that wish to retain poliovirus and/or poliovirus materials as eradication progresses. Individual countries that choose to retain poliovirus materials are encouraged to institute national containment policies in line with the containment requirements for all poliovirus materials in advance of final eradication and containment whenever possible. A proactive approach to containment will ensure that the risk of facility-associated exposure post-eradication is minimized.

Due to the dynamic nature of eradication, containment requirements for a given strain may be temporarily suspended by the GCC in specific regions where a decision by WHO has been made to use mOPV to respond to emerging or re-emerging WPV/cVDPV transmission. A regional suspension of containment requirements does not represent a suspension of containment requirements worldwide.

The components of these lines of effort and details about how they apply to the poliovirus containment effort are outlined in Table 2 below.

1 **Table 2. Inventory, Destruction and Containment**

	Component	Applicable Facilities	Timeline	Justification	Applicable Materials
Inventory and Destruction	Continuous Assessment and Validation	Applies to all locations where PV materials and/or PIM may be found	Ongoing effort for all facilities nationwide	Ensures that no PV infectious material or PIM is unaccounted for	All PV infectious materials and PIM
Containment	Establish Authorities	Countries that wish to house PEFs	Before 'Verification' can begin for countries housing PEFs	Ensure that national authorities and containment certification procedures are in place	Any contained PV infectious material and/or identified PIM to be stored, worked with, or otherwise manipulated
	Verification and Final Containment	Applies to PEFs and/or facilities that wish to become PEFs	As containment efforts progress for a given PV strain ¹	Ensures that PEFs institute appropriate ongoing safeguards for containment of PV material and/or PIM	Contained strains of PV infectious materials and/or PIM ¹
	mOPV Stockpiles	Countries/authorities that will maintain mOPV strategic stockpiles	Ongoing effort if strategic stockpiles are maintained	Ensures rapid deployment of mOPV in the event of a re-release while also ensuring adequate containment provisions for the stockpile	All contained mOPV strain vaccines manufactured and stored to support SIAs

2

¹ GPEI Website Link to Containment Status Table

Inventory and Destruction

The efforts undertaken to ensure Inventory and Destruction are Continuous Assessment and Validation. An important aspect of Continuous Assessment is the national inventory of biomedical facilities that may possess infectious or potentially infectious poliovirus materials and the survey of those materials, including nOPV, S19 and other relevant strains. Maintaining this inventory is an ongoing effort for all regions and all strains. It is also a dynamic process; facilities can and should be added and/or removed from the inventories as they obtain, transfer, and destroy samples. A successful national inventory is maintained through effective communication and outreach to all biomedical facilities in the country, proactive identification of facilities that may house poliovirus, and the regular survey of potentially affected facilities. National authorities are encouraged to verify inventories of PIM and poliovirus infectious materials to ensure inventory reports are complete and accurate.

Both maintaining the national facility inventory and providing annual updates to each country's RCC are the responsibility of the relevant national authority (most commonly the NCC). Due to the changing nature of eradication efforts, including active VDPV outbreaks, the maintenance of national inventories will continue until after global eradication, at which time the GCC may approve changes to the national inventory process.

The Validation component of Inventory and Destruction involves assessment of facilities' compliance with national poliovirus policies and regulations, including validating the status of poliovirus materials and timelines for compliance. Destruction of unneeded poliovirus infectious and potentially infectious materials will be emphasized by the relevant national authority for all facilities identified in the national inventory, and, as eradication progresses, the need for retention of these materials will be continually assessed. The national biomedical community must be notified that as global eradication is achieved, possession of poliovirus materials of any strain will only be permitted at certified PEFs.

A summary of the requirements for Continuous Assessment and Validation are outlined below and in Table 3.

Continuous Assessment

Countries shall:

- Generate, update, and maintain a national inventory of facilities that possess WPV/VDPV and/or OPV/Sabin infectious or potentially infectious materials and other novel poliovirus strains on a continuous basis.
- Provide annual updates to the RCC of the national inventory of facilities that possess WPV/VDPV and/or OPV/Sabin infectious or potentially infectious materials and other novel poliovirus strains.
- Establish national contingency and emergency response plans for responding to a potential WPV/VDPV and/or OPV/Sabin exposure, release, or outbreak.
- Request that all facilities destroy any unneeded WPV/VDPV and/or OPV/Sabin infectious or potentially infectious materials and other novel poliovirus strains and continually reassess the necessity for retention of such materials.

Validation

Countries shall:

- Request that all facilities adopt the requirements outlined in the PIM Guidance.
- Request that facilities on the national inventory submit plans for compliance with the CCS.
- Request that all facilities that are likely to investigate new suspected poliovirus cases or receive faecal or respiratory samples from recent OPV-using countries adopt:
 - o Safe and secure working practices as outlined in the PIM Guidance.
 - o A policy to destroy or transfer to a PEF all identified poliovirus infectious and potentially infectious materials.
- Notify the national biomedical community that retention of infectious WPV, WPV PIM, and/or OPV/Sabin infectious materials will only be permitted at certified PEFs and retention of Sabin PIM will only be permitted at facilities that comply with the requirements outlined in the PIM Guidance.

Table 3. Continuous Assessment and Validation

Effort	Requirements
Continuous Assessment	Generate, update, and maintain a national inventory of poliovirus possessing facilities
	Provide annual updates to the RCC of the national inventory
	Establish national contingency and emergency response plans for PV release
	Request facilities destroy all unneeded PV and/or PIM
Validation	Request all facilities adopt the PIM Guidance
	Request all facilities with PV and/or PIM submit compliance action plans, including the status of possessed materials
	Notify the national biomedical community that retention of PV materials will only be allowed at PEFs or in compliance with the PIM guidance
	Request that all non-poliovirus-essential facilities investigating new PV cases or samples from recent OPV countries adopt: - safe practices outlined in the PIM guidance, and - a destruction/transfer policy for all PV/PIM samples

Containment

The specific components of the Containment line of effort include Establishing Authorities, Verification, Final Containment, and use of mOPV Stockpiles. Each country that wishes to retain poliovirus infectious and/or potentially infectious materials post-eradication must house such materials within a PEF and is required to designate a NAC to oversee containment efforts in the country. Verification and Final Containment requirements are tied to global eradication, with more stringent requirements enacted as eradication efforts progress. The requirements for mOPV storage arise from the containment requirements for each respective strain with more stringent requirements enacted as eradication efforts progress.

To allow for a transition period in which countries can complete containment efforts prior to their enforcement, the status of Verification and Final Containment for each strain can be classified as 'in transition' or 'in full effect.' When a stage is in transition, countries are in the process of enacting the requirements of that stage, whereas when a stage is in full effect, the country has enacted and is actively enforcing all requirements of that stage. In anticipation of eradication, individual countries are encouraged to enact the Final Containment requirements before they are deemed to be in full effect. This will allow countries to shift to post-eradication containment requirements easily when the time comes, and pre-eradication containment may also prevent facility-associated releases that could delay and undermine the progress of eradication. Containment Verification procedures are now in transition for all strains in all regions at this time.

As these response efforts are ongoing, the current status of containment requirements for each applicable strain of poliovirus can be found on the GPEI website.³ Though WPV types 2 and 3 have been declared eradicated, the world currently faces unprecedented challenges with the emergence of cVDPV outbreaks and ongoing WPV1 circulation in endemic countries. These new outbreaks unexpectedly complicated the envisioned progression of containment and did not fit into the previous, rigid framework. To allow for flexibility in enacting containment requirements in the face of challenges moving forward, verification requirements have been classed as in-transition to enable affected countries to adequately respond to the situation on the ground. This enables countries who have been and are still responding to active outbreaks to collect samples, manufacture and distribute OPV, and continue to respond to their current public health emergencies without having to operate outside of the requirements of this standard.

The progression of containment stages is a decision that will be made by the GCC upon receiving annual reports from the RCC of each region that may include the regional status of the sustained level of immunization, surveillance, poliovirus containment, and risk assessment. The GCC will determine the standing status of the Verification and Final Containment efforts on an annual basis, either

³ GPEI Website Link to Containment Status Table

affirming the current status is unchanged or advancing the containment status from 'not in effect' to 'in transition,' or from 'in transition' to 'in full effect' as needed for each type and/or strain. This system enables flexibility in determining the requirements for containment to reflect the dynamic nature of eradication. Moreover, this system will allow for containment requirements to be considered 'in transition' for a period determined by the GCC as necessary for regions to meet containment requirements in a reasonable timeframe. As different regions will progress towards eradication and final containment at different rates, countries are encouraged to enact containment requirements in advance of the GCC status determination whenever possible.

Containment requirements for a given strain will not be reversed but may be temporarily suspended in specific regions where a decision by WHO has been made to use mOPV to respond to emerging or re-emerging WPV/cVDPV outbreaks. A regional suspension of containment requirements does not represent a suspension of containment requirements worldwide.

A summary of the requirements for Establishment, Verification, Final Containment, and mOPV Stockpiles are listed below and in Table 4.

EXAMPLE STATUS TABLE NOT FINAL IMAGE

Current Containment Status*

Strain	Containment			
	Establishment	Verification	Final Containment	mOPV Stockpiles
WPV1	a	y		
WPV2	a	y	y	
WPV3	a	y	y	
OPV/Sabin1	a	y		y
OPV/Sabin2	a	y		y
OPV/Sabin3	a	y		y

*a = as needed, y = in-transition, x = in full effect

Establishment

Countries that wish to retain poliovirus infectious or potentially infectious materials post-eradication must:

- Weigh the risks and benefits of retaining poliovirus in-country and the responsibilities inherent in complying with the crucial facility, immunization coverage, and environmental safeguards.
- Designate a NAC that will certify PEFs against the requirements of this standard as outlined in the *Containment Certification Scheme to support the WHO Global Action Plan for Poliovirus Containment*.
- NACs must establish national certification procedures compliant with the requirements for WPV and/or OPV/Sabin retention as outlined in this standard.

Verification

Countries that wish to house PEFs and retain poliovirus infectious or potentially infectious material outside of the requirements defined in the PIM Guidance after the declaration of eradication of VDPV of a given strain and type must:

- Require candidate PEFs assess their compliance with the required facility, immunization coverage, and environmental safeguards described in the Biorisk Management section of this standard and submit to their NAC documentation of this compliance.
- Prohibit the retention of all poliovirus infectious or potentially infectious materials subject to this requirement in any facility that is not a PEF.
- Require that all facilities that are unable to meet the retention requirements for WPV and/or OPV/Sabin either destroy their poliovirus materials or transfer them to PEFs.

- Implement national certification procedures compliant with the requirements for WPV and/or OPV/Sabin retention.
- Reassess certified PEFs against the requirements for WPV and/or OPV/Sabin retention annually.
- Require that all non-PEFs destroy or transfer to a PEF any unneeded poliovirus infectious or potentially infectious materials subject to this requirement.
- Request that all non-poliovirus-essential facilities that will investigate new suspected poliovirus cases or receive faecal or respiratory samples from recent OPV-using countries adopt:
 - o Safe and secure working practices as outlined in the PIM Guidance.
 - o A policy to destroy or transfer to a PEF all identified poliovirus infectious and potentially infectious materials.

Countries and/or facilities may apply through their national authorities for WHO verification of PEFs, certified by the MoH or another designated national authority, and declared to meet all biorisk management criteria consistent with the Biorisk Management Standard outlined in this document.

Final Containment

Countries that wish to house PEFs and retain poliovirus infectious or potentially infectious material after the worldwide withdrawal of OPV vaccination must meet the following requirements, as endorsed by SAGE:

- Implement annual national certification procedures compliant with the requirements for OPV/Sabin and/or WPV Final Containment retention requirements as outlined in the Biorisk Management Standard of this document.
- Reassess certified PEFs against the Final Containment requirements for WPV and/or OPV/Sabin retention annually.
- Prohibit the handling and storage of WPV and/or OPV/Sabin outside of PEFs.
- Require all non-poliovirus-essential facilities that will investigate new suspected poliovirus cases or receive faecal or respiratory samples from recent OPV-using countries adopt both:
 - o Safe and secure working practices as outlined in the PIM Guidance.
 - o A non-retention policy for all poliovirus infectious and potentially infectious materials.
- Recall and either destroy or contain at a certified PEF all OPV stocks nationwide.

Countries and/or facilities may apply through their national authorities for WHO verification of PEFs, certified by the MoH or another designated national authority, and declared to meet all biorisk management criteria consistent with the Biorisk Management Standard outlined in this document.

mOPV Stockpiles

- Storage of OPV stockpiles (frozen bulk and finished product) and the replenishment of OPV stockpiles must be performed under the required containment provisions applied to the respective strain as outlined in this document.
- Any OPV that cannot be stored under appropriate containment conditions must be recalled and destroyed in accordance with international requirements.

1 **Table 4. Containment Requirements**

	Requirements	
Establishment	Designate a NAC that will certify PEFs.	Request that all PNEFs investigating new PV cases or samples from recent OPV countries adopt: (1) safe practices outlined in the PIM guidance; and (2) a destruction/transfer policy for all PV/PIM samples
	Establish national certification procedures.	
Verification	Require PEFs submit immunization coverage, and environmental safeguard documentation to NAC.	
	Prohibit retention of PV materials at non-poliovirus-essential facilities. All PV material must be destroyed or transferred to a PEF.	
	Implement national certification procedures for PEFs.	
	Reassess PEFs annually for compliance with standards.	
Final Containment	Implement national certification procedures for PEFs compliant with Final Containment requirements.	
	Reassess PEFs annually for compliance with Final Containment standards.	
	Prohibit retention of PV materials at non-poliovirus-essential facilities. All PV material must be destroyed or transferred to a PEF.	
	Recall and destruction or containment of all OPV stocks nationwide.	
mOPV Stockpiles	Storage and replenishment of OPV stockpiles only allowed at PEFs.	
	Any OPV that cannot be stored under appropriate containment conditions must be recalled and destroyed.	

2

Annex 1

Biorisk Management Standard for Poliovirus-essential Facilities Holding Wild and/or OPV/Sabin Poliovirus Materials

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1 Introduction

2
3 During the Endgame Strategy period, following eradication and cessation of oral polio vaccine (OPV)
4 use, an infection or environmental release of poliovirus associated with an incident at a polio facility
5 would be a public health event of international proportions, threatening to undo decades of gains in
6 global health and the hard work of millions. The *Global Action Plan* addresses the risk of accidental
7 infection and release of poliovirus by establishing a post-eradication/post-OPV cessation goal of
8 retaining poliovirus in a limited number of poliovirus-essential facilities (PEFs) worldwide.
9 Implementation of the *Global Action Plan* further reduces the risk of accidents in these facilities by
10 establishing international standards for facility, immunization coverage, and environmental
11 safeguards. These safeguards are bolstered via assurance through national and international
12 oversight that such standards are met.

13
14 The safeguards required for poliovirus facilities are determined by the nature of the facility and the
15 stage of global and local eradication as summarized in the Strategy section and Table 1 above.

16
17 This *Biorisk Management Standard for Poliovirus-essential Facilities Holding Wild and/or OPV/Sabin*
18 *Poliovirus Materials* describes the international requirements for the facility safeguards established for
19 two groups of poliovirus-essential facilities (PEFs): (1) laboratories handling and/or storing WPV
20 materials or Salk-inactivated polio vaccine (IPV) production facilities, and (2) laboratories handling
21 and/or storing OPV/Sabin poliovirus materials or Sabin-IPV production facilities. This standard builds
22 on the principles contained within ISO35001: *Biorisk management for laboratories and other related*
23 *organisations* [24], the principles of the WHO *Laboratory Biosafety Manual, Fourth Edition* [16] and
24 the extensive poliovirus scientific literature spanning nearly seven decades.

25
26 Using the above documents, this standard emphasizes a risk-based approach to containing poliovirus
27 that can be applied globally despite the variability among PEFs. This standard relies upon local risk
28 assessments, as the responsibility of the PEF and the NAC, to determine appropriate risk control and
29 management techniques to meet the overarching goal of containment.

30
31 This standard serves as the framework for national certification and WHO verification that certified
32 poliovirus-essential facilities comply with GAPIV (*Containment Certification Scheme to support the*
33 *WHO Global Action Plan for Poliovirus Containment – GAP-CCS*) [25], consisting of 14 elements and
34 sub-elements based on the principles of a quality management system. This standard assumes that
35 the organization best understands the risks associated with its work and can manage those risks in
36 ways acceptable to the national and international bodies responsible for facility oversight. This
37 standard further assumes that poliovirus-essential facility personnel and management at all levels fully
38 appreciate the enormity of the consequences of accidental or deliberate poliovirus release in the post
39 eradication/post OPV era and are prepared to demonstrate that the appropriate systems and controls
40 are fully implemented to manage those risks.

Poliovirus Facility-associated Risks

Ingestion is the natural route of transmission for poliovirus and presents the highest risk for facility personnel as this may occur via contact with contaminated fomites, splash to the oral mucosa or by inhalation of large droplets, some of which will deposit in the pharyngeal region. Immunization with OPV or IPV prevents disease, but immunization neither fully inhibits asymptomatic poliovirus infection nor prevents reinfection of the gut. Estimated infectious doses (ID₅₀) by ingestion, based on studies with infants and children, are $\pm 10^1$ CCID₅₀ for wild polioviruses and $\pm 10^3$ CCID₅₀ for Sabin strains. Immunized adult laboratory workers are likely more resistant than immunologically naïve children, but resistance is dose related and may be overcome by larger ingested doses. Droplets created by sprays, spills and the splash of poliovirus cell cultures (up to 10^8 CCID₅₀) and concentrates (10^{11} CCID₅₀) constitute one of the highest personnel exposure risks (Figure A2.1) [26].

While biosafety measures continue to evolve and improve, workplace acquired infections still occur. Several literature reviews and surveys of workplace acquired infections and exposures (laboratory, clinical and vaccine manufacturing settings) found the most commonly identified routes of exposure to infectious agents in the facility environment are parenteral inoculation, spills and splashes to the skin or mucous membranes, ingestion, and animal bites or scratches. These incidents comprise approximately 20% of clearly attributable causes of exposure [27-31].

While the respiratory tract does not appear to be a significant portal of entry for poliovirus, whether small particle aerosols deposited in the lower airways may be cleared to the pharyngeal region through mucociliary transport and infect the alimentary tract is an unresolved question. Antibodies acquired through immunization greatly reduce infection risks from injection or breaks in skin or mucous membranes. Identified instances of documented workplace acquired infections and exposures have concluded that up to 80% of exposures may occur via the aerosol route [27-31].

Polioviruses under moist conditions in clinical or environmental samples can survive indefinitely in the laboratory freezer (<-20 °C), for many months in the refrigerator and for weeks on the bench top at ambient temperatures [18]. The virus is inactivated by dehydration, heat (>50 °C) or treatment with dilute solutions of formaldehyde or bleach at appropriate concentrations. In the poliovirus facility, poliovirus content of common materials ranges from a mean of $10^{3.7}$ CCID₅₀/g (Sabin) to $10^{4.3}$ CCID₅₀/g (wild) in stool samples, to 10^8 CCID₅₀/ml in cell culture harvests, and 10^{11} CCID₅₀/ml in concentrates in vaccine production facilities [26]. Sabin strains are less pathogenic than wild and have lower secondary infection rates, but all three Sabin virus types have been linked to vaccine-derived poliovirus (VDPV) outbreaks.

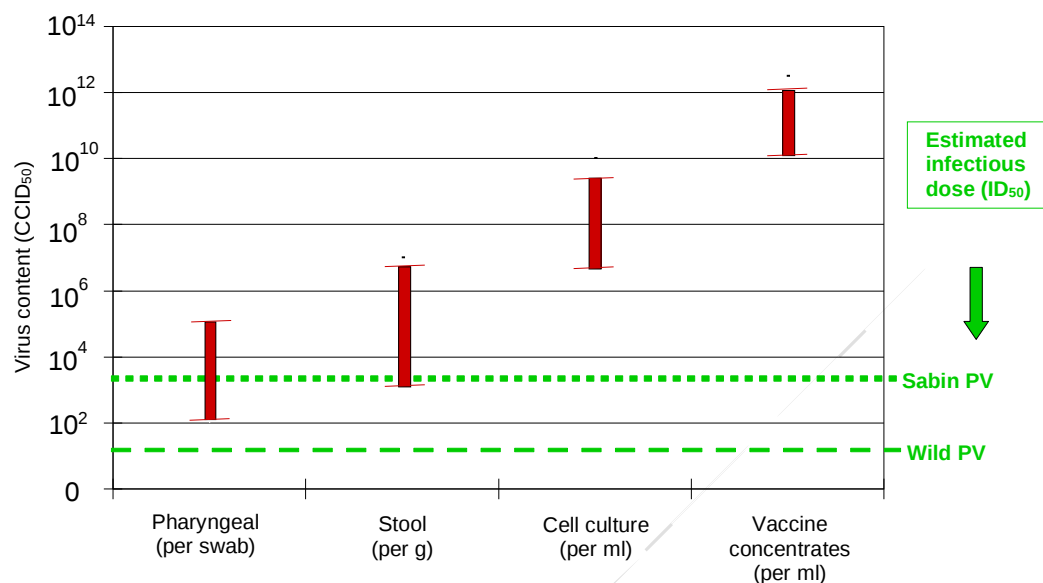
Peer-reviewed research has examined facility-associated release of poliovirus and poliovirus workplace acquired infection and incidents and underscores the need for heightened biosafety and biosecurity practices, comprehensive risk assessment and control strategies, appropriate facility design and operations and emergency plans [32, 33]. Community members may be exposed to infectious agents from the laboratory through:

- workers' contaminated skin or clothing or unrecognized infection;
- the release of contaminated air;
- contaminated effluents and wastewater recovered from secondary sewage treatment plants;
- the uncontrolled transport of infectious material;
- solid waste transported to landfills;
- contaminated equipment or materials removed from the facility;
- the escape of infected animals; and
- a theft or deliberate release of infectious agents from a facility.

Exposure risks through the last four routes are low for poliovirus facilities that adhere to international regulations for the transport of infectious substances, those outlined in the *Good Laboratory Practice* handbook and the WHO guidelines on *Good Manufacturing Practice*. Risks are also likely low for the inhalation of contaminated air effluent where facilities maintain low relative humidity environments and exhaust air away from direct human exposure. Exposure risks through the ingestion of effluents range between high and low, depending on the poliovirus content of facility effluent, sewerage system size and integrity, and the potential for human consumption. Risks of community exposure are highest through facility personnel unknowingly contaminated or infected with poliovirus.

Effective poliovirus risk management is achieved by the careful assessment of exposure risks, the implementation of risk-appropriate worker protection measures, administrative, and environmental controls as well as the operation of a facility designed to minimize the risk of poliovirus contamination and dissemination to the community. The main risk is the infection of laboratory workers by ingestion. Infection through inhalation is a conceivable risk pathway but has not been demonstrated and infection through parenteral exposure such as needlestick is unlikely in immunized individuals.

Figure A2.1: Estimated poliovirus content and infectious dose⁴



⁴ Estimated infectious doses (ID₅₀) are based on studies with naive infants and children. Immunized adult laboratory workers are likely to be much more resistant than immunologically naive children. However, dose-related resistance may be overcome by ingesting sufficient poliovirus particles.

Organization of Management System Elements

The content of this Biorisk Management Standard outlines the requirements for facilities that handle or store wild and/or OPV/Sabin poliovirus and potentially infectious materials as outlined in the *Global Action Plan*. It is organized into 14 elements and their sub-elements as enumerated in the element introductions. Throughout, guidance on meeting the requirements of this standard is incorporated into the sections for which the guidance is most relevant.

All requirements are listed in the body of the text, with guidance relating to the requirement provided in boxes following the requirement. Where applicable, national legislation supersedes the requirements set forth in this standard. All guidance is made available to inform facilities about the ways in which requirements can be met, and the guidance should not itself be considered a requirement. That is, facilities will not be assessed against the implementation of items listed in the guidance boxes.

The facility safeguard requirements outlined in this standard apply to facilities that handle or store WPV and/or OPV/Sabin materials, unless otherwise noted. Enhanced requirements that apply to WPV facilities only upon the global achievement of eradication and Final Containment are specifically noted under relevant sub-elements entitled '**WPV Final Containment Only**'; upon institution of Final Containment, these additional requirements supersede any others. Required immunization coverage and environmental safeguards that apply to these facilities and their implementation requirements are outlined in the 'Strategy' section of GAPIV above.

Additional resources for the National Authorities for Containment (NACs) and discussion regarding this standard can be found in the NAC group on the TechNet-21 Platform. Access will be granted to verified NAC members by contacting containment@who.int.

Element 1 – Biorisk Management System

The biorisk management system element describes a system (and associated policy) in place to manage laboratory biorisk. Commitment from all levels of management in an organization is vital to the success of the system. Top management must define clear objectives, from which roles and responsibilities are allocated, implemented and monitored. Without effective leadership and a structured system, all other initiatives for managing risk will be ineffective. More detailed guidance on the implementation of a biorisk management system can be found in the WHO Laboratory Biosafety Manual Fourth Edition Associated Monograph: Biosafety Programme Management [34].

Sub-elements

- 1.1. Biorisk Management System
- 1.2. Biorisk Management Policy
- 1.3. Objectives, Targets and Programme
- 1.4. Roles, Responsibilities and Authorities
- 1.5. Contractors and Suppliers
- 1.6. Records, Documents and Data Control
- 1.7. Analysis of Data
- 1.8. Programme of Work
- 1.9. Change Management
- 1.10. Consultation and Communication
- 1.11. Legal Requirements
- 1.12. Preventive Action
- 1.13. Inspection and Audit
- 1.14. Control of Nonconformities
- 1.15. Corrective Action
- 1.16. Continual Improvement
- 1.17. Biorisk Management Review

1.1 Biorisk Management System

- 1.1.1 The organization must establish, document, implement and maintain a biorisk management system according to the requirements of this polio biorisk management standard.

1.2 Biorisk Management Policy

- 1.2.1. The policy clearly states the overall biorisk management objective and a commitment to improving biorisk management performance.

Biorisk management should be a clearly stated, prominent part of the organization's health, safety, security and environment (HSE) policies. Depending on the relevance of biorisk management to the organization, the biorisk management policy should complement the general HSE policies. As appropriate, the biorisk management policy may be integrated into the organization's HSE policies.

- 1.2.2 Management demonstrates commitment to the policy concerning the management of laboratory biorisk (laboratory biosafety and laboratory biosecurity) including development of the organizational biorisk policies, authorization of resources to meet the requirements of the policies and signing of institutional biosafety policies.

The policy should require that all projects/work areas be assessed for risks and a full assessment be prepared before approval is given to commence work.

- 1.2.3 The policy is appropriate to the nature and scale of the risk associated with the facility and associated activities.

- 1.2.4 The policy commits to:

- 1. protecting staff, contractors, visitors, the community and the environment from poliovirus materials that are stored or handled within the facility;

2. reducing the risk of the unintentional release of, or exposure to, poliovirus materials to an acceptable level;
3. reducing the risk of the unauthorized intentional release of hazardous biological materials to an acceptable level;
4. complying with all legal requirements applicable to the poliovirus materials that will be handled or possessed and with the requirements of this standard;
5. ensuring that effective biorisk management takes precedence over all non-"health and safety" operational requirements;
6. effectively communicating individual obligations regarding biorisk to all personnel and relevant third parties;
7. continuously improving biorisk management performance;
8. conduct risk assessments and implement the required risk and evidence-based control measures.

1.3 Objectives, Targets and Programme

1.3.1. Objectives and targets for effective biorisk management throughout the organization are established, implemented and maintained

1.3.2. Management must establish the biorisk controls and enact documented procedures for monitoring the effectiveness of those controls to reduce or eliminate the risks identified in the risk assessment process.

Regular audits or other routine checks develop a proactive system for monitoring the effectiveness of biorisk controls by utilizing corrective-action reporting processes where problems have been identified, by ensuring adequate resources are provided to maintain the effectiveness of the controls, and by investigating incidents and accidents and subsequently improving controls and their implementation. Refer to Element 2 Risk Assessment.

1.4 Roles, Responsibilities and Authorities

1.4.1. Top management takes ultimate responsibility for the organization's biorisk management system.

Top management is the person or group of people who directs and controls an organization at the highest level. Top management includes officers (Director-General, Chief Executive Officer, Chief Operating Officer, Chief Financial Officer, etc.) and directors of the organization. Overall responsibility for managing biorisk rests with top management, but tasks may be delegated to senior management provided they are passed to individuals with adequate resources, skills and training to perform the activities safely and securely. In smaller organizations, one individual may hold more than one role described in this standard. It is important to define roles and responsibilities, have clear communication within the organization regarding actions that need to be taken, and establish who has the required authority.

1.4.2. Top management ensures that roles, responsibilities and authority related to biorisk management are defined, documented and communicated to those who manage, perform and verify work associated with the control of polioviruses.

In assigning roles and responsibilities, potential conflicts of interest should be considered. This standard has identified roles that should be assigned in the organization and uses titles only to illustrate examples of these roles; the titles in this standard may not be equivalent to those used in specific organizations.

1.4.3. Top management demonstrates its commitment by ensuring the availability of resources to establish, implement, maintain and improve the biorisk management system.

Resources include human resources and specialized skills, organizational infrastructure, technology and financial resources.

- 1.4.4. A senior manager is designated operational responsibility to oversee the biorisk management of the facility. An alternate is assigned should the senior manager be unable to fulfil their oversight role.

Senior managers are those with significant operational, budgetary and personnel authority at the departmental or higher level.

- 1.4.5. The designated senior manager is responsible for:
1. providing appropriate resources to ensure the adequate provision of personnel, facilities and other resources deemed necessary for the safe and secure operation of the facility;
 2. reporting to top management on the performance of the biorisk management system and any need for improvement;
 3. ensuring adoption and promotion of the biorisk management system throughout the organization;
 4. instituting review, audit and reporting measures to provide assurance that the requirements of this standard are being implemented and maintained effectively.

The designated senior manager should be an individual with decision-making authority at a level whereby they can allocate resources required to conduct risk assessments and other management and administrative activities. They should be positioned to make decisions regarding the biorisk management needs of the facility independent of the need to implement the programme of work.

- 1.4.6. A biorisk management committee is constituted to act as an independent review group for biorisk issues associated with the poliovirus facility.

The biorisk management committee may be a body dedicated to poliovirus risk management or may act as the institutional biosafety committee with a wider remit.

- 1.4.7 The biorisk management committee reports to the designated senior manager and:
1. has documented function and scope;
 2. includes a representative cross section of expertise, appropriate to the nature, scale, safety and security concerns of the activities undertaken;
 3. ensures issues addressed are formally recorded, and actions are allocated, tracked and closed out effectively;
 4. is chaired by a senior individual;
 5. meets at a defined and appropriate frequency, and when otherwise required.

Members of the biorisk management committee may include the scientific manager, additional scientific specialists, the biorisk management adviser(s), the security manager and the occupational health professional. Others, such as the facility manager, animal care supervisor, and/or worker and community representatives, may be included depending on the nature of the agenda or work. Whenever possible the committee should include members independent of the activities that are being reviewed.

The functions of the committee can include:

- a. contributing to the development of institutional biorisk policies and codes of practice;
- b. approving proposals for new work or significant modifications to the potential risk associated with existing activities;
- c. reviewing and approving protocols and risk assessments for work involving polioviruses;
- d. reviewing information related to significant accidents or incidents, data trends, associated local or organizational actions and communication needs.

The list of roles for the biorisk management committee is not exhaustive but includes several main areas that should be addressed.

- 1.4.8 One or more competent individuals are designated to provide advice and guidance on biorisk management issues.

The competent individual providing advice and guidance on biorisk management is often recognized as a biorisk management adviser, biological safety officer or biological safety adviser. This function should normally be regarded as an advisory position and not one directly responsible for managing biorisk, as that rests with those conducting and managing the work within the organization (e.g., the scientific director, principal investigator, department head, laboratory manager, group leader). The role and knowledge of the biorisk adviser are important to develop, implement, maintain and continually improve a biosafety and biosecurity programme. In the context of vaccine production facilities, the biorisk adviser should be knowledgeable in poliovirus vaccine production, current GMP and containment. The adviser should have adequate skills and training to perform the role and be allocated sufficient time and other resources to do the job effectively.

1.4.9 The role of the biorisk management adviser is independent of the functions of those responsible for implementing the programme of work.

In the execution of their biorisk management duties, advisers have direct access to the designated senior manager and top management when necessary.

1.4.10 The biorisk management adviser:

1. reports directly to the designated senior manager;
2. has delegated authority to stop work in the event that it is considered necessary to do so;
3. participates in laboratory biosafety and laboratory biosecurity risk assessments.

The functions of the biorisk management adviser may include:

- a. verifying, in conjunction with other relevant personnel, that all relevant biorisk considerations have been addressed;
- b. advising or participating in the reporting, investigation and follow-up of accidents/incidents and, where appropriate, referring these to management and/or the biorisk management committee;
- c. ensuring relevant and up-to-date information and advice on biorisk management are made available to scientific and other personnel as necessary;
- d. advising on biorisk management issues within the organization (e.g., management, biorisk management committee, occupational health department, security);
- e. contributing to the development and/or delivery of biorisk training activities;
- f. ensuring all relevant activities are performed in compliance with biorisk regulations, and the required biorisk authorizations for work are in place;

The list of roles for the biorisk management adviser is not exhaustive but includes several main areas that should be addressed.

1.4.11 One or more individuals responsible for the scientific programme within the facility are designated with responsibilities relevant to biorisk management.

The scientific manager should be responsible for managing the scientific programme within the facility on a day-to-day basis and for implementing and monitoring biorisk controls in association with other facility personnel (e.g., adhering to policies and procedures, monitoring staff performance and participation in inspections and audits). The individual may have an in-depth knowledge of the work programme and the facility, be in a supervisory/management position and may be referred to as Head of Department, Principal Investigator, Laboratory Supervisor/Manager or Group Leader. Competence is required in technical/scientific aspects of the poliovirus under their control and in the management of the facility, its personnel and systems. More than one individual may hold similar roles, but in such instances, the responsibilities should be clearly defined to avoid any omissions and ensure consistency.

1.4.12 The scientific manager is responsible for:

1. ensuring all work is conducted according to established policies and guidelines described in this standard;
2. supervising workers, including ensuring only trained, competent and authorized personnel can enter and work in the facility;

3. planning and conducting work activities, and ensuring adequate staffing levels, time, space and equipment are available;
4. ensuring required authorizations for work are in place;
5. ensuring laboratory biosafety and laboratory biosecurity risk assessments have been performed, reviewed and approved, and the required control measures are in place;
6. ensuring all at-risk personnel have been informed of risk assessments and/or provisions for any recommended precautionary medical practices (e.g., vaccinations or serum collections).

1.4.13 One or more individuals responsible for occupational health within the facility are designated with responsibilities relevant to biorisk management.

The occupational health professional should be a medical doctor or occupational health nurse with an understanding of the poliovirus materials handled within the facility. The role should include assessing and managing risk from a worker health perspective, advising on first aid/emergency treatment measures and liaising with first responders and external healthcare providers. They may also coordinate medical examinations, surveillance and vaccination programmes. The roles and responsibilities of the occupational health professional should be determined in accordance with the requirements established in this standard. See Element 3 Worker Health Programme and Element 13 Emergency Response and Contingency Planning.

1.4.14 The organization must establish an occupational health programme commensurate with the facility's activities and risks.

1.4.15 One or more facility managers are designated with responsibilities relevant to the facilities and equipment requirements established in this polio biorisk management standard.

The facility manager should be an engineer or a person with an in-depth knowledge of containment equipment, laboratory facilities and buildings. They should liaise with the biorisk management adviser to assess and manage risk from a facility perspective as well as coordinate maintenance, building work and contractors. The roles and responsibilities of the facility management personnel should be determined in accordance with the requirements established in this standard. More than one individual may hold similar roles, but in such instances, the responsibilities should be clearly defined to avoid any omissions and ensure consistency.

1.4.16 A security manager is designated with responsibilities conforming to the security requirements established in this polio biorisk management standard.

The security manager should have an in-depth knowledge of laboratory and facility security, liaise with other personnel (e.g., the biorisk management adviser) and implement effective and proportionate laboratory biosecurity measures based on the biological risk. The role should include participating in risk assessments and managing risk from a security perspective. The roles and responsibilities of the security personnel should be determined in accordance with the requirements established in this standard.

1.4.17 In laboratories where animals are kept, an animal-care manager is designated with animal-related responsibilities conforming to the requirements established in this polio biorisk management standard.

The animal-care manager should have an in-depth knowledge of animal handling, the risks associated with animal research and human pathogens associated with animal research. The animal-care manager should liaise with other personnel (e.g., biorisk management adviser, occupational health professional) to implement effective and proportionate laboratory biosafety and biosecurity measures. A qualified veterinarian should be available for additional advice. The role should include assessing and managing risk from an animal-care perspective.

1.5 Contractors and Suppliers

1.5.1. Purchases (including services) must conform to specified requirements. Controls on purchases (including services) are applied depending on the potential impact to the biorisk involved.

1.5.2. Suppliers are evaluated and selected based on their ability to provide products/services that meet the requirements of this polio biorisk management standard.

While not all suppliers will provide products/services that may have an impact on biorisk, many may. Suppliers that should be considered include, but are not limited to, those that provide:

- a. cleaning services;
- b. laboratory equipment;
- c. waste management or disposal services;
- d. information technology support services;
- e. equipment and facility maintenance or certification services;
- f. security services.

1.5.3. Criteria for selection, evaluation and re-evaluation of suppliers are established.

1.5.4. Records are maintained of evaluation results and any necessary actions arising from the evaluation.

1.6 Records, Documents and Data Control

1.6.1 Records, documents and data are established, controlled and maintained to provide evidence of conformity to the requirements of this polio biorisk management standard.

1.6.2 Records, documents and data are handled in such a way that they remain legible, readily identifiable and retrievable.

Documented records are maintained in paper or electronic form for a minimum of six years and are available for review during containment certification audits.

If not already in place, the collection and retention of records, documents and data must start immediately.

Controlled documents may include, but are not necessarily limited to:

- a. standard operating procedures (SOPs) and safety manuals;
- b. job hazard analyses and charts of authority;
- c. design records and commissioning/test plans, maintenance plans and records, and all associated data;
- d. audit and inspection checklists;
- e. laboratory biosecurity manuals, authorizations and other security documents;
- f. biosafety and security risk assessments;
- g. training records;
- h. incident reports and corrective actions;
- i. evaluations of suppliers;
- j. containment equipment certifications.

This list of controlled documents is not exhaustive but includes several main areas that should be formally recorded and subjected to document control. Electronic data, spreadsheets, databases, and other media in which information related to the above list are stored should be considered documents of the purpose of this requirement. A procedure should be established to define the controls needed for the identification, storage, protection, retrieval, retention period and disposal of records. A procedure should be established to define the controls needed for the approval of documents prior to their issue or public release, to ensure sensitive information, such as personnel medical records or the specific freezer locations of pathogen repositories, is not inadvertently released. Procedures should also be established to define the controls needed for the review, update and reapproval of documents, and for the control of change and revision process.

1.7 Analysis of Data

- 1.7.1 The suitability of the biorisk management system is assessed by identifying, collecting, and analysing appropriate data. This analysis is used to evaluate where continual improvement of the system can be made.

The analysis should include data generated by monitoring, measurement, audits, analysis and from other sources. Such analyses should be conducted at least annually, and more often if justified by the risks and scope of operations. The results of the analysis should be applied in the management review.

1.8 Programme of Work

- 1.8.1 The programme of work for the facility is defined, documented and reviewed.

The programme should include the nature of the activities authorized to be conducted in the facility and their definitions (e.g., diagnostics, research, small scale/large scale). All activities associated with the work programme should be specified and supported by formal SOPs approved in line with the requirements for controlled documents, as defined by this standard. Any changes to the programme of work should be subject to a formal change management process.

- 1.8.2 Work that requires prior approval is defined by established criteria.

Any change to the poliovirus programme of work or processes that affect biorisk are required to be reported to the NAC to maintain certification, as outlined in the Containment Certification Scheme to support the WHO Global Action Plan for Poliovirus Containment (GAP-CCS) [25].

1.9 Change Management

- 1.9.1 All changes associated with the design, operation and maintenance of the facility are subject to a defined and documented change management process.

These changes should be reviewed, verified and validated as appropriate, reviewed by the biorisk management committee and approved by top management before implementation. This should include an evaluation of the effect of the changes on the risk assessment.

Examples of changes that should be subject to the change management process include:

- a. modifications to buildings and equipment or their operation that may affect biorisk;*
- b. introduction of altered staffing arrangements (such as the temporary presence of on-site contractors or students, temporary reassignments of personnel);*
- c. changes to the programme of work, including changes to strains used, volume or workflow, should be evaluated based on impact to biorisk;*
- d. alterations to SOPs, including significant changes in materials or reagents;*
- e. modifications to entry/exit protocols;*
- f. modifications to personnel policies and visitor protocols;*
- g. modifications to disinfection, decontamination and other waste management methodologies;*
- h. changes associated with the provision and use of personal protective equipment (PPE).*

1.10 Consultation and Communication

- 1.10.1 Relevant biorisk information related to an organization's activities is communicated to and received from personnel and other relevant parties.

The organization should implement mechanisms to ensure relevant information that may affect personnel operations and/or safety is defined, documented and delivered effectively at appropriate intervals. Communication mechanisms could entail regular team meetings and briefings in the workplace, as well as formal training sessions. In addition to facility personnel, it may also be appropriate to engage others, including:

- a. local, national and international governmental organizations;*
- b. relevant regulatory agencies;*

- c. equipment and/or facility certifiers;
- d. emergency services and healthcare providers;
- e. contractors and suppliers (e.g., cleaners, maintenance providers, security personnel);
- f. local community representatives (e.g., through a community liaison committee).

Systems should be put in place to identify existing or emerging technologies and other information relevant to the containment of poliovirus materials. This information should be shared with relevant staff through appropriate media, including the posting of appropriate signage, circulation of documents, holding of team briefings and the maintenance of reference libraries.

1.10.2 Involvement of personnel in communication and consultation arrangements is documented.

1.10.3 Personnel have access to adequate and up-to-date information about the biorisks and biorisk management of the organization.

1.11 Legal Requirements

1.11.1 The organization ensures that all relevant legal requirements are identified and fulfilled within the biorisk management system. Legal requirements include national/federal, regional/state, provincial, city and local regulations with which the organization must comply. National legislation supersedes other regulations. If this standard differs from regulations or legislation, facilities must satisfy the more rigorous requirements, provided these standards are allowable under prevailing law.

The organization should adopt measures to identify the legal requirements for the poliovirus materials being held and used but also other regulations such as worker protection and rights, environmental impact, and general health and safety (e.g., fire, electrical). The organization should monitor for new and upcoming requirements, as well as those that already exist. This information should be kept up-to-date, and the requirements should be incorporated into the facility's biorisk management system.

1.12 Preventive Action

1.12.1 Action is taken to identify and eliminate the causes of potential nonconformities to prevent their occurrence.

A procedure should be established to:

- a. determine the potential nonconformities and their causes;
- b. evaluate the need for action to prevent the occurrence of nonconformities;
- c. determine and implement the action needed;
- d. record the results of action taken;
- e. review the preventive actions taken and their effectiveness through Key Performance indicators or other appropriate metrics.

1.12.2 Preventive actions must be commensurate to the effects of the potential nonconformities.

1.13 Inspection and Audit

1.13.1 An inspection and audit programme that is appropriate to the risk associated with the facility is conducted in alignment with the guidance provided in the GAP-CCS and AQAS plan [25, 35].

Inspections may be frequent checks of specific areas, conducted to ensure sufficient standards are being maintained (e.g., disinfectant levels/concentrations, air exchange rates/maintenance of directional air flow) or may be more extensive but less frequent inspections of laboratories, facilities or other operations. The frequency of inspections should be set as part of performance monitoring. Random, unannounced inspections and inventory audits can help ensure compliance at all times and not just in time for scheduled inspections. Audits should be performed by competent individuals unaffiliated with the audited activity. Records of inspection/audit findings should be maintained, including action taken to close out any nonconformities or pursue improvement opportunities.

1.13.2 Internal inspections and audits are conducted at planned intervals to determine if the biorisk management system conforms to the documented plans and the requirements of this Biorisk Management Standard and if it is effectively implemented and maintained.

An external audit programme is conducted regularly by the relevant national authorities to determine if the biorisk management system conforms to the requirements of this standard and is functioning properly and to ensure necessary corrective actions are taken and verified without undue delay.

Facilities that meet these requirements under their National Authority for Containment (NAC) in accordance with the GAP-CCS will be eligible for certification and endorsement by the Global Commission for the Certification of the Eradication of Poliomyelitis (GCC). The NAC issues, suspends or revokes certificates of containment, in consultation with the GCC.

Top management ensures that information relevant to the audit and certification process is made available in English to the GCC and the WHO secretariat to the GCC.

1.13.3 Management responsible for the area being inspected/audited ensures that any corrective actions are taken without undue delay to eliminate detected nonconformities and their causes.

1.13.4 Follow-up activities include verification of the actions taken and reporting of the verification results to top management.

1.14 Control of Nonconformities

1.14.1 Situations that do not conform to the requirements of the site-specific biorisk management policy are identified and controlled to prevent undesirable consequences.

The controls, authorities and related responsibilities needed to address nonconforming situations should be defined in a standard operating procedure.

1.14.2 Records of the nature of the nonconformity and any subsequent corrective action taken are maintained.

1.15 Corrective Action

1.15.1 To prevent the recurrence of any nonconformities, action is taken to develop a procedure that enables elimination of their causes using the requirements of this polio biorisk management standard.

A procedure should be established to define requirements to:

- a. review the nonconformities;*
- b. determine the root cause of nonconformities;*
- c. evaluate the need for action to ensure nonconformities do not recur;*
- d. determine the corrective action needed;*
- e. verify the action per a change management process, as described above;*
- f. implement the approved corrective action;*
- g. record and review the results of action taken.*

1.15.2 Corrective actions are in proportion to the effects of the nonconformities encountered. They are prioritized by the classification of the nonconformity as major (category 1) or minor (category 2), as described in the GAP-CCS [25].

The time frame for completion is detailed in the GAP-CCS [25], but nonconformities should be resolved in a manner that prevents future adverse outcomes by preventing the persistence or recurrence of the nonconformity.

1.16 Continual Improvement

1.16.1 The organization continually improves the effectiveness of the biorisk management system through:

- 1 the policy;
- 2 its objectives;
- 3 the internal audit programme;
- 4 audit results;
- 5 the analysis of available data;
- 6 risk assessments;
- 7 corrective and preventive actions;
- 8 management review.

The organization should strive to continue developing and refining the systems in place to ensure that further opportunities to improve the biorisk management system are identified and implemented, which may be achieved by setting objectives and giving targets to those working within the facility and by monitoring progress to ensure the objectives are achieved.

1.17 Biorisk Management Review

1.17.1 Management reviews the biorisk management system at planned intervals to ensure its continued suitability, adequacy and effectiveness.

The management review may be conducted by top or senior management and should be conducted regularly, at a frequency determined by the needs of the organization but at least annually. The biorisk management system should be reviewed against the requirements outlined in this standard, with deviations documented and corrective actions recorded.

1.17.2 The review includes assessing opportunities for improvement and determining the need for changes to the system, procedures, policies and objectives.

Review input should include information on:

- a. the results of audits;
- b. compliance with SOPs and work instructions;
- c. compliance with training programs and their effectiveness;
- d. meetings of the biorisk management committee;
- e. the status of risk assessment activities and control strategies;
- f. the status of preventive and corrective actions;
- g. follow-up actions from previous management reviews;
- h. changes that could affect the system;
- i. recommendations for improvement;
- j. the results of accident/incident investigations.

1.17.3 Records are maintained from the management review.

Review output should include decisions and actions related to:

- a. improvement of the effectiveness of the biorisk management system;
- b. improvement related to the requirements and risk assessments;
- c. justification for changes deemed necessary;
- d. resource needs
- e. performance indicators to confirm changes to the program are performing to the level required

Element 2 – Risk Assessment

Risk assessment and control is a critical element in developing and implementing a robust Biorisk Management System. Risk assessment is a systematic process involving a team of personnel who have the knowledge and competence to identify, assess, control, and evaluate risks. While risk in a poliovirus facility is driven by poliovirus, other infectious agents and laboratory risks should be identified and addressed in a holistic manner. The General Risks sub-element examines the processes in place to ensure hazards associated with the personnel's work in the facility are identified and managed while also addressing their implications to impact biorisk. Organizations should take both a preventive and proactive approach to establish measures to identify, detect, mitigate and respond to emergencies. Risk assessment is only a part of the entire Biorisk Management System and should be reviewed as a part of the system. More detailed guidance on general biological risk assessment can be found in the WHO Laboratory Biosafety Manual Fourth Edition Associated Monograph: Risk Assessment [36].

Sub-elements

- 2.1. General Risks
- 2.2. Process, Methodologies and Procedures
- 2.3. Assessment Timing and Scope
- 2.4. Roles and Responsibilities for Risk Assessment
- 2.5. Hazard Identification
- 2.6. Risk Evaluation and Control
- 2.7. Implementing Risk Control Measures
- 2.8. Monitoring Effectiveness

2.1 General Risks

- 2.1.1 A formal process is in place to identify and manage risk that may compromise general safety.

The organization should adopt a preventive and a proactive approach to managing such sources of risk, both to protect workers from the direct hazards associated with their work and to address the implications for biorisk in the event of an accident/incident resulting from such sources. Measures should be identified and implemented to prevent, detect, control and respond to emergencies, taking into consideration the potential implications for poliovirus control in such measures. Issues addressed should include but are not limited to:

- a. general laboratory risks;
- b. fire risks;
- c. electrical risks;
- d. radiation risks;
- e. chemical risks;
- f. the use of gases (including risk of asphyxiation);
- g. work with hot and cold sources;
- h. risks with pressurized equipment;
- i. laboratory animal care and use;
- j. health emergencies;
- k. general housekeeping, including storage requirements and tidiness, and risks with general waste.

2.2 Process, Methodologies and Procedures

- 2.2.1 The organization ensures that a risk assessment system is established, implemented and maintained.
- 2.2.2 The performance of the risk management system is reported to the designated senior manager for review. This review is used as a basis for improvement.
- 2.2.3 Relevant personnel within the organization identifies those operations and activities associated with risks, including possible biological risk and where control measures are to be applied.
- 2.2.4 Activities associated with possible biological risk, including maintenance, are carried out under conditions specified by the risk management system.

2.3. Assessment Timing and Scope

2.3.1 The approach to risk assessment is defined according to its scope, nature and timing to ensure it is proactive rather than reactive.

The following should trigger either a new risk assessment or the review of an existing one:

- a. commencement of new work or changes to the programme of work, including the introduction of new biological agents or alterations to workflow or volume;
- b. new construction/modifications to laboratories, plants and equipment or their operation;
- c. introduction of altered and unplanned staffing arrangements, including those concerning contractors, visitors and other noncore personnel;
- d. significant alterations to SOPs or working practices (e.g., disinfection/waste management methodologies, changes in strains, reagents or disposables, PPE provision, usage entry, exit protocols);
- e. unexpected events that may be relevant to the management of biorisks;
- f. actual or potential nonconformity with internal/external rules and regulations (e.g., the introduction of new legislation or major accident exposure);
- g. consideration of emergency response and contingency planning requirements;
- h. the existing management system review process (e.g., annually or at another appropriate and predetermined frequency).

Many defined methodologies and approaches are available to conduct hazard identification, risk assessment and control; the approach taken will vary depending on the nature of the situation and the level of detail required. One framework that organizations may consider adopting can be found in the WHO Laboratory Biosafety Manual Fourth Edition Associated Monograph: Risk Assessment [36].

2.4. Roles and Responsibilities for Risk Assessment

2.4.1 Resource requirements are identified, and adequate resources are allocated, including assigning competent personnel to perform risk assessments and evaluation activities, such as internal review of risk control measures in place.

Risk assessment teams may consist of supervisors, staff who perform the work, safety personnel, maintenance staff and any others who understand the procedure, hazards, and activities being assessed.

The roles and responsibilities of personnel who perform and verify work affecting risk management should be defined and documented, particularly for people who need the organizational freedom and authority to:

- a. initiate action to prevent or reduce the adverse effects of risk;
- b. control the further treatment of risks until the level of risk becomes acceptable;
- c. identify and record any problems related to managing risks;
- d. initiate, recommend or provide solutions through designated channels;
- e. communicate and consult internally and externally as appropriate.

2.5. Hazard Identification

2.5.1 The hazards associated with proposed work are identified and documented.

The first stage in the risk management process is to identify all hazards relevant to biorisk. It is useful to involve the whole work team in this process and to use inputs from organizational experts on safety and risk management.

Existing standard operating procedures, work instructions, experimental protocols, and manufacturers protocols should be reviewed to identify hazards and assess for risk.

Hazards can be associated with:

- a. Material (e.g., infectious agents or clinical samples, volume, concentration and stability of the poliovirus at the site),

- b. *Equipment/facility (e.g., centrifuge, incubators, room layout, ventilation, availability of biosafety cabinet, potential results of minor and major systems failures)*
- c. *Process (e.g., pipetting, plating, PCR, ELISA),*
- d. *Human factors (e.g., level of competency or training), and*
- e. *Any other factor that may affect laboratory operations.*

Some hazards may belong to more than one category.

Defined methodologies and approaches are available to conduct hazard identification exercises. Unless hazards are identified effectively, it is not possible to characterize the risk associated with the facility and its activities. More detail on one approach to hazard identification can be found in the WHO Laboratory Biosafety Manual Fourth Edition Associated Monograph: Risk Assessment [36].

2.6. Risk Evaluation and Control

- 2.6.1. Suitable methodologies for assessing and recording risks are identified, implemented and maintained. Risk assessment methodology and outcomes are documented.

The risk assessment should identify and categorize risks associated with the identified hazards. Separate risk assessments can be performed for individual hazards if required. Questions to consider can include but are not limited to:

- a. *How could an exposure and/or release occur? How likely is it that they occur?*
- b. *What are the consequences of exposure/release?*
- c. *What is the overall risk (combined likelihood and consequence of exposure/release) of the activities?*
- d. *Is this risk acceptable? Is this risk unacceptable?*
- e. *Can the unacceptable risks be controlled or reduced to an acceptable level?*

For each characterized risk, controls should be identified. Controls can include but are not limited to:

- a. *engineering methods such as directional air flow, biosafety cabinets, physical separation of some procedures etc.;*
- b. *administrative methods such as SOPs, work instructions, training and competency, supervision, etc.;*
- c. *Personal Protective Equipment (PPE) such as double-gloves or respiratory protection;*
- d. *remove and/or cease all activities with the identified hazard.*

Risk assessments can be qualitative, semi-quantitative or quantitative. Wherever possible and considered necessary, a quantitative method for risk assessment should be used. When a quantitative method is not possible (which is often the case in biological risk assessment), a qualitative or semi-quantitative method can be used.

In conducting the assessment, due consideration should be given to the inherent risk from polioviruses (e.g., from agent specific information sheets).

After defining and implementing control measures, the risks assessments should be reviewed to decide whether the remaining risk is acceptable or additional controls need to be identified and implemented. Multiple risk control measures are often implemented in combination to minimize residual risk.

2.7. Implementing Risk Control Measures

- 2.7.1. Suitable methodologies for assigning actions that result from risk assessments are identified, implemented and maintained., including timelines, responsible persons and associated reporting and approval mechanisms.

The risk management approach should have a documented control plan that includes:

- a. *who is responsible and accountable for implementing the plan;*
- b. *what resources are to be used (e.g., personnel, budget);*
- c. *ensures availability of the required resources;*

- d. a timetable for implementation;
- e. details of the mechanism and frequency of reviewing compliance with the plan;
- f. review and approval of the plan by the biorisk management committee and biosafety officer or biological safety adviser.

Once risk control measures have been selected and the risk control plan has been approved, actions to take before reviewed work begins include but are not limited to:

- a. ensure that risk control strategies have been communicated to relevant personnel;
- b. update Standard Operating Procedures or work instructions to include the identified risk control strategies;
- c. ensure that relevant operational and maintenance procedures have been put into place;
- d. ensure that personnel have been properly trained to implement the identified risk control measures.

2.8 Monitoring Effectiveness

2.8.1 Risk controls are monitored for effectiveness and revised when needed.

Monitoring the effectiveness of risk assessment is part of performance monitoring of the biorisk management system, including audits and inspections as described in Element 1.12 Inspection and Audit. Internal inspections and audits should include review of laboratory process and procedures to ensure that the risk control methods documented in the risk control plan are being followed and continue to be effective.

Risk assessment documents should be reviewed periodically as a part of the internal audit process, when there is any change in circumstances, or in response to an incident or near-miss. Risk assessment documents may be adjusted and modified based on changing work needs.

Element 3 – Worker Health Programme

The Worker Health Programme element evaluates the systems in place to protect workers from injuries and illnesses resulting from exposure to poliovirus and how workers are supported in the event of an accident or exposure. Subject areas covered include exposure control, health care, health monitoring, immunization and the availability of competent first aid and external assistance.

Sub-elements

3.1 Worker Health Programme

3.2 Vaccination of Personnel

3.3 Medical Emergencies

3.1 Worker Health Programme

3.1.1 The organization ensures that the risk to worker health, and that of other personnel whose health could be directly harmed by exposure to poliovirus materials, is managed effectively, including through preventive and protective measures.

The programme should address the needs of all individuals associated with the facility, including providing assurance that contractors and visitors receive the required level of protection suitable for the activities they perform, as well as safeguarding workers' families.

3.1.2 The requirements of the health surveillance programme are determined by a defined health hazard identification and risk assessment process that involves all relevant personnel.

The programme should consult relevant personnel that may include:

- a. the biorisk management adviser;
- b. the occupational health professional;
- c. facility personnel and personnel representatives;
- d. external experts, including emergency responders;
- e. biorisk management committee members;
- f. veterinary and animal-care facility staff;
- g. human resource representatives;
- h. the communicable disease specialist;
- i. scientific management.

Organizations should identify personnel considered to have significant risk of exposure and assess their healthcare needs, including the need for vaccination, PPE provision and emergency measures that encompass isolation/testing in the event of exposure. The individual's health and immune status should be considered and periodic checks appropriate to work conditions should be established.

Although the primary focus of the assessment is exposure to the poliovirus materials being handled, other conditions that could harm personnel associated with the facility should also be addressed. These may include medical conditions that could affect the work (e.g., epilepsy, heart attack, impaired vision, physical mobility/dexterity), the ability to safely use appropriate PPE, other workplace hazards (e.g., chemical exposure, radiation, fire hazards) or factors affecting general well-being (e.g., stress, depression, pregnancy, immune status, substance abuse).

Information covered by the worker health programme should be treated confidentially. All individuals should have access to consultation with a corporate or institutional occupational health facility or an independent healthcare provider. They should be informed of the nature of any treatments/vaccinations they may receive and their inherent risks and benefits.

3.2. Vaccination of Personnel

3.2.1 Relevant personnel, contractors, and visitors must demonstrate established immunity to poliovirus through evidence of poliovirus antibodies before accessing the containment facility. The need for subsequent vaccination and antibody titre testing is determined based on risk assessment and is consistent with national occupational health guidelines.

The Global Polio Laboratory Network (GPLN) may provide support for assessing poliovirus antibody titres in workers to ensure demonstrable immunity to poliovirus. Organizations should implement measures to identify those who are not protected after vaccination (depending on the vaccine's response rate) and implement a policy to address these individuals. Individuals considered unfit for work in the facility on health grounds should be identified and prevented from accessing areas with likelihood of exposure. Areas requiring vaccinations to enter should be posted.

. Reasonable measures should be taken to ensure that the vaccinations have been given and current certificates are valid. These measures may include examining original certificates and cross-checking with medical practices responsible for administering the vaccine. The organization should ensure the required or recommended vaccines are made available to concerned personnel. Vaccination should be seen as a risk control strategy that addresses consequences of an exposure. This should not impact any effort within the facility in minimizing the likelihood of exposure by any mitigation measures and controls that can reasonably be implemented, such as the use of good microbiological practices or PPE, because vaccination does not necessarily prevent onward transmission. Personnel, temporary workers, contractors and visitors who enter the containment facilities (or other areas where work was conducted with poliovirus) may be exempted from the immunization requirement if the area was decontaminated using a validated procedure.

3.2.2 A vaccination policy is defined and implemented.

Vaccination policies for containment facilities should be defined by risk assessment, documented, and approved by the relevant NAC.

3.2.3 Access to laboratories or work is restricted for individuals until they comply with the vaccination policy.

3.3. Medical Emergencies

3.3.1 A system is established to effectively manage medical and emergencies, including but not limited to identifying potentially infected workers and providing immediate medical care to exposed, ill or injured workers. This system is in alignment with the legal framework for reporting public health events involving polioviruses set forth in Annex 2 of the International Health Regulations 2005 (IHR) [14].

Procedures should ensure that adequate emergency planning is provided to address worker health needs in the event of an accident or emergency. Additional guidance can be found in Public Health Management of Facility Related Exposure to Live Poliovirus [19].

This provision should extend to first responders and their families, to members of the broader community and to environmental conditions that may have been affected by the incident. It should include identifying emergency scenarios (e.g., involving an infected worker/family member) and necessary support measures (e.g., liaison with emergency services/local authorities) and providing equipment and other resources required to manage the emergency (e.g., prophylaxis, post-exposure treatment, disinfectants, isolation requirements, vaccines). The necessary plans and other materials for managing medical emergencies should be prepared, tested and maintained.

Procedures should ensure that adequate first aid is available in relation to credible accident scenarios, as identified during risk assessments. The procedures should address the need for adequately trained personnel and their availability, as well as equipment and other materials that may be required to provide treatment.

Procedures should ensure additional competent medical support is identified and made available (e.g., hospitals, isolation units). See Element 13 Emergency Response and Contingency Planning.

Element 4 – Competence and Training

The Competence and Training element covers the processes in place to ensure that only people with appropriate qualifications are recruited, that they are subsequently trained in all aspects of the work programme, and that their competency is assessed and monitored in a structured way. This element also examines how capacity issues are addressed and how staff turnover is managed to ensure the organization is not left vulnerable when critical roles are vacated.

Sub-elements

4.1 Recruitment

4.2 Training

4.3 Competence

4.4 Human Factors

4.5 Continuity and Succession Planning

4.6 Exclusion and Reinstatement

4.1. Recruitment

4.1.1 Qualifications, experience, and reliability to observe appropriate codes of practice and aptitudes related to biorisk are considered as part of the recruitment process.

Prior to employing a candidate, the organization should ensure that:

- a. *personnel were subject to a formal selection process, including relevant background checks based on risk (e.g., employment references, security checks);*
- b. *appropriate controls are implemented should existing personnel be transferred to areas where there may be an increased risk profile;*
- c. *an assessment is made of the need for the above controls for non-core personnel (e.g., contractors, visitors, students), and measures are implemented to ensure they are applied where necessary.*

4.2. Training

4.2.1 Requirements and procedures for biorisk-related training of personnel are identified, established and maintained.

For all persons working within the containment perimeter as defined in Element 8.3.3 Infrastructure and Operational Management as well as all those who may need to enter the perimeter, including medical support staff, quality control staff, emergency responders, maintenance and cleaning staff, training procedures should:

- a. *define biorisk training needs, including training specific to the characteristics of poliovirus, biosafety and hygiene relevant to work conducted and the procedures for minimizing risk within the facility;*
- b. *provide the required biorisk training;*
- c. *include determinations of the effectiveness of the biorisk training;*
- d. *provide for refresher biorisk training;*
- e. *ensure individuals are restricted from performing tasks for which they are not trained;*

The content of a biorisk training programme will be specific to the organization, however a list of training topics outlined in this standard may include:

- a. *general biorisk awareness, including the relevance of human factors;*
- b. *SOP-specific training for relevant personnel;*
- c. *training on the contents of the biosafety manual;*
- d. *PPE training;*
- e. *animal husbandry, handling, and manipulation;*
- f. *waste management;*
- g. *security;*
- h. *insider threat awareness.*

4.3 Competence

- 4.3.1 Personnel who have responsibilities and/or perform tasks within the poliovirus facility that may impact biorisk management are competent to execute those responsibilities and/or tasks. No personnel are exempt from demonstrating competence, irrespective of rank, experience or background.
- 4.3.2 Competence levels are judged on appropriate education, training, experience together with a demonstrated ability to correctly perform their assigned responsibilities in a safe and secure manner.
- 4.3.3 The organization must define required levels of competency in alignment with any existing legal regulations. The designated manager is responsible for ensuring only competent personnel access the facility (See Element 1.4.12 Roles, Responsibilities and Authorities).
- 4.3.4 Records are maintained that show staff members have attained and demonstrated those levels of competency.
- 4.3.5 Personnel who conduct activities within the facility are under close supervision until they have demonstrated competency.

4.4 Human Factors

- 4.4.1 The organization establishes and maintains a programme to address risk associated with human behaviour, including the management of how personnel interact, the facility and its equipment.

Many laboratory incidents are caused by inappropriate behaviour or human error and a preventive and proactive approach to managing these risks should be pursued, including the specific inclusion of such issues in risk assessments. The use of competent experts in assessing this area should be considered.

Measures should be put in place to promote:

- a. human reliability and behavioural safety, including adherence to procedures;*
- b. team building and motivation;*
- c. communication, consultation and feedback;*
- d. conflict management and resolution;*
- e. the management of stress and fatigue;*
- f. empowerment of all levels of personnel, including authority to correct unsafe practices or stop work if potentially unsafe or unsecure conditions are identified;*
- g. access to counselling;*
- h. a culture of willingness to report accidents, incidents or unsafe conditions/behaviours, and protection of workers who do so, including the avoidance of a "blame culture";*
- i. ergonomics, including equipment and work practice design to take account of individual needs;*
- j. respect for individual privacy and dignity.*

4.5 Continuity and Succession Planning

- 4.5.1 Adequate backup and contingency measures are in place to address the need for continuity and succession planning.

The organization should identify roles and individuals that require a substitute, ensuring the integrity of the facility is not compromised through short- or long-term absence. Such measures should include succession planning for personnel (technical, management and scientific, including contractors) to guarantee that all critical knowledge regarding the safe and secure operation of the facility is available to others even in the event of an individual's departure or unavailability.

4.6 Exclusion and Reinstatement

- 4.6.1 Measures are put in place for the removal and exclusion of personnel (both temporary and, if appropriate, permanent) from the facility, where deemed necessary through risk assessment.

The measures should:

- a. remove access to the facility (e.g., taking away passes, changing locks and keys and access codes, and other security devices);*
- b. withdraw access to information related to the facility, including documentation, computerized records and data;*
- c. allow the immediate physical removal of personnel if deemed necessary.*

4.6.2 Measures are put in place and documented for re-evaluation of temporarily excluded personnel when deemed appropriate through risk assessment.

Element 5 – Good Microbiological Practice and Procedure

The Good Microbiological Practice and Procedure (GMPP) element examines how an organization identifies appropriate microbiological techniques and controls and how they are implemented and reviewed. A major part of this element is the development of a biosafety manual, which identifies hazards that may be encountered and specifies practices and procedures designed to minimize or eliminate risks. The biosafety or operations manual is a site-specific guidance document that is developed, implemented and updated as needed and is readily available to personnel who may encounter poliovirus materials during the course of their duties. The manual contains institutional biosafety policies, programme information and plans.

Sub-element

5.1 Biosafety Manual

5.2 Good Microbiological Practice and Procedure

5.1. Biosafety Manual

5.1.1 The biosafety manual contains site-specific information for promoting a safe, secure workplace and reducing the probability of a release of poliovirus containing material and is based on risk assessments focused on hazards associated with poliovirus/poliovirus containing materials.

As appropriate, the site-specific biosafety manual should address, but is not limited to, the following components:

- a. emergency contact information*
- b. scope and purpose;*
- c. roles and responsibilities;*
- d. characteristics of poliovirus and signs and symptoms of infection;*
- e. comprehensive risk assessment process;*
- f. good microbiological practices and procedures;*
- g. special microbiological practices and procedures;*
- h. universal precautions and sharps disposal;*
- i. biological safety training;*
- j. disinfection, decontamination and sterilization processes and their validation;*
- k. laboratory accidents, spills and potential exposure incidents; incident response, reporting, investigation and control/remediation processes;*
- l. occupational health programme;*
- m. biocontainment elements: administrative controls, specific recommended work practices, use of personal protective equipment (PPE), primary containment, facility engineering controls;*
- n. laboratory inspection, audit and testing;*
- o. biosecurity;*
- p. transport, transfer and disposition of biological material;*
- q. biological material record keeping;*
- r. pest control programme;*
- s. laboratory and laboratory support area housekeeping programme;*
- t. references.*

SOPs containing specific and applied information pertinent to these topics should be referenced in the biosafety manual and made available to personnel during training. Elements in the site-specific biosafety manual should meet or exceed the requirements outlined in this biorisk management standard.

5.1.2 All personnel in the facility where poliovirus materials are used or stored or who may encounter poliovirus materials during the course of their job duties must read and adhere to the biosafety Manual.

Training of relevant personnel on the contents of the manual and associated biosafety SOPs is critical to effective Biorisk Management.

5.2 Good Microbiological Practice and Procedure

5.2.1 All personnel handling poliovirus materials must be competent in good microbiological practices and procedures. All manipulations of poliovirus infectious materials are performed within primary containment as described in Element 8.3.4 Infrastructure and Operational Management.

5.2.2 Appropriate resources (including time and equipment) are available to ensure good microbiological practices are adhered to effectively.

As appropriate, procedures should address risks associated with but not limited to the following:

- a. *the handling of infectious poliovirus materials;*
- b. *animal handling;*
- c. *aerosol-producing procedures;*
- d. *handling of needles and sharps;*
- e. *use of vacuum pumps;*
- f. *culture, purification and storage techniques;*
- g. *sonication and other mechanical forms of cell/tissue disruption;*
- h. *use of biological safety cabinets (BSCs);*
- i. *use of disinfectants, including routine decontamination and spill control;*
- j. *handwashing and hygiene.*

This list is not exhaustive and identifies only some activities that may be employed during typical laboratory work. These activities should be undertaken in association with appropriate procedures and working practices to ensure the control measures are effective under all foreseeable and credible operating scenarios.

Good microbiological practices and procedures that should be adhered to include but are not limited to:

- k. *no eating, drinking, smoking or applying of cosmetics in the containment facility;*
- l. *no mouth pipetting;*
- m. *implementing measures to minimize aerosol generation when manually transferring or mixing materials containing live poliovirus;*
- n. *implementing policies on the safe handling of sharps;*
- o. *conducting all manipulations of materials containing poliovirus under conditions of primary containment;*
- p. *decontaminating work surfaces after handling materials containing live poliovirus and after any spill of viable material;*
- q. *decontaminating equipment before removing it from the facility or prior to repair or maintenance.*

Element 6 – Clothing and Personal Protective Equipment (PPE)

The Clothing and PPE element examines how an organization ensures that personnel are provided with the personal protective measures to minimize potential exposures and that PPE is properly maintained. This element specifically addresses the characteristics of some key PPE, for example the use of respirators but also considers other items, including gloves, laboratory coats and footwear. Specific PPE to be used at a facility will be determined based on the site-specific risk assessment.

6.1 Clothing and Personal Protective Equipment (PPE)

6.1.1 PPE needs are identified through site-specific risk assessment.

Management should ensure that:

- a. adequate information is used in selecting PPE (e.g., risk assessments, review and analysis of tasks, personnel feedback, ergonomic requirements);*
- b. the risks associated with PPE itself are identified and controlled (e.g., impaired dexterity or visibility);*
- c. all personnel who use PPE, including scientific staff, visitors and contractors, are identified, trained in PPE use and supplied with correctly fitting equipment (including respirators) and clothing.*

PPE should be used in conjunction with, but never as a substitute for, reasonable and appropriate administrative and engineering controls. PPE should be used in accordance with established standards and manufacturer specifications. Employers should make PPE available to personnel at no cost.

6.1.2 Suitable PPE is specified, made available, used and maintained appropriately within the facility.

Poliovirus-specific PPE needs should be determined by a risk assessment and may include the use of face shields, goggles, gloves, double gloves, surgical masks, HEPA-filtered respirators and clothing strictly dedicated for use within the containment perimeter as defined in Element 8.3.3 Infrastructure and Operational Management, including solid front gowns or other clothing protecting the body from exposure.

Respirators can be used when conducting procedures with a high risk of aerosol generation. Protective clothing is removed when leaving the containment area and should be decontaminated using a validated procedure prior to reuse or disposal.

Routine checks and maintenance of PPE should be defined and carried out based on manufacturers recommendations. Replacement and spare PPE should be made available based on the site-specific risk assessment. Procedures should be in place for the cleaning and, if appropriate, the validated decontamination of used PPE, including safe storage prior to decontamination.

Element 7 – Security

The Security element examines how an organization manages security with regard to biorisk, including laboratory biosecurity. The element examines prevention of unauthorized individuals entering the facility or accessing materials, prevention of unauthorized access to information generated by the facility, and prevention of incidents caused by individuals with authorized access.

Sub-elements

- 7.1 Physical Security
- 7.2 Information Security
- 7.3 Personnel Control
- 7.4 Personal Security
- 7.5 Contractors, Visitors and Suppliers

7.1. Physical Security

7.1.1 A risk assessment process for identifying physical security needs is in place. Controls are implemented and maintained for the physical security of cultures, specimens, samples, animals and potentially contaminated materials or waste, determined as part of the risk assessment process.

Measures should be put in place to minimize the potential for release or removal of poliovirus materials from the facility due to a breach in security. These measures should proactively identify vulnerabilities and implement effective control and monitoring mechanisms.

In planning and conducting security risk assessments, the organization should consider the likelihood as well as the consequence of:

- a. break-in and intrusion;*
- b. sabotage, including cyberthreats, vandalism, picketing, occupation and barricade;*
- c. labour issues and disputes, including workplace violence;*
- d. the failure of utilities;*
- e. weather-related emergencies (e.g., earthquake, tsunami, flood, tornado, hurricane);*
- f. acts of terrorism, civil unrest or war;*
- g. theft or diversion of poliovirus materials or related equipment, documents or data.*

Care should be taken to coordinate biosecurity and biosafety measures to manage and minimize conflicting priorities.

Security breaches should be reported, recorded and investigated. External authorities, such as law enforcement, should be involved if necessary.

Facilities should consider including Insider Threat Awareness training for all personnel with access to the containment facility as a part of their standard training schedule.

Procedures for the physical security of poliovirus materials, including cultures, specimens, samples and potentially contaminated materials, should be implemented and maintained to ensure:

- a. the containment facility is located on a secure site with perimeter control to prevent unauthorized access;*
- b. the containment facility is located away from uncontrolled traffic flows (e.g., entrance is via a locked door with two-factor access control measures requiring an electronic pass and personal access code);*
- c. a second person within the containment perimeter as defined in Element 8.3.3 Infrastructure and Operational management or in close proximity is aware of the work being conducted during poliovirus work, is available for contact, and can provide assistance if needed;*
- d. the facility perimeter is subject to constant monitoring (e.g., through the use of alarms, security personnel and/or closed-circuit television);*
- e. measures are implemented to identify and record all personnel in the facility at any point in time;*
- f. anti-intrusion alarms and sensors are installed, including interfaces with police and other security services;*

g. panic buttons and “silent” emergency alert measures are implemented (e.g., key codes to alert security in the event of a hostage situation);

How the facility perimeter is defined may vary based on the nature of each specific facility and therefore should be determined by risk assessment and approved by the NAC.

7.2 Information Security

7.2.1 A policy and procedures are in place to identify sensitive information.

The information generated by an organisation can be as valuable and/or dangerous as the poliovirus materials stored at the facility. Adequate measures to prevent the unauthorized release of such information are critical.

Procedures addressing information security should consider:

- a. the secure storage of all sensitive written records and data (e.g., virus inventories, security plans, security inspection reports, design drawings, maintenance plans, human resource information including worker contact details), including electronic records and electronic signatures;
- b. computer security, including robust Internet firewalls and encryption protocols;
- c. strict policies regarding PCs, laptop computers, storage media and cameras, among others, entering or leaving the facility;
- d. compliance with local and national laws regarding information security;
- e. the thorough destruction of paper files to be discarded, and complete erasure of unwanted electronic files.

7.2.2 A review and approval process is used to control access to sensitive information.

7.3. Personnel Control

7.3.1 A personnel reliability policy is defined and implemented.

The nature and extent of the measures required for the personnel reliability assessment should be determined as part of the risk assessment process. The organization should ensure that unescorted access to poliovirus containment areas is limited to personnel who have been screened for subversive behaviours/associations or criminal records. Personnel who have not be screened (as in the case of visitors, contractors, etc.) should be accompanied at all times by authorized individuals.

Factors screened for should include:

- a. association with organizations that could present a threat to the integrity of the facility;
- b. previous involvement in scientific misconduct or fraud;
- c. criminal records and financial probity;
- d. medical conditions, both mental and physical, that could lead to unstable/undesirable behaviour;
- e. dependency on drugs or alcohol.

7.3.2 The organization ensures that personnel access to facilities or work is controlled, according to the policy.

7.4 Personal Security

7.4.1 A policy is in place to provide personal security awareness training, where appropriate. Documented security drills and exercises are conducted and prepare personnel to learn from any deficiencies.

7.5. Contractors, Visitors and Suppliers

7.5.1 The organization ensures that suppliers, contractors, visitors and subcontractors adhere to the requirements of the management systems and do not compromise the facility's biorisk management system.

Element 8 – Facility Physical Requirements

The Facility Physical Requirements section sets standards for how to assess the influence of the physical characteristics of the facility on biorisk. Change in biorisk could arise due to previously unidentified shortcomings or changes in the building, equipment or scientific programme. Issues addressed include identifying the people who need to be involved and consulted, incorporating biorisk into planning, approaching commissioning in a structured way (including the role of suppliers), considering the physical characteristics of the facility and carrying out any certification that may be needed.

Sub-elements

8.1 Planning, Design and Verification

8.2 Commissioning and Decommissioning

8.3 Infrastructure and Operational Management

8.1. Planning, Design and Verification

8.1.1 A formal planning, design and redesign process is adopted for the facility, based on an assessment of risk associated with the materials to be used and activities undertaken.

A formal design process means a structured and documented approach, where the needs of the facility are determined through risk assessment. The design process incorporates engineering and operational solutions that are consistent with the risk posed by poliovirus materials to be stored and handled in the facility. Additional design measures to address facility biorisk control can be found in the WHO Laboratory Biosafety Manual Fourth Edition Associated Monograph: Laboratory Design and Maintenance [37].

Suitability of new facilities as well as retrofitting existing facilities are determined based on risk assessment. Factors to consider include, but are not limited to:

- a. adjacent spaces and whether adequate separation from the rest of the facility can be achieved;*
- b. entry and exit control;*
- c. location of equipment including BSCs;*
- a. ability to meet waste management requirements;*
- d. isolation of HVAC to maintain containment;*
- e. provisions for Building Management System in case of an alarms;*
- f. redundancy for emergency planning, such as an on-site generator;*
- g. the ability for equipment to fit through doors and be moved through corridors due to space considerations.*

Refurbishing of existing facilities should achieve the same final performance standard as constructing a new facility.

8.1.2 The design process identifies and incorporates all relevant legislative requirements, recognized standards, considers guidelines from the WHO Laboratory Biosafety Manual Fourth Edition and associated monographs [16], industry good practices and facility-specific risk assessments.

The design process considers relevant legislation and codes of practice (including building codes as well as those related to laboratory biosafety/laboratory biosecurity) and is based on the facility-specific risk assessment. The design process should also, when applicable, consider needs for compliance to Good Manufacturing Practise (GMP). The requirements identified from these sources are incorporated into the design plans. The design is fully documented, including a description of the tests and standards of acceptance to ensure required performance. The process is documented and transparent to provide assurance that it has been comprehensive and thorough.

8.1.3 The design process identifies and facilitates consultation with all relevant parties associated with the facility and its operation.

The design process includes identifying and consulting relevant stakeholders involved in the planning, construction, operation and maintenance of the facility.

The following roles and groups should be considered for information, requirements and consultation:

- a. scientific personnel and other end users;*
- b. the biorisk management adviser and biorisk management committee;*
- c. biosecurity and/or security personnel;*
- d. designers (architects and engineers);*
- e. contractors;*
- f. maintenance engineers;*
- g. material and equipment suppliers;*
- h. commissioning agents;*
- i. certifiers;*
- j. regulators including National Regulatory Authorities;*
- k. NAC;*
- l. first responders;*
- m. other relevant parties identified in risk assessments.*

A peer review process involving independent, competent third parties from the roles listed above should be conducted to ensure the design specifications meet requirements..:

8.1.4 All design features, construction techniques, materials and equipment selected are documented in line with the needs of the design specifications.

8.1.5 New construction and physical facility modifications, including refurbishing and retrofitting, are carried out according to an approved plan.

8.2 Commissioning and Decommissioning

8.2.1 A formal process exists for the initial commissioning of facilities and the final decommissioning of facilities.

Commissioning will ensure that the facility is constructed and performs as designed. The commissioning and decommissioning process starts at the design phase, during the first stage of the programme of work definition, to ensure the expectations for the building are achievable. The commissioning plan is developed in detail in parallel with the physical concept to ensure the expectations for the building are measurable. The commissioning plan clearly identifies all the commissioning steps from beginning to end, providing examples and including the conditions of acceptance of each step as a prerequisite for proceeding to the next.

The commissioning plan identifies all steps required before operation is commenced or resumed after any temporary shutdown. The commissioning process provides the benchmark for acceptable facility operation and the description of the programme to be put in place to maintain that level of performance.

The decommissioning process identifies the decontamination procedures and security-related measures that must be in place for temporary or final shutdown of the facility. The decommissioning programme describes not only the procedures but also the standards of acceptance when those procedures are performed. This may be documented through clearance certificates and permits to work, which identify when and under what conditions the decommissioned facility can be re-entered.

8.3 Infrastructure and Operational Management

8.3.1 Facilities, equipment and processes are safely and securely designed and operated. With respect to biorisk management, the poliovirus facility incorporates features that are guided by biosafety and biosecurity risk assessments for the loss of poliovirus from containment, as outlined in the WHO Laboratory Biosafety Manual Fourth Edition and associated monographs [16].

8.3.2 Poliovirus facilities are either poliovirus dedicated or non-dedicated laboratories. Non-dedicated facilities must demonstrate effective segregation and decontamination procedures between work with poliovirus and other pathogens to prevent cross-contamination.

8.3.3 Existing facilities must provide a containment perimeter sealable for gaseous decontamination and with sealed penetrations to prevent uncontrolled outward airflow irrespective of the choice of primary containment. New facilities and those undergoing retrofitting or refurbishing must ensure the sealable containment perimeter, irrespective of the choice of primary containment.

If subsequent renovation, decommissioning or repurposing of a poliovirus laboratory (and its containment perimeter) is planned and gaseous decontamination of the duct work cannot be conducted, a comprehensive risk assessment and control plan should be developed for alternative decontamination of the containment perimeter, including the exhaust ventilation system from the laboratory register to the downstream side of the HEPA filter, utilizing validated decontamination methods.

HEPA filter caissons equipped with a bag-in-bag-out (BIBO) section provide an alternative to gaseous decontamination of HEPA filters. The BIBO system is designed to allow removal and replacement of HEPA filters while maintaining containment of the caisson.

8.3.4 The use of devices (e.g., BSCs) that are validated to maintain primary containment are required for all procedures using live poliovirus.

8.3.5 Controlled entry into the containment perimeter is through a double-door personnel airlock. Features include alarms, interlocking doors or an equivalent system to ensure that more than one door cannot be opened at a time and associated operating procedures to ensure the building systems function effectively at all times. Anterooms and personnel airlocks for entry are considered to be within the containment perimeter, must be sealable for gaseous decontamination and meet all requirements of spaces within the containment perimeter.

8.3.6 All containment facilities where live poliovirus is stored, handled, treated and disposed of must be marked with biohazard signs. Signs are posted in prominent locations at the entry to the working area where poliovirus is being stored, handled, treated and/or disposed of and that only authorized personnel are permitted to enter. An emergency contact phone number must be displayed at all times and kept up to date.

8.3.7 Handwashing sinks operated by a hands-free mechanism with running water and soap are provided near the exit of the containment perimeter.

8.3.8 Controlled exit from the containment perimeter includes appropriate steps and procedures to prevent exposure to contaminated PPE or personnel. Procedures for exiting the containment perimeter and the requirement for an exit shower must be determined by a facility-specific risk assessment.

8.3.9 All exits are clearly marked. Emergency exit doors from the containment perimeter are alarmed.

8.3.10 Throughout the strain-specific containment period where evidence of the satisfactory implementation of facility, immunization coverage, and environmental safeguards (described in GAPIV) is provided, the controlled air system maintaining directional airflow will not require HEPA filtration on exhaust.

WPV Final Containment Only: The controlled air system maintains directional airflow via a dedicated ventilation system with ductwork sealable for gaseous decontamination, HEPA filtration of exhaust, backflow protection on supply, and monitors/alarms to ensure directional airflow can be readily validated.

Use of supply-side HEPA filters directly on the containment perimeter in the absence of downstream interconnections, if correctly maintained and routinely tested, is functionally equivalent to providing a dedicated ventilation system.

When BSC exhaust air is discharged through the building exhaust air system, the air handling system should be designed so it does not disturb the air balance of the BSC or of the room in which the cabinet is located.

8.3.11 The decontamination of all effluent (including emergency shower water, eyewash, handwash, unsterilized autoclave condensate) from within the containment perimeter is achieved through a validated inactivation procedure. Backflow prevention is implemented on all liquid services/utilities passing across the polio containment boundary and measures to prevent release through traps, sinks and emergency shower drains.

8.3.12 The decontamination of all materials exiting the facility is achieved through a validated sterilization/decontamination procedure.

8.3.13 Kill-tank rooms or equivalent must meet all construction, sealing, and HVAC requirements of the primary containment space and are required to have an anteroom/personnel airlock for controlled entry as described in Element 8.3.5.

Guidance on sterilization/decontamination procedures are available in Element 11 Decontamination, Disinfection and Sterilization. Examples include:

- a. a pass-through autoclave with a bioseal, interlocking doors to prevent opening the clean side prior to cycle completion, sterilization of air discharge, cycle recording mechanisms and alarms;*
- b. a material airlock/decontamination chamber sealable for gaseous decontamination;*
- c. a dunk tank containing sufficient active compound to inactivate poliovirus.*
- d. validated procedures for inactivating the contents of a full holding tank/container containing live poliovirus prior to disposal due to product failure, contamination, or other reasons (i.e., sterilize in place or other methods).*

8.3.14 Storage of poliovirus must be performed under appropriate containment conditions, as determined by a risk assessment approved by the NAC and in line with the approach detailed in the GAP-CCS [25].

8.3.15 Whenever possible, manufacturing processes and transfer of intermediates must be carried out in closed systems that have been leak tested and certified.

Consideration should be given to the use of vision panels to allow visual monitoring of activities in the laboratory and production areas inside the containment facility. Other devices such as closed-circuit television cameras may be effective alternatives where vision panels are not appropriate.

8.3.16 A poliovirus animal facility will incorporate features according to risk assessments and will meet all poliovirus containment criteria as described in this biorisk management standard, including:

1. complying with containment criteria for animal facilities, consistent with all other controls outlined in this document;
2. specially training and supervising personnel responsible for safe handling of poliovirus infected animals, including inoculating, harvesting, sampling, performing animal necropsies, and for any other manipulations so as to prevent personal injury and exposure;
3. requiring the use of devices (e.g., BSCs, flexible film isolators, or local exhaust ventilation) that are validated to maintain primary containment for all animal manipulations with live poliovirus;
4. ensuring provisions are in place to manage animal associated waste according to this standard;
5. housing infected animals separately from uninfected animals;
6. maintaining barriers to prevent infected animals from escaping and from introducing poliovirus to unexposed animals;
7. maintaining accurate records and accounting for all infected animals and their final disposition;
8. meeting international criteria and country-specific requirements for laboratory animal care;
9. using security procedures specific for facilities housing animals involved in biomedical research.

1



Element 9 – Equipment and Maintenance

The Equipment and Maintenance element ensures that biorisk management is considered during the selection of all equipment that effects risk. Emphasis is placed on equipment selection, the maintenance equipment inventories, and control over where the equipment may be moved and what it will be used for. Attention is also given to ensuring the equipment functions properly by following regular and predictive maintenance, supported by plans to prepare for, and recover from, breakdowns.

9.1 Maintenance, Control, Calibration, Certification, and Validation

9.1.1 Documented procedures are established and executed to ensure equipment and physical components of the facility that may influence biorisk are maintained, controlled, calibrated, validated, and certified in a manner consistent with the requirements of the biorisk management system and this standard.

9.1.2 Due to their criticality in maintaining containment, biological safety cabinets (BSCs) and other primary containment devices will be certified on a regular schedule in accordance with relevant national standards.

The equipment maintenance programme should apply to all aspects of the physical structure (including finishes and seals, where appropriate) and equipment therein. All materials used should be specified to ensure they can perform in line with predetermined criteria. An appropriate maintenance plan will be addressed as part of that specification process.

Maintenance

In planning and conducting maintenance activities, the organization should consider:

- a. adequately maintaining the physical integrity of the facility and its fixtures and fittings;*
- b. ensuring that the risks associated with the work have been subjected to a risk assessment and that competent individuals perform the maintenance activities;*
- c. ensuring adequate controls are in place to prevent maintenance workers from being exposed to poliovirus during their work;*
- d. identifying and recording maintenance requirements during the construction of facilities or when equipment is purchased/acquired;*
- e. creating and maintaining a maintenance register for all applicable equipment;*
- f. identifying and conducting planned maintenance activities at an appropriate frequency;*
- g. ensuring capacity for unplanned (breakdown) maintenance so the integrity of the facility is maintained at all times or that work is stopped if facility integrity cannot be maintained;*
- h. determining and monitoring predictive maintenance requirements and associated indicators and monitors;*
- i. ensuring essential spare parts are available in line with a frequency appropriate to the risk of failure and need for replacement;*
- j. establishing a pest control programme.*

Control

In planning and conducting equipment controls, the organization should consider:

- a. identifying equipment to match work needs, which can be demonstrated as fit for purpose;*
- b. controlling the purchase/acquisition of equipment to ensure all necessary risk assessments are completed and approval is authorized by competent personnel;*
- c. controlling the entry and exit of equipment to and from the poliovirus facility, including decontamination requirements (e.g., air locks and decontamination);*
- d. ensuring the asset, validation, and calibration register is regularly updated;*
- e. ensuring stocks and supplies of equipment are sufficient.*

Calibration

In planning and conducting calibration activities, the organization should consider:

- a. identifying and documenting calibration requirements at the time of purchase/acquisition;*
- b. identifying the standards/tests to use to ensure the equipment is correctly calibrated;*
- c. establishing procedures to conduct calibrations on equipment used in live virus areas;*

- d. ensuring calibration is scheduled and conducted in line with manufacturer requirements and/or at other specified intervals as identified by risk assessments.

Certification

In planning and conducting certification activities, the organization should consider:

- a. identifying and recording certification requirements at the time of purchase/acquisition of equipment, including relevant and current standards against which to certify;
- b. ensuring competent and independent certifiers are used for the certification process;
- c. ensuring certification is scheduled and conducted in line with manufacturer requirements and/or at other specified intervals as identified by risk assessments.

BSC certification should be conducted according to an appropriate national standard, such as EN 12469, British Standards Institution (BSI), Deutsche Industries Norm (DIN) or National Sanitation Foundation (NSF), as outlined in the WHO Technical Report Series 1016 [38].

Validation

In planning and conducting validation activities, the organization should consider:

- a. identifying and recording validation requirements at the time of purchase/acquisition;
- b. identifying the standards/tests to use to ensure the equipment is correctly validated;
- c. ensuring validation is scheduled and conducted in line with manufacturer requirements and/or at other specified intervals as identified by risk assessments;
- d. ensuring competent and independent validation mechanisms are used for the validation process.

For physical security systems, the analogous concept is performance testing and evaluating the entire physical security system (equipment, policies, procedures and people) to ensure the system works as designed.

Element 10 – Poliovirus Inventory and Information

The Poliovirus Inventory and Information element examines the systems in place to identify, record and review the poliovirus material stored in, received by and transported from a facility. The capabilities of the system depend on the nature of the facility and ranges in complexity from simple lists to secure databases. This element also examines the way materials are stored, including segregation, labelling systems and controls of stocks of cultures.

Sub-elements

10.1 Inventory

10.2 Information and Records

10.3 Transfer of Poliovirus Materials

10.4 Monitoring and Control

10.5 Storage Procedures

10.1 Inventory

10.1.1 An accurate and up-to-date poliovirus materials inventory is established and maintained.

The inventory maintenance process should be based on risk and include:

- a. *identifying all poliovirus materials held, including cultures, specimens and other sources (e.g., infected tissues/samples or animals);*
- b. *storing poliovirus material as outlined in the requirements of this biorisk management standard;*
- c. *ensuring 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;*
- d. *ensuring the movement of poliovirus materials to and from storage meets the standards of Element 12 Transport Procedures;*
- e. *ensuring the surfaces of all storage vessels are decontaminated with a validated method for inactivating polioviruses;*
- f. *restricting access to poliovirus materials to authorized individuals with a demonstrable legitimate need;*
- g. *implementing effective physical security measures according to risk (e.g., locks, alarms, access controls);*
- h. *developing and maintaining a reliable sample identification system;*
- i. *segregating and storing poliovirus materials according to risk;*
- j. *determining what materials should be controlled (e.g., seed stocks, working stocks, infected animals) and what level of information should be captured in the inventory for these materials.*

10.2 Information and Records

10.2.1 Records related to the poliovirus materials inventory are current, complete, and stored securely with adequate backup provisions.

Inventory information should include:

- a. *the name(s) and contact information of the individual(s) responsible for the poliovirus material, and the details of other personnel with access to the poliovirus materials or the immediate area based on the level of risk;*
- b. *restricted access to the detailed inventory records to only those individuals who are authorized to have access to that information;*
- c. *legible and robust identification numbers and other relevant identifiers;*
- d. *records of quantities of poliovirus materials (number of containers/vials or applicable equivalent) at an appropriate level and based on risk, exact location of storage;*
- e. *ability to account for materials at all times;*
- f. *data on origin, including geographical source and date of collection;*
- g. *records of materials removed from storage to conduct work, and the fate of those materials and any newly developed stocks (consumed, destroyed, removed from the facility, returned to storage) following the completion of the work.*

10.3 Transfer of Poliovirus Materials

10.3.1 Transfer of poliovirus materials between laboratories within the facility or into and out of the facility are recorded and controlled. Material containing live poliovirus to be removed from the containment perimeter adheres to the requirements outlined in Element 12 Transport Procedures. Transfer of poliovirus materials to another containment facility is executed only after the receiving containment facility has certified that receiving material is authorized according to national regulations and international agreements.

Facilities should put controls in place to ensure that documented assurances are received to guarantee that requests for poliovirus materials originate from legitimate facilities. Material may be brought into the facility or sent elsewhere only if authorized by those responsible for the facility. For materials deemed to be of high risk, more stringent controls, including shipment tracking and verification of receipt, may be necessary. More detailed guidance on transport procedures can be found under Element 12 Transport Procedures as well as in international sample transport regulations.

10.4 Monitoring and Control

10.4.1 The inventory is reviewed at predetermined intervals and at a level based on risk so that materials can be accounted for in an appropriate manner.

The system for inventory and associated controls should be matched to the nature of the material held and the risk of harm should it be misplaced or removed with the intention of misuse. Poliovirus inventories should be monitored so that materials missing or unaccounted for are quickly identified. Procedures should be in place to investigate potentially missing poliovirus materials. An inventory review should be conducted at least annually.

10.4.2 Measures are put in place to minimize the quantities of poliovirus materials in the inventory.

The organization should demonstrate proactive measures to reduce risk through the elimination, substitution or minimization of volumes/quantities of poliovirus materials used and the number of manipulations conducted. Materials no longer needed should be identified for destruction, consistent with the goal of reducing amounts of live poliovirus materials to the lowest level possible. An inventory review should be conducted at least annually.

10.5 Storage Procedures

10.5.1 Areas used for the storage of poliovirus materials are secured against entry by non-authorized personnel as outlined in Element 7 Security.

10.5.2 For secondary (back-up) storage locations where poliovirus material such as stocks or equivalent are not normally used, the NAC may approve storage in leak-proof containment containers within a dedicated freezer that is subject to labelling requirements, security and access restrictions appropriate for the storage of poliovirus materials, as determined by facility risk assessment.

10.5.3 Outside the containment facility, poliovirus materials must be stored under appropriate containment conditions, as determined by a risk assessment and approved by the NAC.

10.5.4 Movement of stock to and from storage locations outside the containment perimeter must be in line with the requirements outlined in Element 12 Transport Procedures.

10.5.5 The poliovirus material storage area must be equipped with a back-up emergency power source and with recording and alarm systems to monitor freezers.

Element 11 – Waste Management, Decontamination, Disinfection and Sterilization

The Decontamination, Disinfection and Sterilization element describes the procedures necessary to ensure that appropriate decontamination, disinfection and sterilization routines contribute to managing the risk presented by poliovirus and work activities undertaken. The element addresses general requirements for procedures, training and waste management as well as more specific issues, including the potential need for specialized laundering, animal facilities, and inactivation of poliovirus material for work outside the poliovirus containment perimeter.

Sub-elements

11.1. Management of Biological Waste

11.2. Inactivation of Poliovirus Materials and Decontamination of Facilities

11.3. Poliovirus Material Inactivation for Conducting Work Outside the Poliovirus Containment Perimeter

11.4. Decontamination of Equipment Prior to Servicing or Removal

11.1. Management of Biological Waste

11.1.1 The organization establishes and maintains an appropriate waste management policy for poliovirus materials.

No viable poliovirus will be released from the facility unless it adheres to the requirements outlined in Element 12 Transport Procedures. Potential routes whereby viable poliovirus could unintentionally exit the facility are identified and adequate prevention measures put in place through risk assessment.

The organization should have an implemented waste management policy including validated procedures for the decontamination of poliovirus-containing waste.

The following elements should be considered for a waste management policy:

- a. ensure a programme is in place to minimize waste production;
- b. ensure effective waste audit trails are in place and documented;
- c. provide facilities and procedures for the storage of waste (including short-term storage) that meet the requirements of this standard;
- d. ensure methods are available to effectively segregate and decontaminate mixed waste (e.g., biohazardous and radioactive waste);
- e. ensure waste is packaged to contain the waste and to maintain its integrity during storage and transport.

11.1.2 All contaminated or potentially contaminated waste (including those that may result from an emergency) has been identified and documented. All waste is managed according to the waste management policy.

Sources of contamination that should be considered include:

- a. personnel;
- b. clothing and PPE;
- c. glassware;
- d. equipment;
- e. cultures and associated materials;
- f. spill clean-up materials and equipment;
- g. microbiological specimens;
- h. paper and plastic waste;
- i. needles, syringes and sharps;
- j. wastewater, including that from sinks and showers;
- k. air;
- l. filters and air handling systems;
- m. decommissioned equipment used in the facility;
- n. animals exposed to poliovirus;
- o. animal carcasses and bedding;
- p. facility surfaces.

All potential waste streams and other sources of contamination should be identified and documented. Potential routes whereby viable poliovirus could unintentionally exit the facility as result of an emergency should be planned for (e.g., including downstream sewage diagrams in emergency plans) as outlined in Element 13 Emergency Response and Contingency Planning.

Potentially contaminated personnel may include core personnel working within the facility, contractors and emergency response personnel. Cultures and associated materials may be a source of contaminated supernatants, aspirates and culture media. Infected biological materials may also include infectious human, animal or plant specimens. In some instances, contaminated dedicated equipment, such as fire-fighter apparel or ambulance tools, may need to be held on-site if they cannot be effectively decontaminated.

For each of these sources, facilities should implement procedures to validate the decontamination regime. Records should demonstrate that no contaminated persons or materials leave the facility and that inactivation measures have been implemented effectively.

11.2. Inactivation of Poliovirus Contaminated Materials and Decontamination of Facilities

11.2.1 Procedures are established and maintained to ensure appropriate disinfection and decontamination methods are chosen and implemented effectively.

11.2.2 Procedures are established, validated and maintained for the effective poliovirus decontamination of the facility.

The following aspects of inactivation of poliovirus contaminated materials and facility decontamination should be considered:

- a. Heat sterilization (autoclaving) is the preferred method to inactivate polioviruses.*
- b. Decontamination SOPs are available to address both routine and non-routine activities (e.g., daily routines versus major spills).*
- c. SOPs are developed to respond to the failure of the decontamination procedure or equipment.*
- d. SOPs are validated in-house and shown to be effective against poliovirus prior to their use. The validation process includes the use of positive and negative controls.*
- e. All materials leaving the containment perimeter, including clothing and liquid/solid waste, are heat sterilized or subject to chemical treatment of proven effectiveness prior to their removal.*
- f. Any poliovirus materials inactivated for future use and/or equipment leaving the containment perimeter are accompanied by documentation of their decontamination.*
- g. Procedures are available to deal with waste generated by emergencies, accidents and other incidents.*
- h. Any live poliovirus that may be removed from the facility will be taken via a dunk tank, decontamination chamber or other validated mechanism to ensure the disinfection of the exterior surfaces of any packaging materials used.*
- i. The facility inactivates all waste and potentially contaminated material before it is passed to contractors or other third parties for waste disposal.*

11.2.3 Procedures are established and maintained to ensure the complete inactivation of all poliovirus from all materials and solid waste streams leaving the containment perimeter using validated methods. The procedures cover normal conditions as well as response to failure of the decontamination procedure or equipment.

The organization should ensure data are available to demonstrate that the methodology selected can inactivate the poliovirus materials under the specific conditions encountered in the facility. Validation measures should consider such issues as:

- a. the nature of the material being treated (e.g., volume, presence of protein/other potentially inhibitory substances);*
- b. contact times and material compatibility issues (e.g., interaction with stainless steel or rubber seals);*
- c. potential health hazards associated with the disinfectant;*
- d. the need to maintain the required level of active compound, including deterioration over time.*

- Validation of decontamination and/or inactivation should be repeated at least three times to validate the process and should be performed using the type of matrix containing the poliovirus material (i.e., solid, liquid, stool samples, animal carcass, waste culture media with serum, water containing decontaminating chemicals). Validations can be performed on loads meant to mimic operational status using non-contaminated materials and appropriate surrogates, such as *G. stearothermophilus* or another poliovirus surrogate as approved by the biosafety adviser. Examples of methods that demonstrate the validation of poliovirus material decontamination include but are not limited to:
- e. Autoclave cycles that are validated by placing several *G. stearothermophilus* biological indicators (BIs) throughout the load of material that will be autoclaved. Cycles validated using the largest load capacity of the autoclave can be used for smaller loads. BIs should be run periodically in autoclaves to verify continued efficacy over time.
 - f. Batch tank liquid effluent decontamination system cycles that are heat-based and validated using *G. stearothermophilus* BIs at high, medium and low liquid levels inside the tank.
 - g. Continuous flow liquid effluent decontamination system cycles that are heat-based and validated using *G. stearothermophilus* spores (captured in effluent prior to release).
 - h. Batch tank liquid effluent decontamination system and continuous flow liquid effluent decontamination system cycles that are chemical-based and validated using an approved surrogate for poliovirus that is not pathogenic for humans or hazardous to the environment. For each system effluent is captured and tested prior to release to the environment.
 - i. Gaseous/vapor (i.e., hydrogen peroxide, chlorine dioxide, formaldehyde, etc.) room/enclosure decontamination system cycles should be validated using the biological indicator type, placement strategy and number of BIs recommended by the equipment manufacturer.
 - j. Chemicals used for surface, equipment, waste or spill decontamination, and the required concentration and contact time should be validated as effective for inactivating poliovirus. Tests described in the European Standards EN 14476 (liquid phase) or EN 16777 (stainless steel carrier disk) can be modified for testing chemicals for poliovirus inactivation.
 - k. Sterilization-in-place (SIP) system cycles should be validated using an approved surrogate for poliovirus that is not pathogenic for humans or hazardous to the environment. Samples are collected at the end of the cycle and tested prior to release of material to the environment.
 - l. Incinerator cycles should be validated per the manufacturers operating instructions.
- In planning and conducting decontamination activities, the organization should consider:
- m. ensuring all disinfectants used contain sufficient active compound to address the working conditions under which they will be applied, and such concentrations are maintained throughout the process, including conducting specific validation activities where necessary;
 - n. providing adequate facilities and procedures for the storage of waste (including short-term storage);
 - o. ensuring methods are available to effectively decontaminate mixed waste (e.g., infected animals that have received radioactive materials);
 - p. ensuring methods are available, where appropriate, to decontaminate sensitive equipment not suitable for autoclaving (e.g., computers);
 - q. implementing monitoring measures to ensure the methods have been effective (e.g., cycle recording and the use of indicators in autoclaves);
 - r. decontaminating protective clothing by appropriate means prior to leaving the facility;
 - s. ensuring adequate methods and resources are available to deal with routine work and any spillages or other incidents during the handling and transport of materials inside and outside the facility;
 - t. implementing programmes to ensure the amount of contaminated waste is minimized.

11.3 Poliovirus Material Inactivation for Conducting Work Outside the Poliovirus Containment Perimeter

11.3.1 Procedures are established, validated in-house and maintained to ensure appropriate inactivation methods are chosen and implemented effectively for poliovirus material that is to be inactivated for future use.

Each individual conducting a poliovirus material inactivation procedure must verify the inactivation procedure was successful the first time they conduct the procedure.

The organization should ensure data are available to demonstrate that the methodology selected for inactivation of poliovirus enables inactivation under the specific conditions encountered in the facility. Validation data should be in the form of more than one independently performed assay and preferably performed by more than one trained individual.

The organization should have a notification and response process in place in the event poliovirus containing material is removed from the poliovirus containment perimeter and later found to contain infectious poliovirus.

Inactivation methods should take into consideration:

- a. the nature of the material being treated (e.g., volume, presence of organic material/other potentially inhibitory substances);*
- b. compatibility of the inactivation process with the work to be conducted on the material (e.g., need to retain antigenic structure or nucleic acid sequences);*
- c. potential health hazards and disposal requirements associated with the inactivation process (e.g., chemical, heat, other hazards).*

Examples of methods of poliovirus material inactivation include but are not limited to treatment by:

- a. heat;*
- b. nucleic acid extraction reagents;*
- c. chemicals;*
- d. ;*
- e. ionizing radiation;*
- f. germicidal UV light;*
- g. combinations of the above methods (e.g., heat treatment followed by filtration or chemical lysis followed by filtration).*

The validated inactivation procedure should contain positive and negative controls. It should consider the limit of detection and effect of residual inactivation material on the viability of the biological system used in the validation assay.

The validated inactivation procedure provides a process in which treated poliovirus materials no longer contains detectable:

- a. viable poliovirus, with efficacy established by viability testing data; or*
- b. poliovirus nucleic acid that is capable of producing infectious forms of virus, with efficacy established by infectivity testing data.*

Examples of methods that demonstrate the validation of poliovirus material inactivation include but are not limited to:

- a. culture of the treated material in permissive cells and observing for cytopathic effects/cell death;*
- b. inoculation of the treated material into a susceptible animal model for observation of clinical symptoms and viral titre from infected tissues.*

11.4 Decontamination of Equipment Prior to Servicing or Removal

11.4.1 Procedures are established, validated and maintained to ensure equipment, tools and other similar items are appropriately decontaminated before they are serviced in the lab or removed from the poliovirus containment perimeter.

11.4.2 Equipment, tool, or other treated items cannot be serviced or removed from biocontainment until the validation tests demonstrate there is no live poliovirus present. The results of any equipment decontamination are recorded, including documentation of

1. the equipment owner;
2. date of decontamination;
3. equipment description/identity and destination;
4. decontamination method used and how it was validated;
5. contact information of the individual conducting the decontamination;
6. any other relevant information.

The organization should ensure data are available to demonstrate that the decontamination process selected is capable of inactivating poliovirus and the process was properly conducted. A copy of the

documentation of decontamination should accompany any item being serviced or transferred out of the poliovirus containment perimeter.

Decontamination methods may include poliovirus inactivation methods described in Element 11.3.1 Poliovirus Material Inactivation for Conducting Work Outside the Poliovirus Containment Perimeter and should be chosen based on:

- a. compatibility of the decontamination process with the item to be decontaminated (e.g., can it be subjected to a chemical decontaminant or autoclaving, is a vapor or gas decontaminant required to permeate areas that cannot be wiped down with a chemical);
- b. potential health hazards and disposal requirements associated with the decontamination process (e.g., chemical, heat, other hazards).

Examples of methods of decontaminating equipment, tools or similar items are provided below but are not limited to treatment by:

- a. heat;
- b. chemical wipe down;
- c. gaseous/vapor decontamination;
- d. heat and pressure, as in sterilization-in-place (SIP).

The decontamination process should be validated for the equipment, tools or items being treated (e.g., biological indicators (BI) used during autoclaving, BIs used during vapor/gas decontamination, swab samples taken from the most likely place of contamination following chemical wipe down or SIP). Time required for validation is dependent on the validation SOP and manufacturer instructions (e.g., for BIs).

Items should be maintained in such a way as to prevent any potential contact or contamination by poliovirus containing materials until validation tests results are complete and the item can be serviced or removed.

Element 12 – Transport Procedures

The Transport Procedures element outlines how an organization deals with issues associated with the internal and external transport of biological materials. The necessary roles and responsibilities, materials and equipment as well as the need to work with specialized t couriers are examined.

Sub-elements

12.1 Transport Procedures

12.2 Transfer Approval

12.1. Transport Procedures

12.1.1 Procedures for the safe and secure transport of cultures, specimens, samples and contaminated and potentially contaminated materials, both inside and outside the facility containment perimeter, are established and maintained in accordance with legal requirements for the transport of dangerous goods.

In planning and conducting transport activities, the organization should consider:

- a. *ensuring preparation of samples and transport requirements are identified and implemented, including legal requirements and national and international guidelines;*
- b. *ensuring transport within the facility is in sealed, appropriately labelled, surface decontaminated, leak-proof secondary containers by trained staff only;*
- c. *ensuring adequate packaging systems, materials, labels, PPE and documentation are available and used as part of the transport process;*
- d. *selecting a specialized carrier that is qualified to document and handle the package safely and securely;*
- e. *using document controls that allow the traceability of material movements into and out of the facility;*
- f. *identifying and implementing adequate and proportionate emergency response and contingency plans associated with the transport of poliovirus materials.*

The organization should also consider:

- a. *determining whether a request for poliovirus materials is being made by an approved facility (i.e., a facility certified for handling or storing poliovirus material) for a legitimate reason;*
- b. *ensuring controls are applied to the importation of material to the facility;*
- c. *ensuring that material may be brought into the facility or sent elsewhere only if authorized by those responsible for the facility.*

12.2. Transfer Approval

12.2.1 Transport of poliovirus materials must be approved by the competent authority for transfer to another containment facility under controlled conditions.

The organization should identify and consult the national or regional authority that has been delegated the responsibility of overseeing the transfer of poliovirus materials before initiating any intra- or inter-country transport.

Element 13 – Emergency Response and Contingency Planning

The Emergency Response and Contingency Planning element examines the structures and mechanisms in place to cope with working outside normal operating conditions and how to react proportionally to emergency situations. Issues addressed include physical requirements, emergency communications, decision-making authorities, the development of simulations, testing of emergency scenarios and capacity of personnel, facilities and protective and rescue systems. Detailed guidance on emergency management for poliovirus exposure can be found in *Public Health Management of Facility Related Exposure to Live Poliovirus* [19].

Sub-elements

- 13.1 Emergency Scenarios
- 13.2 Emergency Response and Planning
- 13.3 Emergency Plans
- 13.4 Emergency Exercises and Simulations
- 13.5 Contingency Plans

13.1. Emergency Scenarios

13.1.1 All credible and foreseeable emergency scenarios that may impact the organization's handling of biorisks must be identified.

It is unlikely that all potential emergency scenarios will be credible, but all reasonable ones should be considered and recorded. Where appropriate, the rationale for dismissing any issue should be provided.

Scenarios considered should include:

- a. an infected/potentially infected worker or other contact (e.g., family member, emergency responder or community member);
- b. accident or medical emergency of a worker within the containment perimeter and need for evacuation;
- c. a major spillage/aerosol release;
- d. the potential loss of poliovirus materials through theft or any other reason;
- e. unexpected virulence (of unknown biological agents or of biological agents expected to be non-infectious);
- f. fire;
- g. flooding;
- h. explosion;
- i. a natural disaster (e.g., earthquake, extreme weather conditions, disease pandemics);
- j. breach of security;
- a. suspicious packages, including quarantine areas and appropriate explosive stand-off;
- k. utility failure including electricity, gas, steam and water supplies;
- l. physical facility and equipment failure, including a control system failure of the disinfection regime;
- m. environmental release through loss of containment;
- n. an act of terrorism or deliberate vandalism or extortion.

13.2. Emergency Response Planning

13.2.1 Plans and procedures are established and maintained to:

1. Identify and assess risk for incidents and emergency scenarios involving poliovirus and other hazardous materials;
2. prevent their occurrence to the degree possible;
3. respond to emergency situations;
4. report public health events involving poliovirus materials, per the IHR 2005 framework [14];
5. limit the likelihood of illness or other damage that may be associated with the emergency situation.

13.2.2 Emergency planning covers all aspects of biorisk and includes general safety, security and medical issues. The organization must demonstrate that there are effective linkages between the response and contingency plans addressing containment breaches in place at the facility level, as approved by the NAC.

Detailed guidance on the handling of facility-associated poliovirus infections can be found in Public Health Management of Facility Related Exposure to Live Poliovirus [19]. This document includes guidance on meeting these requirements and should be incorporated into facilities emergency planning and response. The reporting mechanism and criteria for a notifiable event involving polioviruses are detailed in Annex 2 of the International Health Regulations 2005 (IHR) [14].

13.3. Emergency Plans

13.3.1 Biorisks are considered when preparing and implementing emergency plans.

A system in accordance with national and international legislation is in place to effectively manage incidents that are determined by the organization to be significant poliovirus exposures, including:

1. implementing measures to prevent exposure of unimmunized individuals, including exposure to stool and associated waste;
2. educating individuals under investigation, their family and close contacts on the risk of poliovirus infection to the community, the procedures for diagnosis and the precautionary measures required to prevent possible transmission;
3. initiating procedures to determine whether exposed individuals are infected, by collecting and testing nose, throat and stool specimens daily for a minimum of seven days post-exposure;
4. communicating with relevant national, regional and local officials;
5. disinfecting areas potentially contaminated by infected individuals within the facility.

Detailed guidance on the handling of facility-associated poliovirus infections can be found in Public Health Management of Facility Related Exposure to Live Poliovirus [19], which includes guidance on meeting these requirements and should be incorporated into facilities emergency planning and response.

The organization should ensure that plans address the following needs at a minimum:

- a. identifying those responsible for devising, implementing and testing the control measures specified, along with ensuring their conclusions are effectively communicated to all relevant personnel;
- b. ensuring the legality and enforceability of proposed emergency response plans;
- c. responding during emergencies occurring outside working hours as well as those occurring during normal working hours;
- d. providing for periods of reduced staff availability (e.g., during weekends and holiday periods);
- e. ensuring emergency access/exit, including the ability to override access controls as appropriate;
- f. providing emergency exit routes that avoid evacuating people through containment areas;
- g. providing for the safe removal, transport, transfer, treatment and accommodation of contaminated persons and objects;
- h. informing visitors and contractors about emergency response plans and the possible consequences of exposure.

13.3.2 Control measures in place are demonstrated as being reasonable and proportionate to the scale and nature of the emergency.

13.3.3 Emergency plans are effectively communicated to all personnel and relevant third parties and tested with the goal of making everyone aware of their roles and responsibilities.

In the event of an emergency, it may be necessary to involve parties external to the organization. Based on the credible scenarios identified, the organization should identify and communicate with such agencies to establish their role in responding to a given situation. The organization may choose to sign memoranda of understanding or agreements with key local responders. It may also be

necessary to inform and educate such parties on their role and any risk (including exposures) they may face. Additionally, the organization should take steps to reasonably ensure their actions will not unnecessarily increase the risk associated with the emergency (e.g., uncontrolled use of water for fires). The organization should coordinate with local or national authorities to implement surveillance plans in response to an incident or emergency. Contact information should be documented and made available to personnel responsible for coordinating the emergency response activity.

External agencies that should be consulted could include:

- a. police and security services;
- b. fire services;
- c. ambulance and local hospitals/healthcare providers;
- d. transport providers/couriers;
- e. local and national government officials;
- f. environmental authorities;
- g. local utilities authorities, including sewage and power;
- h. the WHO.

13.4. Emergency Exercises and Simulations

13.4.1 Structured and realistic emergency exercises and simulations, including security drills, are conducted at regular intervals, based on risk, to test the emergency plans, prepare personnel and learn from any good practices or deficiencies identified.

Facilities should cooperate with external agencies, such as local health authorities and emergency services, to ensure coordination of outside resources. The NAC should serve in an advisory capacity.

Exercises should be planned to realistically represent the events simulated. The results of an exercise should be documented and reviewed for lessons learnt, and feedback on performance should be provided to all relevant personnel, including senior management. Any resulting actions should be recorded and allocated to named individuals, and measures should be put in place to ensure they are closed out as specified in Element 1.14 Corrective Action.

13.5. Contingency Plans

13.5.1 In the event of an emergency, adequate contingency measures are in place to ensure the safety and security of continued operations.

Normal operating conditions may be disrupted in the event of an emergency or unforeseen event. This could range from safely shutting down work during a power failure, to obtaining alternative storage conditions in the event of a breakdown. Such eventualities should be considered proactively, and contingency plans put in place. Activities should address the need for adequate redundancy, replacement and other measures, which could involve the availability of alternative facilities or personnel, the introduction of backup systems (e.g., power supplies), alternative means of decontaminating materials in the event of the failure of critical systems or equipment (e.g., kill tanks or autoclaves), maintaining containment for injured/ill workers in an emergency, or the complete safe shutdown of operations in extreme situations.

Element 14 – Accident/Incident Investigation

The Accident/Incident Investigation element addresses activities that define the facts and circumstances related to an unwanted event, determine the causes and develop remedial action to control biorisk and prevent recurrence. Following an unwanted event, chance often is the only reason a property-damage accident or near-miss incident does not result in infection or personal harm. This element examines the organization's reporting and investigation system in place.

14.1. Accident/Incident Investigation

14.1.1 Documented procedures are established and maintained to define, record, analyse and learn from accidents and incidents involving poliovirus materials.

Facilities should implement procedures to ensure that definitions for what constitutes an accident or incident are clear and communicated to all relevant personnel. Incidents may include events of exposure and accidental release. Accidents and incidents provide an indication that the systems designed to manage biorisk may have failed, so it is essential that lessons be learnt and improvements made where possible.

The accident/incident investigation process should at a minimum:

- a. create a culture of self-reporting incidents, including “near misses” and incidents that may trigger an investigation or emergency response;*
- b. identify personnel responsible for maintaining the accident/incident reporting system;*
- c. define what triggers recording and reporting, with emphasis on events that may result in exposure to live poliovirus (e.g., needle sticks, spills, splashes, sprays, leaks, aerosol generating events);*
- d. define what constitutes a significant poliovirus exposure (e.g., ingestion) and thresholds for initiating procedures to determine whether individuals are infected;*
- e. specify required documentation to support the system, as well as the frequency and distribution of reports generated and communicated to relevant personnel;*
- f. identify the reports that will be generated, as well as their frequency and distribution;*
- g. 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 designated senior manager and recommends such actions as deemed necessary;*
- h. establish and publicize 24-hour accident/incident reporting channels and identifying those responsible for maintaining the system;*
- i. ensure an analysis of trends;*
- j. identify root causes using individuals trained in investigation techniques;*
- k. provide feedback to staff at regular intervals and action-tracking mechanisms to ensure lessons learnt result in action to avoid repeating such events and/or to minimize their potential impact;*
- l. identify where security professionals may be required to coordinate with law enforcement.*

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