Laboratory Containment of Poliovirus in the United States Phase II (Poliovirus Type 2)

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Outline

• Background
• Why PV2 Containment now?
• Previous 2002-03 Survey
• Critical role of US in Global Containment
• What DHHS is doing now for Containment
• US NPCC approach to Containment
• Internal CDC Survey
• External US Facility Survey
• Findings to date
• Lessons learned
• Challenges
• Next steps
Last WPV Cases by Serotype

- **USA**
  - WPV2: before 1965 (indigenous)
  - WPV3: 1968 (indigenous)
  - WPV1: ~1970 (indigenous); 1979 (imported)

- **Americas**
  - WPV2: 1989, Peru (indigenous)
  - WPV3: 1990, Mexico (indigenous)
  - WPV1: 1991, Peru (indigenous)

- **Global**
  - WPV2: **October 1999**, India (indigenous)
  - WPV3: November 2012, Nigeria (indigenous)
  - WPV1: 22 December 2015, Pakistan (indigenous)
WPV2 and VDPV2 Cases and Infections

• Global Certification Commission certified WPV2 eradication on 20 September 2015

• VDPVs (vaccine-derived polioviruses) are genetically divergent phenotypic revertants of Sabin OPV strains (“feral” OPV viruses)

• VDPVs are phenotypically equivalent to WPVs
  • GAPIII Containment recognizes this equivalence

• Type 2 circulating VDPVs (cVDPV2) have repeatedly emerged since 2000
  • ~85% of cVDPVs are cVDPV2; ~95% since 2006
  • cVDPV2 has emerged and caused outbreaks in 24 countries
  • >1 M PV2 infections since 2000 from cVDPV2

• Type 2 immunodeficiency-associated VDPVs (iVDPV2) represent ~65% of total (n ~110) since 1961
## Wild Poliovirus & cVDPV Cases$^1$, Previous 12 Months$^2$

<table>
<thead>
<tr>
<th>Country</th>
<th>Wild poliovirus</th>
<th>cVDPV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Onset of most</td>
<td>Onset of most</td>
</tr>
<tr>
<td></td>
<td>recent case</td>
<td>recent case</td>
</tr>
<tr>
<td></td>
<td>Total WPV1</td>
<td>Total cVDPV*</td>
</tr>
<tr>
<td>Guinea</td>
<td>NA</td>
<td>0</td>
</tr>
<tr>
<td>Nigeria</td>
<td>NA</td>
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</tr>
<tr>
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</tr>
<tr>
<td>Pakistan</td>
<td>22-Dec-15</td>
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<td>18</td>
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<td>EMR</td>
<td>22-Dec-15</td>
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<td>Myanmar</td>
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<td>05-Oct-15</td>
</tr>
<tr>
<td>Global</td>
<td>22-Dec-15</td>
<td>62</td>
</tr>
</tbody>
</table>

*Excludes viruses detected from environmental surveillance.

*Onset of paralysis 27 January 2015 – 26 January 2016

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* cVDPV1 in Madagascar, Ukraine, Laos, cVDPV2 in all other countries.
NA: most recent case had onset of paralysis prior to rolling 12 months.

Data in WHO HQ as of 26 January 2016
Global Action Plan ("GAP III")

- WHO Global Action Plan to *minimize* poliovirus *facility-associated risk* after type-specific eradication of wild polioviruses and sequential cessation of OPV use
- Based on risk assessment and risk mitigation
- Endorsed by World Health Assembly, May 2015
- Survey/inventory of materials
- Type-specific, phased implementation
  - PV2 in 2016
  - PV1 and PV3 possibly as soon as 2019
- All "infectious" and "potentially infectious" poliovirus materials requested to be inventoried by end 2015
- Virus-specific: WPV/VDPV vs. OPV/Sabin
- Reduce number of facilities handling poliovirus to minimum

Or *google* “gap iii polio”
Phases of GAPIII

Phase I: Global Coordination Readiness
- Phase II: Poliovirus Type 2 Containment Period
  - IIa: Wild poliovirus containment in essential laboratories
    - OPV2 withdrawal
  - IIb: Vaccine-derived type 2 poliovirus containment in essential facilities
    - Certified safe handling of new samples containing potentially poliovirus infectious material
Phase III: Long-term Poliovirus Containment
- IIIa: Final containment of all wild poliovirus
  - IIIb: Final containment of all vaccine-derived poliovirus

- Essential facilities holding WPV
  - Inventory Destruction
  - Preparation for Containment
  - Certification
- Essential facilities holding OPV/Sabin only
  - Inventory Destruction
  - Preparation for Containment
  - Certification
- Non-essential facilities
  - Destruction/
  - Safe handling
  - Collection 1991 or before **
  - Adoption of safe measures
  - 1992 – July 2016***

No containment
- Adoption of safe handling measures
- Containment of all WPV
- Final containment of all WPV
What Does “Containment” Mean?

• **Destroy** (and document): Autoclave, incinerate

• **Transfer**: To an “Essential” Laboratory Facility

• **Contain**: Become an “Essential” Laboratory Facility
  • Work with materials in appropriate containment space
Poliovirus “Infectious Materials”

- Presence of poliovirus confirmed and storage consistent with maintaining infectivity (stored at or below –20°C)
- Virus isolates identified as poliovirus by
  - Antigenic typing
  - Nucleic acid hybridization
  - rRT-PCR
  - Sequencing
- Specimens from person known to be infected
  - Example: stool from which a poliovirus isolate was obtained
- Specimens from infected experimental animals
  - Non-human primates
  - PVR-Transgenic mice
Poliovirus “Potentially Infectious Materials”

- Presence of poliovirus unknown but collected in a *place and time* where WPV or cVDPV was circulating or OPV was used
- Storage consistent with maintaining infectivity (stored at or below –20°C or stored for less than one year at +4°C)
- Includes fecal specimens, sewage samples, or respiratory samples, extracted nucleic acid
- Working on risk assessment/management/mitigation language to minimize disruption in non-polio labs, especially for respiratory samples and extracted nucleic acid, which should be low risk

Containment applies to *all* laboratories, not just polio labs (and not just virology/microbiology labs)
Why PV2 Containment Now? The tOPV to bOPV Switch; April 2016 (1)

• Continued use of tOPV (types 1, 2, and 3) has become inconsistent with polio eradication

• The GPEI increased use of bivalent OPV (types 1 and 3) to reduce interference by OPV2
  • Focused on eradication of WPV1 and WPV3
  • tOPV primarily used in routine immunization
  • Routine immunization rates remain low in many settings
  • tOPV campaigns became less frequent
  • cVDPV2 emergences became increasingly frequent

• Synchronized global tOPV to bOPV switch scheduled for April 2016 in countries using OPV

• At least one dose of IPV shall be used worldwide to maintain immunity to PV2

• No tOPV shall be given anywhere after April 2016
Why PV2 Containment Now? The tOPV to bOPV Switch; April 2016 (2)

- Excretion of OPV-related viruses expected to continue for ~3 months (until end-July 2016)
- Very little OPV2-related virus should be detected thereafter
- Apart from prolonged VDPV2 excretors, the main source of PV2 for reintroduction into the community would be the laboratory and vaccine manufacturers
- Similar considerations apply after total OPV cessation
- GAPIII addresses risks from WPV, VDPV, and OPV
- PV2 is top priority
  - Survey covers all three serotypes; sets stage for full Containment
  - Infectious materials can be identified by serotype
  - Potentially infectious, especially for OPV/Sabin, usually not identifiable by serotype
- GAPIII remains a work in progress
Critical Role of US in Global Containment

• 2002–03 US survey and subsequent global surveys found that 34% of all facilities storing WPV infectious or potentially infectious materials were in US
• CDC: Largest WHO Global Polio Reference Laboratory
• Many leading poliovirus research laboratories in US
• No poliovaccine production; ongoing vaccine testing
• Risks of poliovirus spread from US facilities low
  • High IPV coverage rates
  • Good sanitation/hygiene
  • But risk is not zero!
• Risk is much higher in developing country settings
  • cVDPV outbreaks underscore ongoing risk
• US must take leading role in implementing poliovirus Containment
What DHHS is Doing Now for Containment (1)

• Established Office of National Poliovirus Containment Coordinator (NPCC), September 2015
  • Based at CDC; logistical support primarily by CDC
  • Reports to NCC, through Office of Assistant Secretary for Health (OASH), through National Vaccine Program Office (NVPO)

• NPCC responsible for 2015–16 US National Survey

• NPCC Office includes
  • NPCC: Dr. Olen Kew, Technical POC, named 25 September 2015
  • National Poliovirus Containment Program Manager
  • Data Manager

• CDC Epidemiologist: Supported launch of surveys and coordinates with Programmer

• CDC-based Programmer: Set up and support web-based survey and data entry system
What DHHS is Doing Now for Containment (2)

- NVPO (Dr. Bruce Gellin) co-signed with NPCC a letter to Secretaries of key US Government Departments requesting support for Containment
- CDC developed a web-based survey instrument modified from WHO/PAHO template
- Two slightly different survey instruments were distributed
  - Internal CDC survey
    - Sent to 149 laboratories on 14 December 2015; requested return by 31 December 2015
  - External survey
    - Sent to 109 laboratories on 22 December 2016; requested return by 12 January 2016
    - Sent to Federal, academic, industrial, state and local government, and hospitals
    - Top-tier labs identified by results of 2002–03 survey
    - Very highest-tier labs known to have recently stored WPV2 were contacted directly by email and phone in addition to deployment of survey
U.S. Poliovirus Containment Program
2015 2016
As of: January 26, 2016

Organizations
Karen Fowler’s 60-day detail ended
Lines of Authority, Org and Admin Structure, Appointment of NPCC

Staffing / Contracting
Project Mgr., Data Mgr., Policy Communications, Public Health Analyst(2), NPCC Olen Kew

Survey Development and Distribution
Survey Content PDF Pilot Elec. Pilot Internal Survey External Survey

Database Environment Update
Update Data Model, History Load, Facilities Lit Search, Standard Input Format

Communications and Tracking
WHO Alignment, Key Messaging, Tools, Email Account, Website

Additional Program Iterations

Ongoing Database Analysis
Original WPV2 Containment Target Date

OPV2 Containment Target Date

Process Refinement

Post Delivery
Ongoing Tools Usage of Polio Email Account and Website

NCC Meeting

Poliovirus Containment receives and reviews survey results

Karen Fowler’s 60-day detail ended
US NPCC Approach to Containment (1)

• Distribution of survey was prioritized by estimated risk
  • WPV2/VDPV2 infectious materials to be contained first
  • WHO target date of 31 December 2015 not achievable
  • Requested return ASAP from top-tier labs
  • Sent request directly to Laboratory Directors
    • Personal letters/emails to close colleagues
  • Facilities storing WPV2/VDPV2 potentially infectious materials will be second priority

• OPV2-related materials to be contained before 1 August 2016
  • Facilities storing OPV2/Sabin 2 infectious materials are third priority
  • Facilities storing OPV/Sabin potentially infectious materials will be fourth priority

• Priority categories will overlap in many facilities
  • Opportunity to contain all PV and be removed from list

• Potentially infectious materials will be prioritized by risk
  • Highest risk assigned to stool material, sewage
Surveys will be launched in successive waves prioritizing from highest to lowest estimated risks.

Containment is an ongoing process:
- Immediate goal: PV2 Containment in 2016
- Overall goal: All poliovirus containment (~2019)

Analysis of results from internal CDC survey (especially) and first round of external survey will guide priorities for subsequent survey rounds:
- What other external laboratories should be contacted?

Will take a collaborative approach as described in Introduction to GAPIII:
- Will continue to work with Laboratory Directors

Will request assistance of Institutional Biosafety Office Directors for further follow-up:

May request additional high-level OASH/DHHS assistance as needed.
Structure of 2015 Electronic Surveys

- Modular Organization
  - A. General Information
    - Institution, lab, who filled out the survey, capacity to store samples
  - B. Type of Stored Samples or Specimens
    - Specimen types, whether from place/year of interest
  - C. Specification and Inventory Information
    - Infectious and potentially infectious materials, estimated number
  - D. Disposition of Materials
    - Decision to destroy, inactivate, or transfer
  - E. Attestation Statement

- Appendix A: Countries/years of last WPV, by type, and last use of tOPV
- Appendix B: Definitions
Internal CDC Survey (1)

- CDC is the largest facility storing poliovirus infectious and potentially infectious materials
- Containment receives strong institutional support
- The Polio and Picornavirus Laboratory Branch (PPLB) within the Division of Viral Diseases is the major WHO Global Polio Reference Laboratory
  - Contains the largest poliovirus collection in the world, including
    - WPV2 isolates dating from the 1950s to 1999
    - cVDPV2 isolates through 2015
    - OPV2-related isolates to present
    - Poliovirus-infectious and potentially infectious materials from the US and abroad
- Other CDC laboratories store poliovirus potentially infectious materials
  - Historical US specimens; international specimens up to present
- 140 of 149 laboratories (94%) completed the survey by 28 January 2016
• Only laboratories within the Polio and Picornavirus Laboratory Branch (PPLB) reported retaining WPV2/VDPV2 infectious materials

• Only PPLB and the CDC Viral Gastroenteritis Laboratory reported storing OPV2/Sabin 2 infectious materials

• Nine (9) laboratories reported storing WPV2 potentially infectious materials
  • Laboratories handling enteric specimens
    • PPLB
    • Gastroenteritis and Respiratory Virus Laboratory Branch
  • Laboratories handling respiratory specimens
    • Measles, Mumps, Rubella, and Herpesvirus Laboratory Branch
    • Influenza Division Laboratories
    • Bacterial Meningitis and Vaccine-Preventable Diseases Branch

• Ten (10) of these laboratories (except Bacterial Meningitis) reported storing OPV/Sabin potentially infectious materials
CDC Polio Lab (PPLB) Compliance

- All WPV2/VDPV2 were moved to a BSL-3 containment laboratory
- The laboratory is in compliance with GAPIII guidelines
- Vials retained by Polio Molecular Epidemiology Team
  - 2664 VDPV2 and OPV2/Sabin 2 from environmental samples
  - 2358 WPV2 and VDPV2 isolates from AFP cases
  - 56 VDPV2 transfected cells
- Vials retained by Polio Vaccine Development Team
  - 1857 WPV2 (primarily MEF-1 and derivatives; some VDPV2)
- 178,615 vials were autoclaved by 31 December 2015
  - NPEVs
  - OPV1, 2, and 3
  - Potentially infectious negative stool specimens
  - Specimens for years 1955-2007; will complete by April 2016
External US Survey

• CDC sent surveys to Directors of 109 top-tier external laboratories identified in 2002–03 survey

• Timeline of CDC external survey
  • Launch: 22 December 2015
  • Requested due date: 12 January 2016

• 37 of 109 (34%) external laboratories have completed the survey as of 28 January 2016

• Among the 37 external laboratories that completed the survey by 28 January 2016

• Six (6) report storing WPV2 infectious materials
  • Academic: 3
  • Government Public Health: 1
  • Industrial: 1
  • Biomedical research: 1

• Four (4) report storing OPV2/Sabin2 infectious materials
“Essential” vs. “Non-Essential” Facilities

• Essential: It is essential that facility retains live poliovirus materials
  • Vaccine (IPV and OPV) manufacturers
  • Vaccine testing laboratories (QC, serologic studies)
  • Key reference laboratories
  • Key laboratories performing essential research to directly inform endgame and post-eradication decision-making

• Non-essential: It is not essential that facility retains live poliovirus materials

• Diagnostic labs—can perform diagnostics regardless of specimen source
  • Global Polio Laboratory Network (GPLN) will continue routine diagnostic work under BSL-2 conditions
  • Detection of OPV viruses or VDPV implies presence in community; laboratory does not contribute significant additional risk
  • GPLN continues shift to all-molecular detection methods
Technical Requirements for Containment in Essential Facilities

- Biorisk Management
- Poliovirus inventory and information
- General safety
- Personnel and competency
- Good microbiological technique
- Clothing and personal protective equipment
- Human factors
- Healthcare
- Emergency response and contingency planning
- Accident/incident investigation
- Facility physical requirements
- Certification
- Decontamination, disinfection, and sterilization
- Transport procedures
- Security
- Certification
Lessons Learned

• Mid-December is not the best time to launch a survey due by the end of the year!
• High response rate at CDC result of strong institutional support
• Importance of regular follow-up
• Absence of statutory authority could limit compliance outside of Federal Government facilities
• Legitimate concerns by non-polio laboratories (laboratories handling and storing enteric and respiratory specimens) must be addressed by WHO, PAHO, and NPCC
• Effective engagement with lab directors, clear communication of overarching goals, and collaborative problem-solving are essential
• Many non-polio labs remain unaware of Containment
• Containment taps reservoir of good will toward polio eradication
• Awareness, a major objective of Containment, coupled with good microbiological practice, can mitigate risks
• Poor specimen records in many labs impede survey completion
Challenges (1)

• GAPIII is defined as an evolving document
• Some interpretations at WHO/HQ of GAPIII requirements and processes are far too prescriptive
• High-risk infectious materials and low-risk potentially infectious materials (such as respiratory specimens, nucleic acids) are grouped together for strict Containment
• Overly strict interpretation of GAPIII will impede compliance
• WHO is aware of these challenges and will empanel an expert Technical Advisory Group to help guide way forward
• Once clear, achievable guidelines are established for potentially infectious materials, we can contact Institutional Biosafety Office Directors for further assistance
• Process for issuing Certificates of Participation incompletely defined
Challenges (2)

• Potentially infectious materials, especially of OPV/Sabin variety, present challenges for outreach

• Respiratory virology/microbiology labs have particular concerns about how poliovirus Containment might adversely impact their vital work

• Academic labs, with frequent student turnover, present special challenges to specimen management and containment

• Absolute poliovirus containment is not feasible
  • Undetected iVDPV excretion is likely to continue for some time
  • Poliovirus can be easily prepared by synthetic biology
    • GenBank sequence data exists in perpetuity

• The goal is major reduction of risk, which is feasible, if colleagues are constructively engaged
Next Steps for US External Survey

• Follow up on first-wave external surveys
• Internal CDC survey and results from top-tier labs will cover the large majority of labs thought to store WPV2/VDPV2
  • Containment of these viruses will sharply reduce PV2 risk
• Analysis of results from internal CDC survey (especially) and first round of external survey will guide priorities for subsequent survey rounds
• Launch successive survey waves, prioritizing from highest to lowest estimated risks
• Challenge: Potentially infectious materials
  • Non-poliovirus labs, non-virus labs are not generally aware of poliovirus containment
  • Many store potentially infectious materials
  • Enteric virology/microbiology labs would have the next highest-risk specimens
  • Respiratory specimens carry much lower risk
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