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# WHO global action plan for laboratory containment of wild polioviruses

Second edition



Vaccines and Biologicals

World Health Organization

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# Purpose

To provide a systematic global plan of action  
to minimize the risk of reintroduction of wild polioviruses  
from the laboratory to the community.



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# Abbreviations

BSL	biosafety level
CNS	central nervous system
GCC	Global Commission for the Certification of the Eradication of Poliomyelitis
HEPA	high efficiency particulate air filter
IPV	inactivated polio vaccine
OPV	oral polio vaccine
PVR	poliovirus receptor
SOP	standard operating procedure
VAPP	vaccine-associated paralytic poliomyelitis
VDPV	vaccine-derived poliovirus
WHO	World Health Organization





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# Executive summary

The world will be declared polio-free when the Global Commission for the Certification of the Eradication of Poliomyelitis (GCC) is satisfied that all regions have documented the absence of wild poliovirus transmission for at least three consecutive years and that laboratories holding wild poliovirus materials have adopted appropriate measures of containment. (1) The probability of wild poliovirus transmission from laboratory to community is small but the potential consequences of such transmission become more serious as polio-free countries increase in number and immunization decreases or stops. It is crucial to achieve the safe handling and, ultimately, the appropriate laboratory containment, of wild poliovirus infectious materials and potential wild poliovirus infectious materials.

The first edition of the *Global action plan for laboratory containment of wild polioviruses* (WHO/V&B/99.32) was issued by WHO in December 1999. It was based on broad input from biosafety experts, epidemiologists, laboratory scientists, ministries of health and vaccine manufacturers.

This second edition of the global action plan replaces the first. It incorporates lessons learned from biomedical laboratory surveys and inventories in more than 100 countries in five of the six WHO regions. It expands previous recommendations to include vaccine-derived polioviruses (VDPVs). It defines biosafety requirements in terms of risks. It describes two phases of activities leading to containment: the laboratory survey and inventory phase and the global certification phase. Finally, it examines the implications of post certification immunization policies on poliovirus biosafety requirements.

## Laboratory survey and inventory

During this phase, when the numbers of polio-free countries and regions are increasing but wild polioviruses continue to circulate somewhere in the world, countries:

1. Survey all biomedical laboratories to identify those with wild poliovirus infectious materials or potential wild poliovirus infectious materials, and encourage the destruction of all unneeded materials.
2. Develop an inventory of laboratories that retain such materials and report to the Regional Certification Commission.
3. Instruct laboratories retaining wild poliovirus infectious materials or potential infectious materials to institute enhanced biosafety level-2 (BSL-2/polio) measures for safe handling (Annex 3).
4. Plan for global certification.

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## **Global certification**

During this phase, which begins when one year has elapsed without the isolation of wild poliovirus anywhere in the world, countries will:

1. Notify biomedical laboratories that wild poliovirus transmission has been interrupted.
2. Instruct laboratories on national inventories to choose one of the following options:
  - render materials non-infectious with respect to poliovirus or destroy under appropriate conditions (Annex 2);
  - transfer wild poliovirus infectious materials and potential infectious materials to laboratories capable of meeting the required biosafety standards;
  - implement biosafety measures appropriate to the laboratory procedures being performed (BSL-2/polio or BSL-3/polio).
3. Document the fulfilment of all containment requirements for global certification.

## **Post global certification**

It is anticipated that the containment requirements for global certification will remain in force together with concurrent immunization policies. At some time in the future, international advisory bodies are expected to re-examine post certification immunization policies in the light of research outcomes, post eradication experiences, containment assessments and assurances that surveillance, vaccine stockpiles and emergency response plans would be adequate should polio re-emerge. If oral polio vaccine (OPV) immunization is stopped, with or without universal replacement with inactivated polio vaccine (IPV), the biosafety requirements for both wild and OPV viruses will become more stringent than those outlined in this document, consistent with the consequences of inadvertent transmission of poliovirus from the laboratory to an increasingly susceptible global community.

## **Publication of the plan**

The present document provides the background, rationale and strategy for ensuring that laboratory facilities and biosafety practices are consistent with the risk of inadvertent transmission of poliovirus to the community. In a separate WHO document (2) guidelines are given for the safe production and quality control of IPV manufactured from wild polioviruses. Full cooperation and commitment at all levels are essential in order to ensure that polio will not be a threat to future generations.

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# Poliomyelitis

## Description

Poliomyelitis, or polio, is an infectious disease caused by poliovirus, a member of the genus *Enterovirus*. There are three serotypes of poliovirus: 1, 2 and 3. A specific protein receptor on susceptible human cells allows the attachment and entry of poliovirus. The virus infects cells of the oropharynx, the tonsils, the lymph nodes of the neck, and the small intestines. Infection progresses through cycles of virus replication. Once infection is established in the gastrointestinal tract, poliovirus can invade the central nervous system (CNS) by penetrating the blood/brain barrier or by spreading along nerve fibres.

When non-immune persons are infected with poliovirus the outcome varies from infection without symptoms to mild illness, aseptic meningitis or paralytic poliomyelitis. (3) About 1% of infections result in recognized neurological illness. The incubation period ranges from 4 to 35 days but is typically between 7 and 14 days. The initial clinical symptoms may include fever, fatigue, headache, vomiting, constipation, stiffness of the neck and pain in the limbs. The virus multiplies and destroys motor neurons, which may result in the permanent paralysis of muscles activated by the affected nerves.

## Mode of transmission

Poliovirus is transmitted from person to person either through droplets from the upper respiratory tract during the early days of infection or, more commonly, through the ingestion of infectious faecal material in circumstances of poor hygiene. (4)

## Poliovirus in nature

Following infection, poliovirus can be found in the oropharynx for one to two weeks, in the blood for about one week, and in faeces for one to two months, even in individuals without symptoms of disease. Poliovirus has been recovered from faeces, intestinal contents, lymph nodes, brain tissue and spinal cord tissue in autopsies conducted on persons who have died of the disease.

Fewer than 1% of infections result in poliomyelitis. Many clinically healthy children shed poliovirus during periods of high prevalence. Poliovirus in the environment is the direct result of recent poliovirus infections in the human community. Soil may be contaminated as a result of human defecation near dwellings, crop fertilization with untreated or inadequately treated night soil or sewage, and the recycling of

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wastewater for irrigation. Surface water may become contaminated through the discharge of untreated or inadequately treated sewage or through run-off from contaminated soil.

Humans are the only natural reservoirs of poliovirus. Higher non-human primates (chimpanzees and gorillas) are susceptible to infection and disease but their populations are too small to sustain poliovirus transmission in the absence of human infection. (5)

### **Poliovirus survival**

Poliovirus is resistant to inactivation by common laboratory disinfectants such as alcohol and cresols. The virus is rapidly destroyed by exposure to temperatures of 50°C or more, autoclaving or incineration. (3) It is readily inactivated by dilute solutions of formaldehyde or free residual chlorine (bleach), ultraviolet light, heat and drying. Inactivation is slowed by the presence of extraneous organic matter. Chlorine bleach (0.5%) is the recommended disinfectant for laboratories working with polioviruses.

Under stable laboratory conditions, poliovirus in clinical or environmental specimens may survive at freezing temperatures for many years, under refrigeration for many months, and at room temperatures for days or weeks. (3)

Rates of poliovirus inactivation in nature are greatly influenced by the immediate environment. It has been estimated that poliovirus infectivity in soil decreases by 90% every 20 days in winter and every 1.5 days in summer, and that at ambient temperatures a 90% decrease in infectivity occurs in sewage every 26 days, in freshwater every 5.5 days, and in seawater every 2.5 days. (5)

### **Polio vaccines**

Protective immunity against poliomyelitis is conferred through immunization or natural poliovirus infection. Immunity is poliovirus serotype-specific. Protection against disease is associated with antibodies that circulate in the bloodstream and prevent the spread of the virus to the central nervous system. Protection against infection is associated with both circulating antibodies in the blood and secretory antibodies in the gut and upper respiratory tract. (6)

Both live attenuated oral polio vaccine (OPV) and injectable inactivated polio vaccine (IPV) give protection against paralytic poliomyelitis. (7) However, neither vaccine provides absolute protection against infection or reinfection with the virus itself. IPV stimulates protective antibodies in the blood (i.e. circulatory immunity), thus preventing poliovirus in the gut from entering and replicating in the CNS. IPV use in Northern European countries succeeded in effectively eliminating wild poliovirus circulation. (8, 9) OPV, containing a live virus that replicates in the gut, additionally induces mucosal immunity that inhibits replication of the virus in the intestine. The resulting reduction in faecal shedding of virus is associated with decreased transmission to other persons, making the choice of OPV critical for the global polio eradication initiative. OPV use by many of the countries involved with the global polio eradication initiative has effectively eliminated wild poliovirus circulation. (10)

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However, live OPV has been associated with vaccine-associated paralytic poliomyelitis (VAPP) at a rate of about one in every 2.5 million doses administered. (11) Immunocompromised patients with B-cell deficiencies may continue to shed vaccine virus for extended periods, eventually leading to an accumulation of genetic changes in the excreted virus. (12) Approximately 19 such cases have been identified. The continuous person-to-person circulation of vaccine polioviruses over extended periods in poorly immunized populations may result in genetic changes where neurovirulence and transmissibility profiles are characteristic of wild poliovirus. (13) Such viruses pose risks similar to those presented by naturally occurring polioviruses.

### **Interruption of wild poliovirus transmission**

Polio occurred worldwide before the advent of immunization in the mid-1950s. Immunization has been highly effective in reducing the number of cases. (14) Further reductions in areas where the disease is highly endemic have been achieved through improved routine childhood immunization and the strategic use of OPV in the polio eradication initiative. (15) The concept of interrupting wild poliovirus transmission is based on the assumption that the circulation of wild poliovirus will cease when the virus is deprived of its susceptible human host through immunization. (16) The continued decrease in the incidence of polio in many countries and the progressive disappearance of poliovirus genetic lineages suggest that the interruption of human-to-human transmission is achievable.

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# The rationale for containment

Less than a year after smallpox was eradicated in 1977, two cases occurred in the United Kingdom, both linked to a smallpox laboratory. The index case worked in a room located directly above the laboratory. Two persons died: the index patient as a result of infection and the director of the laboratory, who took his own life because of the accident. (17) When polio is eradicated every effort must be made to ensure that wild poliovirus is not similarly transmitted from the laboratory to an increasingly susceptible community.

In theory, polioviruses may be transmitted to persons outside the laboratory through contaminated laboratory effluents released into sewage, solid wastes transported to landfills, spent air exhausted to surroundings, or contaminated workers' skin or clothing. However, transmission through such routes is extremely difficult to document against a background of high levels of immunity acquired through natural infection or immunization.

More readily documented are poliovirus infections of laboratory workers with potential for transmission to the community. Twelve laboratory-associated poliomyelitis cases, including two deaths, were recorded between 1941 and 1976. (18–21) Accounts of seven of these cases were unpublished. Most cases occurred in the pre-vaccine era and before the advent of cell culture.

The first report of a laboratory-associated infection, published in 1941, described a case of poliomyelitis which was probably acquired as a result of the washing and grinding of infected tissues in preparation for inoculation into monkeys. (22) In 1943 two laboratory workers were infected with the prototype Lansing (Armstrong) strain while attempting to infect mice. (23) Two additional reported cases of poliomyelitis in laboratory workers were fatal: one in the USA, (24) the other in South Africa. (25)

The paucity of reports of laboratory-associated poliomyelitis since vaccines were introduced testifies to the effectiveness of vaccines and vastly improved laboratory facilities, technologies and procedures. (26, 27) Nevertheless, recent evidence indicates that the potential remains for transmission of poliovirus from the laboratory to the community. In 1992 a wild-type 1 strain used for IPV production was documented as being transmitted from a worker in a vaccine production facility to his young son. (28) In another incident a child was reported to have been infected with a prototype strain of type 3 commonly used in laboratories for research and IPV vaccine production. The source of this infection was not determined.

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IPV is highly effective in preventing disease but its use cannot be assumed to prevent silent infection among laboratory workers. OPV provides a more effective barrier but silent infections may still occur. The incidence of poliovirus infections without clinical symptoms among laboratory workers is unknown.

In the absence of vaccines that can fully eliminate infection in the gut and subsequent faecal shedding, appropriate biosafety measures are crucial for the prevention of poliovirus infection of laboratory workers and subsequent transmission. Absolute containment cannot be assured. Questions of intentional or unintentional non-compliance will always remain. But effective containment, i.e. reducing the risk of inadvertent reintroduction of wild poliovirus into the community, is a realistic goal. (29)



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# Definitions

## Polioviruses (box 1)

Polioviruses are defined by standard neutralization tests with specific antisera. The three poliovirus serotypes form a unique genetic group of human enteroviruses that initiate infection by binding to a specific cellular receptor (PVR:CD155). Other enteroviruses may occasionally be associated with cases of acute flaccid paralysis but they are not polioviruses and do not bind to PVR.

Wild polioviruses have the capacity to circulate indefinitely within susceptible human populations. Molecular studies have shown that the capsid sequence lineages of wild polioviruses are maintained along chains of transmission, while the non-capsid and non-coding sequences may be exchanged by recombination with other enteroviruses during circulation. The identification of sequences outside the capsid region as “poliovirus” may consequently be arbitrary.

Genetic mutations occur in all circulating polioviruses. Mutations in the VP1 region provide the basis for differentiating wild poliovirus isolates into genotypes and lineages. Mutations further characterize isolates of OPV origin. A difference in the range of 0-1% from the parent OPV strain by sequence homology of the full VP1 region is consistent with normal virus shedding or limited person-to-person spread. A difference in the range of 1-15% is characteristic of isolates from OPV-derived poliovirus (VDPV) outbreaks, consistent with extensive transmission and the capacity to cause paralytic disease. (13)

For purposes of containment, all polioviruses are considered wild except those strains currently approved by national control authorities for use as OPV. By extension, also considered “not wild” are the common OPV-like viruses found in clinical materials from recent vaccine recipients. Laboratories wishing to work with “not wild” poliovirus should use authenticated approved seed stocks of OPV strains.

For most of the world, the approved OPV strains are the attenuated Sabin-original (SO) strains, which are type 1 (Li and Schaefer), **LS-c, 2ab/KP3**; type 2 (Fox and Gelfand) **P712, CH, 2ab/KP2**; and type 3 (Kessel and Stimpert) **Leon 12a,b/KP4** (7). In China, the approved type 2 and 3 OPV strains are **Zhong II** and **Zhong III**, respectively.

Other strains are described in the literature as attenuated. Some have undergone extensive field trials. But only the approved OPV strains have the cumulative evidence of attenuation through years of experience in human populations.

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Poliovirus strains currently used for production of inactivated polio vaccine (IPV) are type 1 **Mahoney** (**Brunenders** in Sweden), type 2 **MEF1**, and type 3 **Saukett**. All three strains are wild. IPV produced from Sabin attenuated strains is currently under development.

#### Box 1: Definitions of polioviruses

**Polioviruses:** human enteroviruses that exist as three well-defined serotypes and infect cells via a specific receptor, PVR:CD155.

**Wild polioviruses:** isolates known or believed to have circulated persistently in the community and reference strains derived from these isolates.

**Oral poliovirus vaccine (OPV) strains:** attenuated polioviruses approved for use in oral vaccines by national control authorities. Unapproved candidate strains are considered wild.

**OPV-like polioviruses:** isolates consistent with a limited period of virus excretion or person-to-person transmission, usually demonstrating less than 1% difference from parent OPV strains by full VP1 sequence homology. Included are isolates that have not been sequenced but have been shown to be OPV-like by two WHO-recommended methods of intratypic differentiation.

**Vaccine-derived polioviruses (VDPV):** isolates consistent with an extensive period of virus excretion or transmission in the community, usually demonstrating 1–15% differences from parent OPV strains by full VP1 sequence homology. VDPVs are classified as wild for programmatic and containment purposes.

Materials are further categorised as wild poliovirus infectious or potential wild poliovirus infectious. Included in both of these categories are clinical and environmental materials and laboratory products of these materials.

#### Wild poliovirus infectious materials (box 2)

Wild poliovirus (including VDPV) may be present in a variety of clinical materials, most commonly in faeces and throat specimens, less commonly in blood, and rarely in cerebrospinal fluid in non-paralytic and paralytic infections. In fatal infections, wild poliovirus may be present in faeces, intestinal contents, lymph nodes, brain tissue, and spinal cord tissue. (29) Poliovirus may be found in blood during the first week of infection, before neutralizing antibodies appear, but is rarely found in blood after the onset of clinical signs of central nervous system involvement. All such clinical materials from persons with acute poliomyelitis are defined as infectious, even though the presence of virus may not have been confirmed.

Wild polioviruses present in environmental samples, such as sewage and water, reflect the presence of poliovirus in the community. The viral content of sewage may vary widely, depending on many environmental factors.

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Infectious laboratory products include virus stocks and derivative materials from cell cultures, non-human primates, and transgenic mice inoculated with wild polioviruses. (30)

**Box 2: Wild poliovirus infectious materials are defined as:**

Clinical materials from confirmed wild poliovirus (including VDPV) infections, environmental sewage or water samples in which such viruses are present, and replication products of such viruses, including:

- cell culture isolates, reference strains, seeds for inactivated vaccines;
- infected animals or samples from such animals, including PVR transgenic mice;
- derivatives produced in the laboratory that have capsid sequences from wild polioviruses;
- full-length RNA or cDNA that include capsid sequences derived from wild poliovirus;
- cells persistently infected with poliovirus strains whose capsid sequences are derived from wild poliovirus.

**Potential wild poliovirus infectious materials (box 3)**

At least 99% of wild poliovirus infections cause no recognizable paralytic disease, but may result in significant numbers of wild polioviruses being shed in faeces and respiratory secretions. Wild poliovirus isolation rates of 8-19% have been reported from stools of healthy children during polio seasons in areas of endemicity. (31, 32) Laboratories with stored collections of faecal, throat or environmental samples should assess the likelihood of the presence of wild polioviruses in these materials, on the basis of sample treatment, storage history, the country of origin, the year, and the time when the last indigenous wild poliovirus isolates were obtained in the country concerned (Annex 1). Uncharacterized enterovirus-like cell culture isolates or undifferentiated poliovirus isolates from such materials are included as potential wild poliovirus infectious materials until proven otherwise. (33) Frozen stool samples from young children during periods of endemicity are likely to have the highest levels of infectious wild polioviruses. Serum samples and cerebrospinal fluid collected for other purposes in areas where polio is endemic are not considered as potential wild poliovirus infectious materials because of the low probability of infectious poliovirus being present.

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**Box 3: Potential wild poliovirus infectious materials are defined as:**

Faeces, respiratory secretions, and environmental sewage and untreated water samples of unknown origin or collected for any purpose at a time and in a geographical area (Annex 1) where it was suspected that wild polioviruses (including VDPVs) were present, as well as products of such materials in poliovirus-permissive cells or animals, including:

- harvests untested for polioviruses and enteroviruses;
- uncharacterized enterovirus-like cell culture isolates;
- undifferentiated poliovirus isolates.

Potential wild poliovirus infectious materials may also include contaminated laboratory stocks of other viruses, particularly rhinovirus, enterovirus, and Sabin vaccine strains in laboratories that work or have worked with wild poliovirus in the past. (34, 35) Good laboratory practices require confirmation of the identity and purity of all virus stocks in the laboratory.

# Action plan for laboratory containment of wild polioviruses

The purpose of laboratory containment of wild polioviruses is to minimize the risk of reintroducing wild polioviruses from the laboratory to the community. The plan for containment is divided into three phases in recognition of the changing nature of these risks during different stages of the eradication programme. Implementation of each phase is dependent on the achievement of defined eradication goals. Phase I, Laboratory Survey and Inventory, describes the initial steps towards containment and covers the period when the number of polio-free countries and regions is increasing. Phase II, global certification, describes containment requirements that begin implementation when one year has elapsed without isolation of wild polioviruses anywhere in the world and should be in effect by the time two years have elapsed. Documentation that the conditions are in effect should be compiled during the third year in order to be submitted for global certification. Specific biosafety guidelines for the safe production and quality control of IPV produced from wild poliovirus are addressed in a separate WHO document (2). Containment requirements at the time of global certification will remain in effect as long as universal immunization recommendations remain in force. Phase III, post global certification, refers to a time in the future when post eradication data and experiences suggest to some countries the need to consider the option of discontinuing polio immunization (box 4).

Box 4: Containment and progress with global polio eradication	
Progress towards polio eradication	Containment phase
Wild poliovirus cases decreasing worldwide	I. Laboratory survey and Inventory phase
One year passes with no case reported globally	II. Global certification phase <ul style="list-style-type: none"> <li>• implementation of containment begins</li> <li>• containment completed and documentation submitted</li> <li>• global polio eradication certified</li> </ul>
Two years pass with no case reported globally	
Three or more years pass with no case reported globally	
Post global certification immunization policies established	III. Post global certification phase

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# Laboratory survey and inventory

During this phase, when the numbers of polio-free countries and regions are increasing but wild polioviruses continue to circulate somewhere in the world, countries:

1. Survey all biomedical laboratories to identify those with wild poliovirus infectious materials or potential wild poliovirus infectious materials and encourage the destruction of all unneeded materials.
2. Develop an inventory of laboratories that retain such materials and report to the regional certification commission.
3. Instruct laboratories retaining wild poliovirus infectious materials or potential infectious materials to institute enhanced biosafety level-2 (BSL-2/polio) measures for safe handling (Annex 3).
4. Plan for global certification.

National, regional, and global inventories of all institutions/laboratories with stored stocks of wild poliovirus infectious materials or potential wild poliovirus infectious materials provide the basis for achieving global laboratory containment when wild poliovirus transmission is interrupted. The four primary activities of this phase are described below.

## **1. Surveying laboratories**

The purpose of the national survey is to identify all laboratories storing wild poliovirus infectious materials or potential infectious materials. A major function of the survey is to encourage the destruction of materials that are no longer needed. The national survey is hierarchical, beginning with notification to the national government by WHO and proceeding through ministries of health and other concerned ministries to agencies, institutions, and individual laboratories. Because many laboratories that might possess such materials are outside the health sector, the completion of the national survey requires ministries of health to enlist the cooperation of other ministries, such as those of education, defence and the environment (box 5). Each country should designate a national task force and/or a coordinator for planning and implementing the multisectoral national survey and for verifying that all activities have been completed.

Many different types of laboratories may store wild poliovirus infectious materials or potential infectious materials. To identify these laboratories it may be necessary to refer to national laboratory registries, accrediting bodies, professional organizations, national and institutional biosafety networks, and other sources.

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The types of laboratories that may be storing wild poliovirus infectious materials are described below and summarized in box 5.

**Poliovirus/enterovirus laboratories:** Laboratories currently working with polioviruses, or those that have worked with polioviruses in the past, are probable sources of wild poliovirus materials. Such laboratories that conduct research or serve a diagnostic function are most likely to be found in universities or government health agencies.

**General virology laboratories:** Some virology laboratories, not necessarily identified as poliovirus laboratories, may work with wild polioviruses/enteroviruses or may have worked with such viruses in the past for diagnostic testing, research or teaching exercises. Diagnostic and public health laboratories may have stored poliovirus isolates and clinical specimens from past investigations of endemic or imported cases of poliomyelitis. Some have multiple virus strains for test controls or reference purposes. Educational institutions may hold wild polioviruses for teaching exercises. Virus research laboratories may hold poliovirus stocks or infectious materials for studies on the biological, biochemical or genetic properties of viruses. Such laboratories may be found in numerous organizations, including public health institutions, national control agencies, clinical facilities, commercial services, and research and academic institutions.

**Environmental testing laboratories:** Some environmental laboratories may have materials contaminated with wild poliovirus (sewage or water samples; Annex 1) or may hold wild poliovirus isolates as reference strains or controls.

**Industrial laboratories:** Vaccine manufacturers hold wild poliovirus strains for the production of IPV or, often, for testing the quality of OPV. There are few such production laboratories, and they are known to national regulatory authorities. WHO has developed guidelines specifically for the safe production and quality control of IPV manufactured from wild polioviruses. (2) Related companies, such as disinfectant or filter manufacturers, may use wild poliovirus to measure the effectiveness of virucidal compounds or as reference standards.

Laboratories storing potential wild poliovirus infectious materials are more difficult to identify. These materials may include a variety of clinical or environmental samples that have been collected for purposes unrelated to polio investigations, e.g. a laboratory may hold faecal samples that were collected for research on diarrhoeal disease during a period and in a geographical area of wild poliovirus endemicity.

All the above categories of laboratories may have potential wild poliovirus infectious materials. Others that may hold such materials include clinical bacteriology, parasitology, pathology gastroenterology and nutrition laboratories, which are likely to be located in hospitals (both private and government), academic institutions and the private sector. Research laboratories studying enteric diseases, cholera, parasitic infections or nutrition are of particular importance in this connection (box 5).

**Box 5: Sectors, agencies/institutions and laboratories that may possess wild poliovirus infectious materials or potential wild poliovirus infectious materials**

Types of sectors	Types of agencies or institutions	Types of laboratories
Health	Biological standards/control agencies	Virology
Education	Biomedical research institutions	Bacteriology
Defence	Universities	Parasitology
Environment	Culture collections	Gastroenterology
Agriculture	Environmental agencies	Pathology
Science and technology	(water/sewage)	Molecular biology
Sectors peculiar to country structures	Hospitals/clinics	Nutrition
	Military agencies (health/research)	Genetics
	Producers (biological/vaccines/disinfectants)	Environmental
	Public health agencies	Veterinary
	Agencies peculiar to country structures	Medical

Each laboratory should conduct a thorough search for materials that meet the definition of wild poliovirus infectious or potential infectious materials. Laboratories with wild poliovirus potential infectious materials should be asked to consider the place and date of the collection of the materials. Samples are considered polio-free immediately after the year of the last documented case in a given country (Annex 1). Experience has shown that widespread transmission ceases well before the last case is identified. The likelihood of collecting a wild poliovirus-positive specimen at random after that date is remote.

Laboratories should critically examine the need to retain any wild poliovirus materials and dispose of all such materials that serve no programmatic or research purpose. For most diagnostic tests, wild polioviruses may be replaced with OPV strains, inactivated antigens or non-polio enteroviruses (Annex 2). If wild poliovirus materials are required, only viruses readily identifiable by molecular methods should be used. Laboratories retaining wild poliovirus infectious materials or potential wild poliovirus infectious materials should be listed in national inventories and operated under biosafety level-2/polio (BSL-2/polio).

Laboratories that work with poliovirus, enterovirus, or rhinovirus, or have worked with these viruses in the past, should identify all virus stocks, reference strains, and derivatives of such viruses grown in poliovirus permissive cell cultures and replace stocks of uncertain histories or multiple passages with stocks documented to be authentic by the investigators or by an international culture collection, confirm the identities of remaining virus stocks by use of appropriate reference techniques, replace wild poliovirus diagnostic reference strains with authenticated Sabin strains (WHO may be contacted for information on sources), and destroy all remaining virus materials no longer of programmatic value.



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## 2. Developing national inventories

The purpose of a national inventory is to document the location of laboratories retaining wild poliovirus infectious or potential infectious materials, to meet the country requirements for the certification of regions as polio-free, and to maintain a current list of laboratories to be notified about initiating the appropriate containment procedures one year after detection of the last wild poliovirus.

A national inventory is an active record maintained by a national government and updated regularly. The complete inventory with supporting documents are prepared and presented to the national certification committee for review, endorsement and submission to the Regional Certification Commission as a component of national documentation for the certification of polio eradication.

National inventories of laboratories with wild poliovirus infectious or potential infectious materials are assembled in regional inventories maintained by the WHO regional offices. The inventories of all six regions constitute the global inventory maintained by WHO Headquarters.

## 3. Implementing biosafety level 2/polio

Laboratories listed on national inventories as retaining wild poliovirus infectious or potential infectious materials should operate under biosafety level 2/polio (BSL-2/polio) conditions. The purpose of the BSL-2/polio requirement is to reduce the risk of reintroducing wild polioviruses from the laboratory into the community at a time when poliovirus circulation is decreasing or no longer occurring in many areas of the world. The designation BSL-2/polio refers to standard BSL-2 conditions with additional specific requirements for wild polioviruses.

BSL-2 is described as good microbiological practices in an appropriately equipped basic microbiology laboratory. Specific requirements are described in the WHO *Laboratory biosafety manual* (2<sup>nd</sup> edition revised, 2002). (36) In brief, BSL-2 covers safe laboratory practices, appropriate disinfection, sterilization, waste disposal procedures, and the availability and use of equipment designed to reduce or eliminate hazards. A basic microbiology laboratory consists of a facility with an autoclave on site and a certified class I or class II biological safety cabinet for all manipulations with open infectious materials. A mechanical room ventilation system with inward directional airflow is desirable.

BSL-2/polio includes the following precautions specifically for laboratories holding wild poliovirus materials.

- *Operational practices:* Access to laboratories is restricted. All persons entering the laboratories, including support staff (cleaners, maintenance personnel, etc.), are immunized with IPV or OPV, depending on national policy. Accurate records on wild poliovirus stocks are maintained. All manipulations with open wild poliovirus infectious or potential infectious materials are performed using a certified class I or II biological safety cabinet.

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- *Storage:* Wild poliovirus materials are stored in secure areas to which access is limited. Freezers are locked and there is limited access to the key mechanism. A detailed current inventory of all freezer contents and documentation of all withdrawals and additions is maintained. Stored wild poliovirus materials are clearly marked as such. It is desirable that such freezers be located within the BSL-2/polio laboratory or an equivalent facility.
  - *Transfer of materials:* Great care is taken to avoid spillages and breakages when wild poliovirus infectious and potential infectious materials are moved from the freezer. All are transferred in leak-proof, unbreakable secondary containers that can be disinfected if a spillage occurs. Laboratories have standard operating procedures (SOPs) specifically for the safe transfer of materials to and from freezers. SOPs include clear instructions for responding to all spillages, breakages and accidents that may occur when materials are being transferred. (37)

BSL-2/polio requirements are summarized in box 6 and detailed in Annex 3.

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**Box 6: Additional biosafety requirements for wild polioviruses  
(BSL-2 / Polio)**

In addition to BSL-2 biosafety requirements outlined in the WHO *Laboratory biosafety manual, 2nd edition* (36) the BSL-2/polio facility incorporates the following standards.

*Operational procedures*

- Access to the laboratory is restricted.
- All persons entering the laboratory are fully immunized against polio.
- All open manipulations with wild poliovirus infectious or potential infectious materials are performed using a certified class I or II biological safety cabinet.

*Storage*

- Wild poliovirus infectious and potential infectious materials are stored in secure areas with limited access.
- Freezers and refrigerators are locked with limited access to the key mechanism and clearly marked as containing wild poliovirus materials.
- Freezer inventories are current and complete, including nature of material, volume or amount, location in freezer.
- Documentation is current on all materials, including geographical source and date of collection.

*Transfer of materials*

- All materials are transferred to and from the freezer in leak-proof, unbreakable secondary containers.
- Standard operating procedures (SOP) are established and regular training provided on responses to all spills, breakage of virus-containing vessels, and accidents where virus may have been released.

#### **4. Preparing for global certification**

Each country should establish channels for regular communication with laboratories on the national inventory to inform them periodically about progress towards the interruption of wild poliovirus transmission, the need to maintain updated inventories, and modifications of biosafety recommendations. These channels will be used later to notify laboratories of the effective date for implementing appropriate biosafety measures. Countries will have only one year after WHO notification during which to implement global certification requirements. Preparations should be made well in advance. Any country electing to retain wild poliovirus infectious and potential infectious materials should now begin to ensure that the designated laboratories meet the appropriate biosafety requirements for facilities and staff training (Annex 4).

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# Global certification

During this phase, which begins when one year has elapsed without the isolation of wild poliovirus anywhere in the world, countries:

1. Notify biomedical laboratories that poliovirus transmission has been interrupted.
2. Contact laboratories on the national inventories and instruct them to choose one of the following options:
  - render materials non-infectious for poliovirus or destroy under appropriate conditions;
  - transfer wild poliovirus infectious and potential infectious materials to laboratories capable of meeting the required biosafety standards;
  - implement biosafety measures appropriate for the laboratory procedures being performed (BSL-2/polio or BSL-3/polio);
3. Document the completion of all containment requirements for global certification.

The goal of this phase is to reduce the risk of wild poliovirus transmission from stored virus stocks and clinical materials at a time when universal immunization continues and wild polioviruses no longer circulate anywhere in the world.

## **1. Notifying laboratories when poliovirus transmission has stopped**

When one year has passed with no evidence of wild poliovirus circulation anywhere in the world, WHO will notify all countries that wild poliovirus transmission has likely been interrupted. Countries will be asked to notify the general laboratory community that wild poliovirus circulation has been interrupted and request agencies/institutions and laboratories listed on their national inventories to implement biosafety requirements for global certification no later than one year from the date of the announcement, that is, by the second anniversary of the detection of the last wild poliovirus. In the following year, countries will submit documentation to the Global Certification Commission indicating that effective containment is in place (box 4).

## **2. Implementing biosafety options**

An underlying principle of wild poliovirus laboratory containment is that most laboratories do not have a need for long-term retention of wild poliovirus infectious and potential infectious materials. The destruction of such materials is strongly encouraged. Laboratories should critically evaluate the considerable personal and institutional responsibilities inherent in retaining a virus that is no longer transmitted in nature.

Laboratories that do not implement the required containment conditions must render all wild poliovirus materials non-infectious, destroy them by autoclaving or incineration (Annex 2), or transfer them to a laboratory that meets the appropriate containment level.

By definition, no clinical materials collected during the global certification phase are infectious in respect of wild poliovirus unless the virus re-emerges or VDPV is detected. The threat of laboratory infection comes principally from stored materials collected before wild poliovirus transmission has stopped. A small number of laboratories are expected to retain wild poliovirus materials for research purposes.

It is anticipated that other research laboratories in larger institutions will wish to retain valuable collections of potential wild poliovirus infectious materials for studying other diseases. Laboratories retaining such materials should implement biosafety measures appropriate for the activities being performed (box 7). All wild poliovirus infectious materials (box 2) must be handled under BSL-3/polio conditions. All activities with potential wild poliovirus infectious materials (box 3) that involve inoculating poliovirus-permissive cells or animals, i.e. any biological system in which polioviruses replicate, must also be performed under BSL-3/polio conditions.

All other activities involving potential wild poliovirus infectious materials may be conducted safely in a certified class I or II biological safety cabinet in a BSL-2/polio laboratory (box 6). Potential wild poliovirus infectious materials may be centrifuged in the open laboratory if sealed heads or centrifuge safety cups are used and if these are only opened in a biological safety cabinet.

<b>Box 7: Global certification biosafety requirements for wild poliovirus materials</b>		
<b>Category of material</b>	<b>Laboratory activity</b>	<b>Biosafety level</b>
Wild poliovirus infectious materials (box 2)	All activities, including storage	BSL-3/polio
Potential wild poliovirus infectious materials (box 3)	Activities involving poliovirus-permissive cells or animals	BSL-3/polio
	Other activities	BSL-2/polio, in certified class I or II biosafety cabinet

Biosafety level 3/polio (the high containment laboratory) includes all BSL-2 requirements with additional emphasis on protecting personnel in adjacent areas, the community, and the environment. Specific requirements are defined for personal protective clothing, laboratory design, the use of laboratory equipment, and medical surveillance of laboratory staff. The laboratory should be separated from high-traffic areas of the building and access should be restricted to authorized personnel. Biosafety provisions must be made for air, water and materials entering and leaving the laboratory, as described in the *WHO Laboratory biosafety manual* (2nd edition revised, 2002) (36). A comparison of the major features of BSL-2 and BSL-3 is provided in box 8 and a detailed description of BSL-3/polio is provided in Annex 4.

<b>Box 8: Major features of biosafety levels 2/polio (Annex 3) and 3/polio (Annex 4)</b>		
	<b>BSL-2/polio</b>	<b>BSL-3/polio</b>
Good microbiological technique	√	√
Personnel		
• Immunized	√	√
• Medical assessment		√
• Protective laboratory clothing	√	√
Facility		
• Separation of laboratory		√
• Restricted access	√	√
• Surfaces impervious to liquids	√	√
• Sealed for decontamination		√
• Inward directional airflow		√
• HEPA exhaust filters		√
• Certified biological safety cabinet class I or II	√	√
• Autoclave on site	√	
• Autoclave in room		√
Wild poliovirus storage (box 9)	√	√
Listed on national inventory	√	√

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At the time of global certification, all laboratories with wild poliovirus infectious materials or potential wild poliovirus infectious materials must meet the appropriate biosafety standard (box 7) and implement the following (box 9):

- *Operational practices:* Access to laboratories is restricted. All persons entering the laboratories, including support staff (cleaners, maintenance personnel, etc.), are immunized with IPV or OPV, depending on national policy. Accurate records on wild poliovirus stocks are maintained. All manipulations with open wild poliovirus infectious or potential infectious materials are performed using a certified class I or II biological safety cabinet.
- *Storage:* Wild poliovirus infectious materials stored under secure conditions pose no inherent risk of transmission. Risk arises when these materials are removed from storage. They are therefore kept in locked freezers within the BSL-3/polio facility, preferably within the containment perimeter, and access is restricted. Potential wild poliovirus infectious materials are clearly marked as such, stored in locked freezers with restricted access, and are inventoried and documented. These freezers are preferably located in laboratories having a BSL-2/polio facility.
- *Transfer of materials:* As described in BSL-2/polio, a leak-proof unbreakable secondary container should be used to avoid spillages and breakages when materials are being transferred from freezers to safety cabinets. This practice is particularly important when potential wild poliovirus infectious materials are located in freezers outside the laboratory. Written laboratory procedures provide clear instructions for responding to spillages, breakages and accidents that may occur during the transfer of materials.

**Box 9: Additional biosafety requirements for global certification**

In addition to meeting either BSL-2 or BSL-3 biosafety requirements (box 7) as outlined in the WHO *Laboratory biosafety manual* (36), laboratories holding the following types of materials must implement the following to meet the requirements for global certification:

	<b>Wild poliovirus infectious materials</b>	<b>Potential wild poliovirus infectious materials</b>
Storage location	Secure area, preferably inside BSL-3/polio laboratory	Secure area inside facility
Documentation	Current documentation maintained on all materials, including: <ul style="list-style-type: none"> <li>• Geographical source and date of collection/isolation</li> <li>• Nature of collection source</li> <li>• Cell passage history</li> <li>• Genomic sequence of isolate</li> <li>• Complete composition, history, and properties of virus if research product</li> </ul>	Full and updated documentation maintained on all materials, including: <ul style="list-style-type: none"> <li>• Geographical source and date of collection/isolation</li> <li>• Nature of collection source</li> </ul>
Operational procedures	Access to the laboratory is restricted All persons entering the laboratory are fully immunized against polio All open manipulations are performed using a certified class I or II biological safety cabinet	Access to the laboratory is restricted All persons entering the laboratory are fully immunized against polio All open manipulations are performed using a certified class I or II biological safety cabinet
Security	Locked freezers and limited access to key mechanism	
Materials	Stored in leak-proof, screw-cap containers bearing a unique identification number and the name of the responsible person	
Freezer inventory	Full and updated inventory maintained, including: <ul style="list-style-type: none"> <li>• Nature of material</li> <li>• Volume or amount</li> <li>• Position in freezer</li> </ul>	
Transfer of materials	<ul style="list-style-type: none"> <li>• Leak-proof, unbreakable secondary containers</li> <li>• Specified procedures for response to spillage</li> </ul>	



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### 3. Documenting containment for global certification

Each regional certification commission must submit satisfactory documentation to the Global Certification Commission indicating that all laboratories in the region with wild poliovirus infectious materials or potential wild poliovirus infectious materials have:

- implemented appropriate biosafety conditions (BSL-2/polio or BSL-3/polio); OR
- transferred materials to WHO-designated repositories; OR
- rendered such materials non-infectious or destroyed them under appropriate conditions (1).

The documentation should include:

- a current national inventory of all laboratories retaining wild poliovirus infectious materials or potential wild poliovirus infectious materials;
- a quality assessment of the laboratory survey and inventory process;
- evidence that laboratories retaining wild poliovirus materials or potential wild poliovirus infectious materials meet the required biosafety conditions.

Detailed guidelines for assessing and documenting containment will be communicated from the Global Certification Commission.

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# Post global certification

This phase will begin after the Global Commission has certified the world as polio-free and international bodies have agreed on post-certification immunization policies. (38, 39) Global decisions on immunization policies will be based on outcomes of current research, post-eradication experiences, containment assessments and assurances that surveillance, vaccine stockpiles and emergency response plans would be adequate in the event that polio were to re-emerge. If OPV immunization is stopped, with or without universal replacement with IPV, the biosafety requirements for both wild and OPV viruses will become more stringent than those outlined in this document, consistent with the consequences of inadvertent transmission of poliovirus from the laboratory to an increasingly susceptible global community.

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# Annex 1:

## Year of last reported indigenous poliovirus case by country/territory

Country/territory	Year of last polio	Country/territory	Year of last polio	Country/territory	Year of last polio	Country/territory	Year of last polio
Afghanistan	Ongoing	Djibouti	1999 <sup>2</sup>	Libyan Arab Jamahiriya	1991 <sup>1</sup>	Saint Helena	NR
Albania	1978	Dominica	<1980	Lithuania	1972 <sup>1</sup>	Saint Kitts and Nevis	1969 <sup>1</sup>
Algeria	1996	Dominican Republic	1985 <sup>2</sup>	Luxembourg	1963 <sup>1</sup>	Saint Lucia	1970 <sup>1</sup>
American Samoa	1950s <sup>1</sup>	Ecuador	1990	Macao, SAR	1975 <sup>1</sup>	Saint Vincent and the Grenadines	1977 <sup>1</sup>
Andorra	1959 <sup>1</sup>	Egypt	Ongoing	Macedonia, TFRYR	1987 <sup>1</sup>	Samoa	1950s
Angola	Ongoing	El Salvador	1987 <sup>1</sup>	Madagascar	1997	San Marino	1982
Anguilla	1962	Equatorial Guinea	1992 <sup>1</sup>	Malawi	1991 <sup>1</sup>	Sao Tome and Principe	1983
Antigua & Barbuda	1965 <sup>1</sup>	Eritrea	<1992	Malaysia	1985 <sup>2</sup>	Saudi Arabia	1995
Argentina	1984 <sup>1</sup>	Estonia	1961	Maldives	1980 <sup>1</sup>	Senegal	1998
Armenia	1995	Ethiopia	2001	Mali	1999	Seychelles	1980s <sup>1</sup>
Australia	1972 <sup>2</sup>	Federated States of Micronesia	1970s <sup>1</sup>	Malta	1964 <sup>1</sup>	Sierra Leone	1999
Austria	1980 <sup>1</sup>	Fiji	1962 <sup>2</sup>	Mariana Islands	1960s <sup>1</sup>	Singapore	1973
Azerbaijan	1995	Finland	1985	Marshall Islands	1976 <sup>1</sup>	Slovakia	1960
Bahamas	1967 <sup>1</sup>	France	1989	Martinique	NR	Slovenia	1978 <sup>1</sup>
Bahrain	1993 <sup>1</sup>	French Guiana	1983 <sup>1</sup>	Mauritania	1999	Solomon Islands	<1972
Bangladesh Ongoing	2000	French Polynesia	1982 <sup>2</sup>	Mauritius	1980 <sup>1</sup>	Somalia	
Barbados	1967 <sup>1</sup>	Gabon	1996 <sup>2</sup>	Mexico	1990	South Africa	1989
Belarus	1964 <sup>1</sup>	Gambia	1997 <sup>2</sup>	Monaco	1964	Spain	1988
Belgium	1979 <sup>1</sup>	Georgia	1991 <sup>1</sup>	Mongolia	1993 <sup>2</sup>	Sri Lanka	1993
Belize	1981 <sup>1</sup>	Germany	1990	Montserrat	1976	Sudan	2001
Benin	2000	Ghana	2000	Morocco	1989 <sup>1</sup>	Suriname	1982 <sup>1</sup>
Bermuda	NR	Greece	1982	Mozambique	1993 <sup>1</sup>	Swaziland	1989 <sup>1</sup>
Bhutan	1986 <sup>2</sup>	Grenada	1970 <sup>1</sup>	Myanmar	2000	Sweden	1977
Bolivia	1989	Guadeloupe	NR	Namibia	1995	Switzerland	1982
Bosnia and Herzegovina	1961 <sup>1</sup>	Guam	1964 <sup>1</sup>	Nauru	1910 <sup>1</sup>	Syrian Arab Republic	1998
Botswana	1989 <sup>1</sup>	Guatemala	1990 <sup>1</sup>	Nepal	2000	Tajikistan	1997 <sup>2</sup>
Brazil	1989	Guinea	1999	Netherlands	1993	Thailand	1997
British Virgin Islands	NR	Guinea-Bissau	1999	Netherlands Antilles	1981	Togo	1999

Country/territory	Year of last polio	Country/territory	Year of last polio	Country/territory	Year of last polio	Country/territory	Year of last polio
Brunei Darussalam	1978 <sup>2</sup>	Guyana	1962	New Zealand	1962 <sup>1</sup>	Tokelau	1950s <sup>1</sup>
Bulgaria	1982	Haiti	1989 <sup>1</sup>	New Caledonia	1982	Tonga	1982 <sup>1</sup>
Burkina Faso	2000	Honduras	1989 <sup>1</sup>	Nicaragua	1981 <sup>1</sup>	Trinidad & Tobago	1972
Burundi	1999 <sup>2</sup>	Hong Kong, SAR	1983	Niger	Ongoing	Tunisia	1994
Cambodia	1997	Hungary	1969	Nigeria	Ongoing	Turkey	1998
Cameroon	1999	Iceland	1960 <sup>1</sup>	Niue	1950s <sup>1</sup>	Turkmenistan	1996
Canada	1979	India	Ongoing	Norway	1969	Turks and Caicos Islands	1977
Cape Verde	1988 <sup>1</sup>	Indonesia	1995	Oman	1993 <sup>1</sup>	Tuvalu	1936 <sup>1</sup>
Cayman Islands	1958 <sup>1</sup>	Iran (Islamic Republic of)	1997	Pakistan	Ongoing	Uganda	1996
Central African Republic	2000	Iraq	2000	Palau	1940s <sup>1</sup>	Ukraine	1996 <sup>2</sup>
Chad	2000	Ireland	1965 <sup>1</sup>	Palestine N.A.	1988	United Arab Emirates	1992 <sup>1</sup>
Chile	1975	Israel	1988	Panama	1972 <sup>1</sup>	United Kingdom	1982
China	1994	Italy	1982	Papua New Guinea	1996 <sup>1</sup>	United Republic of Tanzania	1996
Colombia	1991	Jamaica	1982	Paraguay	1985 <sup>1</sup>	United States of America	1979
Comoros	1983 <sup>1</sup>	Japan	1980	Peru	1991	Uruguay	1978 <sup>1</sup>
Congo	2000	Jordan	1988 <sup>1</sup>	Philippines	1993	US Virgin Islands	
Cook Islands	1959	Kazakhstan	1995 <sup>1</sup>	Poland	1984	Uzbekistan	1995
Costa Rica	1972	Kenya	1988 <sup>1</sup>	Portugal	1986	Vanuatu	1989 <sup>2</sup>
Côte d'Ivoire	2000	Kiribati	NR	Puerto Rico	1974	Venezuela	1989
Croatia	1990	Kuwait	1985 <sup>1</sup>	Qatar	1990 <sup>1</sup>	Viet Nam	1997
Cuba	1962 <sup>1</sup>	Kyrgyzstan	1993	Republic of Korea	1983 <sup>2</sup>	Wallis and Futuna	1972 <sup>2</sup>
Cyprus	1995	Latvia	1962 <sup>1</sup>	Republic of Moldova	1991 <sup>2</sup>	Yemen	1999 <sup>2</sup>
Czech Republic	1960	Lao People's Democratic Republic	1996	Reunion	1979 <sup>1</sup>	Yugoslavia	1996
Democratic People's Republic of Korea	1996	Lebanon	1994 <sup>1</sup>	Romania	1992	Zambia	1995
Democratic Republic of the Congo	2000	Lesotho	1987 <sup>1</sup>	Russian Federation	1996 <sup>2</sup>	Zimbabwe	1991 <sup>2</sup>
Denmark	1976	Liberia	1999	Rwanda	1999 <sup>2</sup>		

**Note:** The year of the last indigenous virologically confirmed case is used. Cases attributable to imported wild poliovirus or circulating vaccine-derived poliovirus are not reflected in this table. “Ongoing” refers to countries where wild poliovirus was still endemic in 2002 (shaded).

<sup>1</sup> Details of case unknown.

<sup>2</sup> Clinically confirmed case.

NR – not reported

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# Annex 2:

## Methods for disposal of wild poliovirus infectious materials or potential wild poliovirus infectious materials

### **Sterilization (use of autoclaves)**

The use of moist steam under pressure is the most effective method for sterilizing laboratory materials.

- All cultures and contaminated materials should normally be autoclaved in leak-proof containers, e.g. autoclavable colour-coded plastic bags, before disposal.
- Packaging should allow the penetration of steam.
- After being autoclaved the materials may be placed in transfer containers for transportation to the disposal point.
- Autoclaves should be validated in order to ensure that sterilizing conditions are fulfilled under all loading patterns.

### **Incineration**

Incineration is the method of choice for the final disposal of contaminated waste, including carcasses of laboratory animals, preferably after autoclaving. The incineration of infectious materials is an alternative to autoclaving only if the incinerator:

- is under laboratory control;
- has an efficient means of temperature control and a secondary burning chamber.

### **Final disposal**

The disposal of laboratory and medical waste is subject to various national regulations. In general, ash from incinerators may be treated in the same way as normal domestic waste and removed by local authorities. Autoclaved waste may be disposed of by off-site incineration or in licensed landfill sites.



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# Annex 3:

## BSL-2/polio biosafety requirements

**BSL-2/polio consists of the standard BSL-2 requirements as described in the *WHO Laboratory biosafety manual* with additional specific requirements for wild poliovirus:**

### **Specific requirements for wild poliovirus**

Access to the laboratory is restricted.

All persons entering the laboratory are fully immunized against polio.

All open manipulations with wild poliovirus infectious or potential infectious materials are performed using a certified class I or II biological safety cabinet.

Wild poliovirus infectious and potential infectious materials are stored in secure areas with limited access.

Freezers and refrigerators are locked with limited access to the key mechanism and clearly marked as containing wild poliovirus materials.

Freezer inventories are current and complete, including nature of material, volume or amount, location in freezer.

Documentation is current on all materials, including geographical source and date of collection.

All materials are transferred to and from the freezer in leak-proof, unbreakable secondary containers.

Standard operating procedures (SOP) are established and regular training provided on responses to all spills, breakage of virus-containing vessels, and accidents where virus may have been released.

### **Standard biosafety level 2 requirements (*WHO Laboratory biosafety manual*, 2<sup>nd</sup> edition revised):**

#### ***Access***

The international biohazard warning symbol and sign must be displayed.

Laboratory doors should be kept closed.

Children under the age of 16 years should not be allowed to enter laboratory working areas.

“No smoking” “No eating” and “No drinking” signs should be displayed clearly inside and outside the laboratory.

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### *Personal protection*

Laboratory coveralls, gowns or uniforms must be worn at all times for work in the laboratory.

Appropriate gloves must be worn for all procedures that may involve direct or accidental contact with blood, infectious materials or infected animals. After use, gloves should be removed aseptically and hands must then be washed.

Personnel must wash their hands after handling infectious materials and animals, and before they leave the laboratory working areas.

Safety glasses, face shields (visors) or other protective devices must be worn when it is necessary to protect the eyes and face from splashes, impacting objects and sources of artificial ultraviolet radiation.

It is prohibited to wear protective laboratory clothing outside of the laboratory, e.g. in canteens, coffee rooms, offices, libraries, staff rooms and toilets.

Open-toed footwear should not be worn in laboratories.

Eating, drinking, applying cosmetics and handling contact lenses is prohibited in the laboratory working areas.

Storing human foods or drinks anywhere in the laboratory working areas is prohibited.

Protective laboratory clothing is not stored in the same lockers or cupboards as street clothing.

### *Procedures*

Pipetting by mouth must be strictly forbidden.

Materials must not be placed in the mouth. Labels must not be licked.

All technical procedures should be performed in a way that minimizes the formation of aerosols and droplets. Whenever there is an increased risk of aerosolization, work should be conducted in a biological safety cabinet.

The use of hypodermic needles and syringes should be limited. They must not be used as substitutes for pipetting devices or for any purpose other than parenteral injection or aspiration of fluids from laboratory animals.

All spills, accidents and overt or potential exposures to infectious materials must be reported to the laboratory supervisor. A written record of such accidents and incidents should be maintained.

A written procedure for the clean up of all spills must be developed and followed.

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### *Laboratory working areas*

The laboratory should be kept neat, clean and free of materials not pertinent to the work.

Work surfaces must be decontaminated after any spill of potentially dangerous material and at the end of the working day.

All contaminated materials, specimens and cultures must be decontaminated before disposal or cleaning for reuse.

Packing and transportation must follow applicable national and/or international regulations.

When windows can be opened, they should be fitted with arthropod-proof screens.

### *Biosafety management*

It is the responsibility of the laboratory director (the person who has immediate responsibility for the laboratory) to ensure the development and adoption of a biosafety management plan and a safety or operations manual.

The laboratory supervisor (reporting to the laboratory director) should ensure that regular training in laboratory safety is provided.

Personnel should be advised of special hazards and required to read the safety or operations manual and follow standard practices and procedures. The laboratory supervisor should make sure that all personnel understand these. A copy of the safety or operations manual should be available in the laboratory.

When appropriate, there should be an arthropod and rodent control programme.

Appropriate medical evaluation, surveillance and treatment should be provided for all personnel in case of need, and adequate medical records should be maintained.

Baseline serum samples may be collected from laboratory staff and other persons at risk. These should be stored appropriately according to national or local guidelines. Additional specimens may be collected periodically depending on the organisms handled and the function of the laboratory.

### *Design features*

Ample space must be provided for the safe conduct of laboratory work and for cleaning and maintenance.

Walls, ceilings and floors should be smooth, easy to clean, impermeable to liquids and resistant to the chemicals and disinfectants normally used in the laboratory. Floors should be slip-resistant. Exposed pipes and ducting should be avoided where possible.

Bench tops should be sealed to the walls, impervious to water and resistant to disinfectants, acids, alkalis, organic solvents and moderate heat.

Illumination should be adequate for all activities. Undesirable reflections and glare should be avoided.

Laboratory furniture should be sturdy. Open spaces between and under benches, cabinets and equipment should be accessible for cleaning.

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Storage space must be adequate to hold supplies for immediate use and thus prevent clutter on bench tops and in aisles. Additional long-term storage space, conveniently located outside the laboratory working areas, should also be provided.

Space and facilities should be provided for the safe handling and storage of solvents, radioactive materials, and compressed and liquefied gases.

Facilities for storing outer garments and personal items should be provided outside the laboratory working areas.

Facilities for eating and drinking and for rest should be provided outside the laboratory working areas.

Hand-wash basins, with running water if possible, should be provided in each laboratory room, preferably near the exit door.

Doors should have vision panels, be self-closing and have appropriate fire ratings.

An autoclave should be available in the same building as the laboratory.

Safety systems should cover fire, electrical emergencies, emergency shower and eyewash facilities.

First-aid areas or rooms suitably equipped and readily accessible should be available.

There are no specific ventilation requirements for BSL-2 laboratories. However, consideration should be given to the provision of mechanical ventilation systems that provide an inward flow of air without recirculation. If there is no mechanical ventilation, windows should be able to be opened and should be fitted with arthropod-proof screens.

A dependable supply of good quality water is essential. There should be no cross-connections between sources of laboratory and drinking-water supplies. An anti-backflow device should protect the public water system.

There should be a reliable and adequate electricity supply and emergency lighting to permit safe exit. A stand-by generator is desirable for the support of essential equipment, such as incubators, biological safety cabinets, freezers, etc., and for the ventilation of animal cages.

There should be a reliable and adequate supply of gas. Good maintenance of the installation is mandatory.

Three aspects of waste disposal need special attention to meet performance and pollution-control requirements:

- autoclaves for the treatment of solid waste need specially designed accommodation and services;
- incinerators should be of special design, equipped with afterburners and smoke-consuming devices;
- contaminated wastewater must be decontaminated.

Laboratories are occasionally the targets of vandals. Physical and fire security must be considered. Strong doors, screened windows, and restricted issue of keys are compulsory. Other measures should be considered and applied, as appropriate, to augment security.

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### *Essential biosafety equipment*

Pipetting aids – to avoid mouth pipetting. Many different designs are available.

Biological safety cabinets, to be used whenever:

- infectious materials are handled; such materials may be centrifuged in the open laboratory if sealed centrifuge safety cups are used and if they are loaded and unloaded in a biological safety cabinet;
- there is an increased risk of airborne infection;
- procedures with a high potential for producing aerosols are used; these may include centrifugation, grinding, blending, vigorous shaking or mixing, sonic disruption, opening of containers of infectious materials whose internal pressure may be different from the ambient pressure, intranasal inoculation of animals, and harvesting of infectious tissues from animals and eggs.

Plastic disposable transfer loops. Alternatively, electric transfer loop incinerators may be used inside the biological safety cabinet (BSC) to reduce aerosol production.

Screw-capped tubes and bottles.

Autoclaves to decontaminate infectious materials.

Plastic disposable Pasteur pipettes, whenever available, to avoid glass.

Equipment such as autoclaves and biological safety cabinets must be validated with appropriate methods (usually by a certified examiner) before being taken into use. Recertification should take place at regular intervals, according to the manufacturer's instructions.

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# Annex 4:

## BSL-3/polio containment requirements

**BSL-3/polio consists of the standard BSL-3 requirements as described in the *WHO Laboratory biosafety manual* with additional specific requirements for wild poliovirus:**

### **Specific requirements for wild poliovirus**

Access to the laboratory is restricted.

All persons entering the laboratory are fully immunized against polio.

All open manipulations are performed using a certified class I or II biological safety cabinet.

All wild poliovirus materials are stored in a secure area, preferably inside the BSL-3/polio laboratory.

Current documentation is maintained on all wild poliovirus materials, including:

- geographical source and date of collection/isolation;
- nature of collection source;
- cell passage history;
- genomic sequence of isolate;
- complete composition, history, and properties of virus if research product.

Laboratory maintains a full and updated inventory of all wild poliovirus materials including:

- nature of material;
- volume or amount;
- position in freezer.

All wild poliovirus materials are stored in locked freezers with limited access to the key mechanism

All wild poliovirus materials are stored in leak-proof, screw-cap containers bearing a unique identification number and the name of the responsible person

The laboratory has written procedures for response to spillage

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### **Biosafety level 3 requirements (*WHO Laboratory biosafety manual, 2<sup>nd</sup> edition revised*):**

Biosafety level 3 includes all biosafety level 2 requirements with the following modifications:

#### ***Access***

The two-person rule should apply, whereby no individual ever works alone in the laboratory.

The international biohazard warning symbol and sign displayed on laboratory access doors must identify the microorganism(s) handled and the name of the laboratory supervisor who controls access, and indicate any special conditions for entry into the area, e.g. immunization.

#### ***Personal protection***

Laboratory protective clothing must be of the type with solid-front or wrap-around gowns, scrub suits, coveralls, head covering and, where appropriate, shoe covers or dedicated shoes. Front-buttoned standard laboratory coats are unsuitable. Laboratory protective clothing must not be worn outside the laboratory, and it must be decontaminated before it is laundered.

#### ***Laboratory design and facilities***

The laboratory should be separated from the areas that are open to unrestricted traffic flow within the building. Additional separation may be achieved by placing the laboratory at the blind end of a corridor, or constructing a partition and door or access through an anteroom or basic laboratory – biosafety level 2.

Entry for personnel must be through a vestibule (i.e. double-door entry).

Access to the laboratory area must be designed to prevent entrance of arthropods and other vermin.

Access doors must be self-closing and interlockable. A break-through panel may be provided for emergency exit use.

The surfaces of walls, floors and ceilings should be water-resistant and easy to clean. Openings in these surfaces (e.g. for service pipes) should be sealed to facilitate decontamination of the room(s).

The laboratory room must be sealable for decontamination. Air-ducting systems must be constructed to permit gaseous decontamination.

Windows must be closed, sealed and break-resistant.

A foot- or elbow-operated or automatically controlled water source at the hand-wash basin should be provided near to each exit door.

There must be a ventilation system that establishes a directional air flow from access spaces into the laboratory room. Staff must at all times ensure that proper directional air flow into the laboratory room is maintained.

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The building ventilation system must be so constructed that air from the laboratory is not recirculated to other areas within the building. Air may be HEPA filtered, reconditioned and recirculated within that laboratory. Exhaust air from the laboratory (other than from biological safety cabinets) must be discharged to the outside of the building, so that it is dispersed away from occupied buildings and air intakes. It is recommended that this air is discharged through high-efficiency particulate air (HEPA) filters.

Biological safety cabinets should be sited away from walking areas and out of cross-currents from doors and ventilation systems

The exhaust air from Class I or Class II biological safety cabinets, which will have been passed through HEPA filters, must be discharged in such a way as to avoid interference with the air balance of the cabinet or the building exhaust system. All HEPA filters must be installed in a manner that permits gaseous decontamination and testing.

An autoclave for the decontamination of contaminated waste material should be available in the containment laboratory. If infectious wastes have to be transported out of the containment laboratory for disposal, they must be transported in sealed, unbreakable and leak-proof containers according to national or international regulations, as appropriate.

Anti-backflow devices must be fitted to the water supply.

Effluents should be decontaminated before being discharged to the sanitary sewer.

### ***Biosafety management***

Medical examination of all laboratory personnel who work in biosafety level 3 containment laboratories is mandatory. This should include recording of a detailed medical history and a physical examination.

A baseline serum sample should be obtained and stored for future reference.

Individuals who are immunocompromised should not be employed in facilities with biosafety level 3 containment laboratories.

Special consideration should be given to the employment of pregnant women

After a satisfactory clinical assessment, the examinee should be provided with a medical contact card stating that he or she is employed in a facility with a containment laboratory – biosafety level 3. It is suggested that this card should include a picture of the card holder, should be wallet-sized and should always be carried by the holder.





The Department of Vaccines and Biologicals was established by the World Health Organization in 1998 to operate within the Cluster of Health Technologies and Pharmaceuticals. The Department's major goal is the achievement of a world in which all people at risk are protected against vaccine-preventable diseases.

Five groups implement its strategy, which starts with the establishment and maintenance of norms and standards, focusing on major vaccine and technology issues, and ends with implementation and guidance for immunization services. The work of the groups is outlined below.

The *Quality Assurance and Safety of Biologicals team* ensures the quality and safety of vaccines and other biological medicines through the development and establishment of global norms and standards.

The *Initiative for Vaccine Research* and its three teams involved in viral, bacterial and parasitic

diseases coordinate and facilitate research and development of new vaccines and immunization-related technologies.

The *Vaccine Assessment and Monitoring team* assesses strategies and activities for reducing morbidity and mortality caused by vaccine-preventable diseases.

The *Access to Technologies team* endeavours to reduce financial and technical barriers to the introduction of new and established vaccines and immunization-related technologies.

The *Expanded Programme on Immunization* develops policies and strategies for maximizing the use of vaccines of public health importance and their delivery. It supports the WHO regions and countries in acquiring the skills, competence and infrastructure needed for implementing these policies and strategies and for achieving disease control and/or elimination and eradication objectives.

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