U.S. National Inventory for Poliovirus Containment: Survey Guidance and Resources

The U.S. National Authority for Containment of Poliovirus (NAC), located in the Centers for Disease Control and Prevention (CDC), Center for Preparedness and Response, appreciates your participation in this survey. For most participants, the survey should take less than 10 minutes to complete, although this time will vary depending on your awareness of your inventory and the availability of needed information. It is designed to collect relevant laboratory inventory data to ensure compliance with requirements established in the World Health Organization (WHO) Global Action Plan (GAPIII), as adapted for the WHO Region of the Americas. Per GAPIII, each country is required to complete a national inventory of poliovirus-containing materials.

This survey focuses on institutions that may have poliovirus potentially infectious materials (PIM). **While you may not work with poliovirus, the virus may be present in clinical and environmental materials collected from areas where polio was endemic, or at a time when the live virus vaccine was in use, whether collected for purposes directly related to polio or not.** Researchers may be unaware that such materials may harbor poliovirus. The survey questions are designed to help you to determine if your materials are potentially infectious.

The information collected in the survey will be used to determine if a facility must register as a Poliovirus-Essential Facility (PEF) following the WHO Containment Certification Scheme (CCS). The information collected is confidential and only reported in aggregate to the WHO.

This document provides a brief overview of the survey. A comprehensive version, including the survey questions, can be requested by e-mail to poliocontainment@cdc.gov. There are six modules, each with subsections. The

survey is dynamic and your response to the questions will determine which sections of the survey you will be asked to complete. Definitions for terms used in this document and the online survey can be found in Appendix A and on the U.S. NAC website.

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for Containment of Poliovirus

Module A: Facility Information

Module A gathers information about the parent-institution, facility, or company to which your survey responses relate. Sections 1 and 2 include questions about physical address, primary funding source, general area of work, and primary/secondary work objectives. Sections 3-5 focus on the specific laboratory(s) that the survey represents and the individual who is completing the survey.

Depending on the responses provided in Module A, you may be routed to Module B: Types of Stored Material. If your responses indicate that your laboratory does not work with or store biological or environmental materials (e.g., a computational lab), the survey branching logic will route you to Module E: Key Facility Personnel and Attestation to complete the survey.

Module B: General Material Types

Module B is used to identify general biological or environmental materials common to most laboratories and worked with or stored in your specific laboratory or storage site. The categories in this module are intentionally broad but help to identify material types relevant to this survey and filter responders who have no relevant materials, thus reducing the time needed to complete the survey for many.

Note that if the clinical specimens/samples or isolates that you report in Module B: Section 1 were collected in the United States after the year 2000, it is unlikely that they contain poliovirus as the oral polio vaccine (OPV) was no longer in use at that time. As such, these materials do not fall within the scope of GAPIII. International samples and specimens are addressed in Module C of the survey. Novel poliovirus strains, nucleic acid extracted from poliovirus, and recombinant or synthetic derivatives containing poliovirus capsid sequences are considered infectious poliovirus material[1] and should be reported in Module B: Section 1.

If you are unsure whether your facility possesses any of the materials listed in Module B, select 'Unsure' or work with your facility staff or the laboratory director before continuing with the survey.

Depending on the responses given, you may be routed to Module C: Inventory of Materials. If your responses indicate that you do not possess known poliovirus infectious materials (IM), material collected outside the United States, or in the United States prior to the year 2000, the integrated branching logic will route you to Modules E and F: Key Facility Personnel and Attestation to complete the survey.

Module C: Inventory of Materials

Module C drills down on the materials reported in Module B by asking about specific material types that are at higher risk of containing poliovirus, whether they are known to contain infectious poliovirus (e.g., seed stocks, isolates) (Sections 1-2) or are regarded as PIM (Sections 3-4).

Potential infectious material includes biological specimens or environmental samples collected from areas where polio was endemic or at a time when the OPV was in use, whether those materials were collected for purposes directly related to polio or not. This includes materials such as human respiratory secretions, fecal specimens, sewage, wastewater, standing water, etc. Historical domestic and international specimens often fall into these categories. Additionally, PIM cultured in certain cell lines in order to isolate other viruses of interest may have unintentionally amplified poliovirus; therefore, respiratory or enteric viral isolates obtained from PIM specimens may also be considered PIM. See Appendix C for information about poliovirus susceptible/sensitive cell lines and animals.

It is highly recommended that you take these next steps prior to beginning the survey. In Module C: Section 3, it is critical that you use the WHO Country and Territory-Specific Poliovirus Data table (WHO table) to determine which, if any, poliovirus serotype may be contained in your samples. If wild poliovirus (WPV) was circulating at the time and location that your samples were collected, the table will help you to determine which serotype to report. Like the country table, the trivalent Oral Polio Vaccine (tOPV) table is used to determine if tOPV was in use at the time of collection and which serotype your samples could contain. See the instructions below on using the WHO Country-Specific data table and tOPV table.

[1] World Health Organization. (2014). Global action plan III: WHO global action plan to minimize poliovirus facility-associated risk. Geneva, Switzerland: World Health Organization; available at http://polioeradication.org/wp-content/uploads/2016/12/GAPII_2014.pdf

Using the WHO Tables to Determine PIM WPV Serotype

To use the WHO table, identify the country in which your sample was collected. Compare the year of collection to the date provided for each wild poliovirus serotype (WPV1, WPV2, WPV3). If your collection date falls at or before the date indicated for that column, those materials are considered potentially infectious for that serotype (see example below). Continue working through each of your sample collections making note of serotype indicated. Return to the survey, select 'Yes' for each applicable material type.

Example: Respiratory samples collected in Venezuela in 1986 may contain WPV types 1 and 3 but are unlikely to contain WPV2 since the last documented case of wild type 1 was seen in 1989, type 2 in 1972, and type 3 in 1988.

Please note that the World Health Organization (WHO) maintains this table, not CDC or the U.S. NAC. Until updated information is provided by WHO, this will remain the standard for assessing PIM.

Using the tOPV Table to Determine PIM OPV Serotype

To use the tOPV table, identify the country in which your sample was collected. Compare the year of collection to the year provided. If your collection date falls within or before the date indicated, those materials are considered potentially infectious for Sabin/OPV types 1, 2, and 3 (see example below). Continue working through each of your sample collections making note of serotype identified. Return to the survey, select 'Yes' for each applicable material type.

Example: Fecal samples collected in Thailand in 2012 may contain OPV1, 2, and 3 as tOPV was in use until 2016.

Poliovirus grows in nearly all human and monkey cell lines, in addition to mouse L cells (L20B, Lα) that express the human poliovirus receptor (CD155). If you indicate having any infectious or potentially infectious materials in Module C, you will be asked if any of those materials were inoculated into cells or animals susceptible to poliovirus. A list of cell lines and animals susceptible to poliovirus can be found on the U.S. NAC website: Appendix C.

Depending on the responses provided in Module C: Sections 1 and 3, you may be asked to complete sections 2 and 4, respectively, to indicate how much of each material type is maintained at your facility. The number of vials/containers is reported in broad ranges (e.g., 1-99, 100-999) and a specific vial count is not required.

Important! The 'Untyped/Unknown' option in Module C: Sections 2 and 4, should **ONLY** be used in situations where the collection date or location are unknown. Unless determined otherwise, such samples are considered PIM**.**

If your responses indicate that you possess relevant poliovirus material, you will be routed to Module D: Disposition of Materials. However, if your responses indicate that you do not possess known poliovirus infectious material or potentially infectious materials then you will be routed to Modules E and F: Key Facility Personnel and Attestation to complete the survey.

Module D: Disposition of Materials

Questions in Module D ask about the materials reported in Module C and what your facility intends to do with those materials. Since serotypes were determined in Module C, you will be able to indicate your intent to destroy, inactivate, transfer, and/or retain materials by specific serotype. Facilities are strongly encouraged to destroy any unneeded materials.

Autoclaving and incineration are the preferred destruction methods for poliovirus infectious and potentially infectious materials. Additional information about these destruction methods for poliovirus can be found on the U.S. NAC website.
If other means of destruction are to be used, contact the U.S. NAC (poliocontainment@cdc.gov) prior to destruction.

If you indicate an intent to destroy material, you will be contacted by a representative of the U.S. NAC and asked to complete a material destruction attestation. If you intend to retain materials (e.g., WPV2/3, VDPV2/3, OPV2, and unknown IM) identified in GAPIII as part of the poliovirus containment scheme, you will be contacted by a U.S. NAC representative to discuss the PEF certification process.

If you intend to destroy materials after your current work is complete or after eradication of wild type 1 has been declared, please select the 'Retain' option in Module D to prevent the U.S. NAC from requesting a material destruction attestation form from you. Use the notes field within each section to provide details about your intent to retain, transfer, inactivate, or destroy materials.

An important note about nucleic acids, poliovirus nucleic acid is RNA, cDNA, and total nucleic acid extracted from poliovirus infectious materials (e.g., a virus isolate) or PIM (e.g., stool, respiratory specimen, sewage) using methods demonstrated to inactivate poliovirus, or synthesized RNA or cDNA (e.g., cDNA clone, synthetic transcript). Poliovirus nucleic acid can be handled outside of poliovirus containment under the condition that these materials will not be introduced into poliovirus-permissive cells or animals with or without a transfection reagent, except under appropriate containment conditions as described in GAPIII Annex 2/3. While nucleic acid containment is not required under GAPIII[2], reporting of poliovirus nucleic acid is required as part of the national inventory.

Modules E and F: Key Facility Personnel and Attestation

All survey participants are required to complete these modules. Please be sure to click the 'Submit' button at the end of the survey to send your responses to the U.S. NAC as the results will not be reported until the button is clicked.

Appendix A. Definitions

The definitions given below apply to the terms as used in the Global Action Plan III (GAPIII) standard or the PIM guidance.

Circulating VDPV (cVDPV)	VDPV isolates for which there is evidence of person-to-person transmission in the community.
Global Action Plan III (GAPIII)	The WHO global action plan to minimize poliovirus facility-associated risk after type-specific eradication of wild polioviruses and sequential cessation of OPV use (GAPIII). The 3rd edition of the Global Action Plan (GAPIII) aligns the safe handling and containment of poliovirus infectious and potentially infectious materials with the WHO Endgame Strategy and replaces both the 2009 draft version of the 3rd edition and the 2nd edition of the WHO global action plan for laboratory containment of wild polioviruses.
Inactivation	Procedures that render PV non-infectious and unable to grow or replicate in the absence of transfection reagents (*e.g.,* transfection) or cellular manipulation (*e.g.,* electroporation). Procedures to inactivate PV may include, but are not limited to, nucleic acid or protein extractions, specimen fixations (*e.g.,* formalin, acetone), irradiation, heat, or enzymes (*e.g.,* lysozymes).
Inactivated Poliovirus Vaccine (IPV)	The inactivated poliovirus vaccine was developed in 1955 by Salk and Youngner. IPV is a killed-virus vaccine and is administered by injection.
Infectious materials (IM)	**Wild Poliovirus/Vaccine-derived Poliovirus (WPV/VDPV)** • 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;

[2] World Health Organization. (2017). Containment Advisory Group: CAG 2 November 2017 Meeting Report; available at http://polioeradication.org/wp-content/uploads/2018/02/poliovirus-containment-advisory-group-meeting-20171130.pdf

Infectious materials (IM) (cont')	• 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 [2], 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 wild poliovirus. **OPV/Sabin** • 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; • Fecal 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 [4, 6] • Cells persistently infected with poliovirus strains whose capsid sequences are derived from OPV/Sabin strains.[5, 6]
Nucleic acids	Full-length [i] 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 specimen, sewage) using methods demonstrated to inactivate poliovirus, or synthesized RNA or cDNA (*e.g.,* cDNA clone, synthetic transcript). Poliovirus nucleic acid can be handled outside of poliovirus containment under the condition that these materials will not be introduced into poliovirus permissive cells or animals (as defined in GAPIII and in the "*Guidance for non-poliovirus facilities to minimize risk of sample collections potentially infectious for polioviruses*") with or without a transfection reagent, except under appropriate containment conditions as described in GAPIII Annex 2 or Annex 3.[7] Note: WHO has exempted full-length PV nucleic acids from GAPIII containment. However, WHO does require that full-length PV nucleic acids are included as part of the facility and national inventories.
Oral polio vaccine /Sabin	Attenuated poliovirus strains (approved for use in oral polio vaccines by national regulatory authorities, principally Sabin strains).[6] Also called 'Sabin vaccine', OPV contains live, attenuated (weakened) poliovirus strains. OPV formulations include: • Trivalent OPV (tOPV) contains all three serotypes of Sabin strains (1 + 2 + 3); use of tOPV ended in April 2016 • Bivalent OPV (bOPV) contains Sabin strains 1 + 3; as of April 2016, only bOPV is used routinely • Monovalent OPV (mOPV) contains only one serotype of Sabin strain
Poliovirus (PV)	A picornavirus consisting of three serotypes: 1, 2 and 3; protective immunity is type-specific. Poliovirus serotypes are further subdivided into wild (circulating in nature) and Sabin strains (attenuated strains used for oral polio vaccines). Poliovirus types 2 and 3 have been eliminated in the wild. In this current stage of polio eradication, only type 1 wild poliovirus continues to circulate in endemic areas. It is highly infectious and causes paralytic polio.
Potentially infectious materials	• Fecal or respiratory secretion samples and their derivatives (*e.g.,* stool suspensions, extracted nucleic acids, etc.) collected for any purpose in a geographic area where WPV/cVDPV is present or OPV is being used at the time of collection

Potentially infectious materials (cont')	• Products of such materials (above) from PV-permissive cells or experimentally infected polio-susceptible animals; • Uncharacterized enterovirus-like cell culture isolates from human specimens from countries known or suspected to have circulating WPV/VDPV or use of OPV at the time of collection; • Respiratory and enteric virus stocks derived from PV PIM and handled under conditions conducive to maintaining the viability or enabling the replication of incidental PV; and • Environmental samples (*i.e.,* concentrated sewage, wastewater) collected from areas known or suspected to have circulating WPV/VDPV or use of OPV at the time of collection.[8]
Sample	1) any material--biological, clinical or environmental sample – taken as a representation of a whole, used for analysis or medical diagnosis. 2) an unknown for which an assay is testing for an outcome.
Specimen	See definition for 'Sample'
Vaccine derived poliovirus (VDPV)	Classified with wild polioviruses and usually demonstrate 1–15% sequence differences from the parental 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).
WHO Regions	WHO Member States are grouped into six WHO regions: Africa, Americas, South-East Asia, Europe, Eastern Mediterranean, and Western Pacific.

[1] For U.S. facilities, PV derivatives must contain a complete full-length WPV capsid sequence to meet the WPV IM definition.

[2] Expert panel will be determined by WHO.

[3] For U.S. facilities, PV strains must contain a complete full-length WPV capsid sequence to meet the WPV IM definition.

[4] For U.S. facilities, PV derivatives must contain a complete full-length OPV/Sabin capsid sequence to meet the OPV/Sabin IM definition.

[5] For U.S. facilities, PV strains must contain a complete full-length OPV/Sabin capsid sequence to meet the OPV/Sabin IM definition.

[6] WHO Global Action Plan III

[7] WHO Containment Activity Group, Report of the Second Meeting of the Containment Advisory Group, November 2017

[8] WHO *Guidance to minimize risks for facilities collecting, handling, or storing materials potentially infectious for polioviruses*

External Resources

Visit the U.S. NAC Website https://www.cdc.gov/cpr/polioviruscontainment/NIPC.htm or polioeradication.org for the following resources:

- Country or Territory-Specific Poliovirus Data (direct link to WHO site)
- Guidance for Potentially infectious poliovirus materials (PIM guidance) (direct link to WHO site)
- PIM frequently asked questions (direct link to WHO site)

Thank you for your support of the global poliovirus eradication and containment effort!

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