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

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Advisory Committee on Immunization Practices Meeting

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Courtesy Mark Papania/CDC

Outline

- Background
- WHO Global Action Plan (GAPIII)
- Role of U.S. in Global Containment
- U.S. National Certification Committee
- Previous 2002–03 U.S. National Survey
- 2015–16 U.S. National Survey
- U.S. NPCC approach to Containment
- Internal CDC Survey
- External U.S. Facility Survey
- Findings to date
- Challenges

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, 2016: 17 cases; only two endemic countries
    - Pakistan, 11 cases (most recent 26 April)
    - Afghanistan, 6 cases (most recent 29 May)

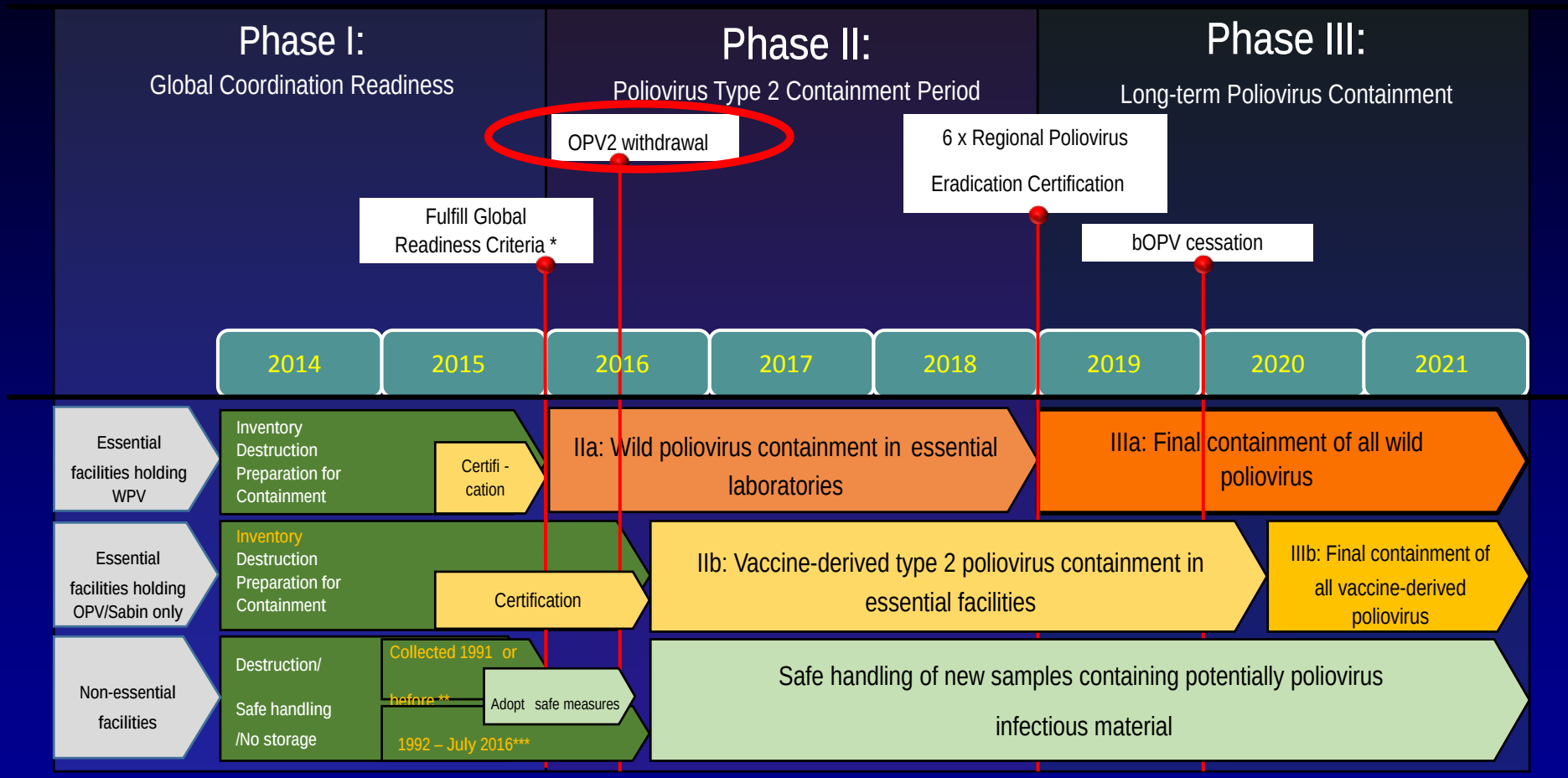
Global Action Plan ("GAP III")

- 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

http://www.polioeradication.org/Portals/0/Document/Resources/PostEradication/GAPIII_2014.pdf

Or *google* "gap iii polio"

Phases of GAPIII



- 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

Role of U.S. in Global Containment

- 2002–03 U.S. survey conducted by Dr Walter Dowdle
  - U.S. had 34% of all facilities storing WPV infectious or potentially infectious materials
- CDC: Largest WHO Global Polio Reference Laboratory
- Many leading poliovirus research laboratories in U.S.
- No poliovaccine production; ongoing vaccine testing
- Risks of poliovirus spread from U.S. facilities low
  - High IPV coverage rates
  - Good sanitation/hygiene
  - But risk is not zero!
- Risk is much higher in developing country settings
- U.S. has responsibility to take leading role in implementing poliovirus containment
- U.S. containment activity reports to U.S. National Certification Committee (NCC)
- NCC reports to Regional Certification Commission (RCC)
- RCC reports to Global Certification Commission (GCC)

U.S. NCC Membership

- NCC Secretariat: Task Force for Global Health, Decatur, GA
- NCC Members
  - Chair: Kenneth I. Berns, MD, PhD, Distinguished Professor Emeritus, Molecular Genetics and Microbiology, University of Florida
  - Charles Brokopp, DrPH, Laboratory Director, Wisconsin State Laboratory of Hygiene
  - Megan Davies, MD, Acting State Health Director, State Epidemiologist and Chief, North Carolina Division of Public Health
  - Joseph Kanabrocki, PhD, CBSP, Associate Vice President for Research Safety, University of Chicago
  - Ruth Lynfield, MD, State Epidemiologist and Medical Director, Minnesota Department of Health
  - José Romero, MD, FAAP, Chief, Pediatric Infectious Diseases; Director, Clinical Trials Research, Arkansas Children's Hospital Research Institute
  - Dominica (Dee) Zimmerman, University of Texas Medical Branch, Environmental Health and Safety

2002–03 U.S. National Survey

- Surveyed 105,356 individual laboratories in 32,429 institutions
  - Only 122 institutions reported storage of WPV infectious or potentially infectious materials
  - Included 12 CDC laboratories
- Polio survey came in wake of Select Agent Act
  - Very high response rate
- Only queried about WPV materials, not OPV/Sabin
- No differentiation by serotype
- Findings from 2002–03 survey was our starting point

2015–16 U.S. National Survey

- Conducted by Office of National Poliovirus Containment Coordinator (NPCC)
  - Based at CDC; comprehensive CDC logistical support
  - Reports to CDC, National Certification Committee (NCC), and Office of Assistant Secretary of Health (OASH), through National Vaccine Program Office (NVPO; Bruce Gellin, MD, Director)
- Distributed web-based survey instrument modified from WHO/PAHO template; initial contact by email
- Two surveys were distributed
  - Internal CDC survey; launched 14 December 2015; n=149
  - External survey; serial launches; first launch 22 December 2015
    - Federal facilities
    - Academic institutions
    - State and local health departments
    - Industrial facilities
    - Commercial diagnostic laboratories
    - Hospitals

U.S. NPCC Approach to Containment (1)

- Distribution of survey was prioritized by estimated risk
  - Phase IIa (original target date: 31 December 2015)
    - First priority: WPV2/VDPV2 infectious materials
      - Top priority: labs known to be currently working with WPV2/VDPV2
    - Second priority: WPV2/VDPV2 potentially infectious materials
  - Phase IIb (completion target date: 31 July 2016)
    - Third priority: OPV2/Sabin 2 infectious materials
    - Fourth priority: OPV/Sabin potentially infectious materials
- Priority categories frequently overlap
- Opportunity to contain all PV and be removed from list
- Potentially infectious materials prioritized by risk
  - Highest risk assigned to stool specimens

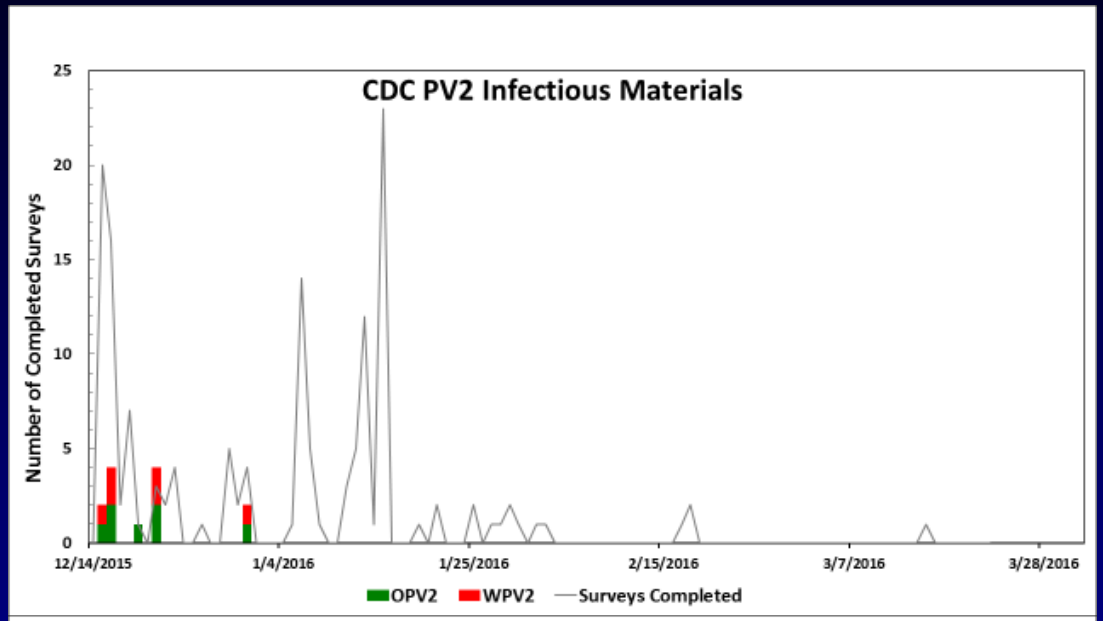
U.S. NPCC Approach to Containment (2)

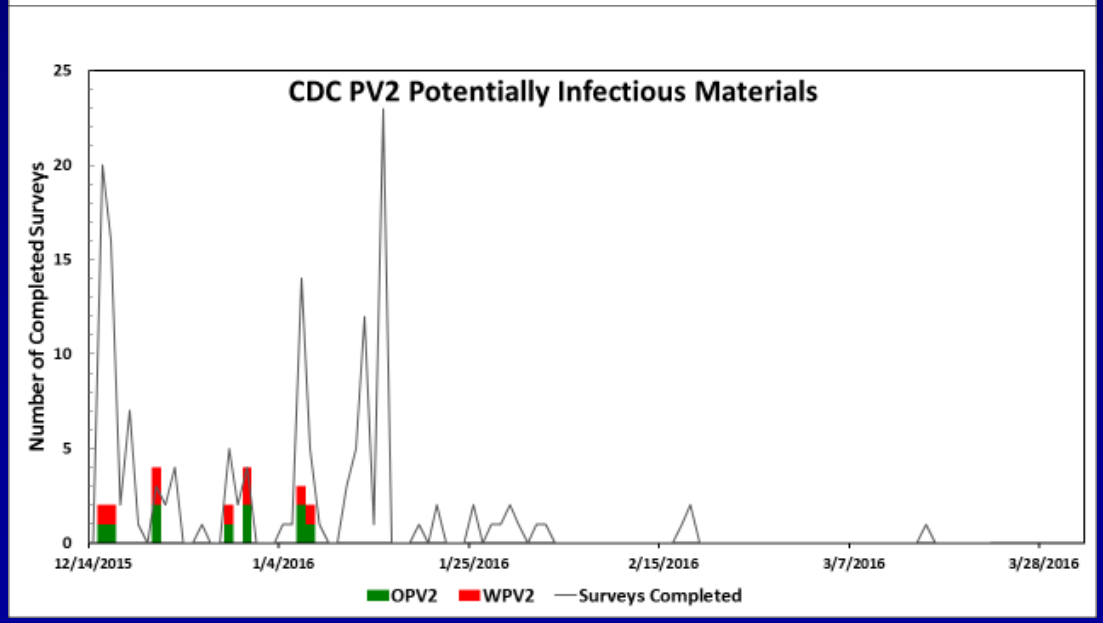
- Surveys are launched in successive waves prioritizing by estimated risks
  - Highest: WPV2 strains; enteric specimens
  - Lowest: domestic respiratory specimens; nucleic acids
- Containment is an ongoing process
  - Immediate goal: PV2 containment in 2016
  - Overall goal: full poliovirus containment (~2019)
- Survey results used to guide priorities for subsequent survey rounds
- Took a collaborative approach to laboratories
- NPCC Office greatly assisted by Biosafety Offices (BSOs) for coordination and further follow-up
- NVPO assistance sought for chronic non-responders

Internal CDC Survey

- CDC is the largest facility storing poliovirus infectious and potentially infectious materials
- Containment receives strong institutional support
- The CDC Polio Laboratory is the major WHO Global Polio Reference Laboratory
  - Contains the largest poliovirus collection in the world
  - Only CDC laboratory with WPV2/VDPV2 infectious materials
  - All WPV2/VDPV2 were moved to a containment laboratory
- 189,763 vials of poliovirus infectious or potentially infectious materials in CDC Polio Laboratory were autoclaved by 24 May 2016
- Other CDC laboratories store poliovirus potentially infectious materials
  - Historical U.S. specimens; international specimens
- All 149 CDC laboratories contacted completed the survey by 15 March 2016

Results: CDC Internal Survey (n = 149)



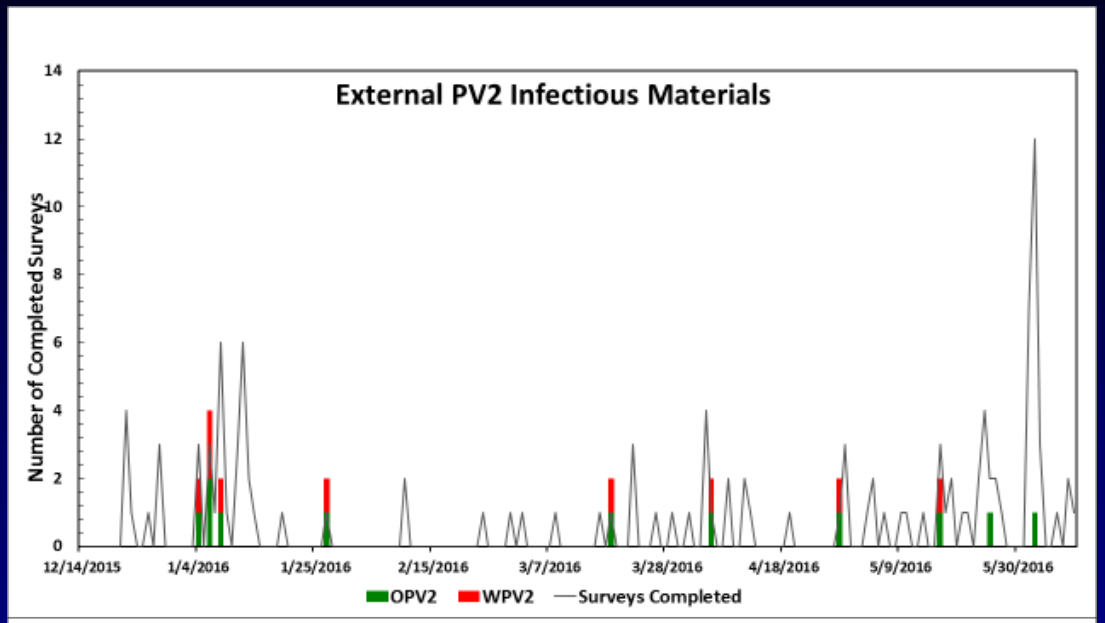


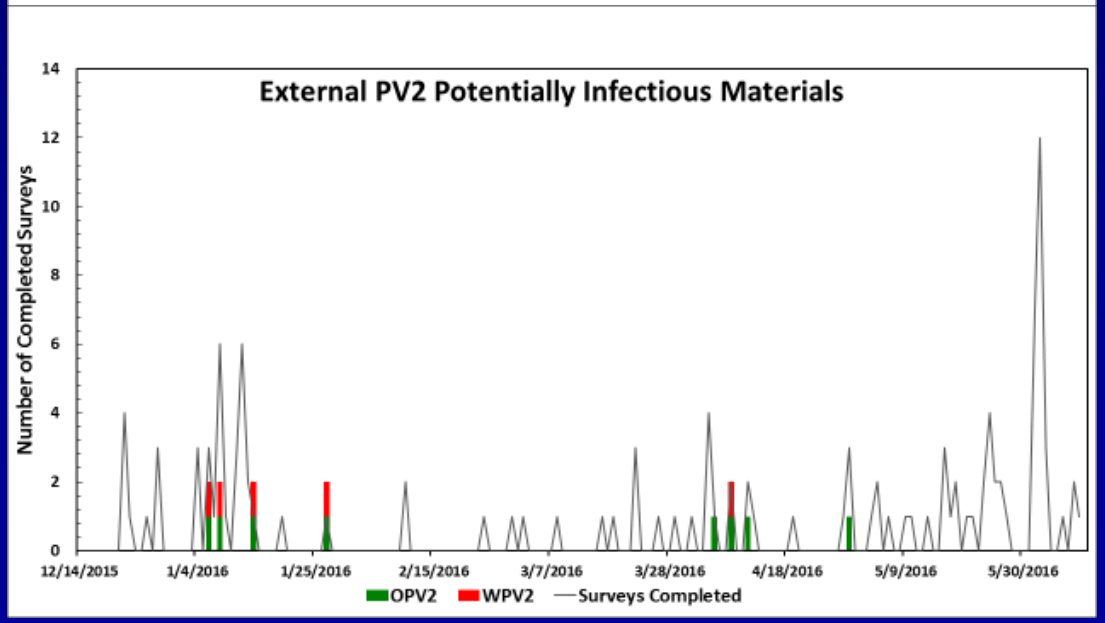
Survey Complete

External U.S. Survey

- Launched in successive waves
  - First Launch: 22 December 2015
  - Distributed to 113 laboratories identified in 2002–03 survey as storing WPV materials
  - Gave special attention to laboratories known to be performing current research/testing with WPV2
- Relaunch to first-round non-responders
- Subsequent launches to
  - Newly identified laboratories
  - State and large municipal health laboratories
  - Other non-polio enteric virology laboratories
    - Rotavirus, norovirus, astrovirus, HAV, HEV, …
    - Note: Enteric bacteriology and parasitology labs do not normally store original stool specimens after isolation of infectious agents
  - BSOs of large institutions to help fill any remaining gaps

Current Results: External Survey (n = 134)





Data as of 06/22/16

Current Overall Survey Results

Stored Poliovirus Materials	Number of Laboratories		
	Serotype		
	1	2	3
WPV/VDPV Infectious Materials	26	**14**	17
OPV/Sabin Infectious Materials	19	**13**	14

	Number of Laboratories
WPV/VDPV Potentially Infectious Materials	10
OPV/Sabin Potentially Infectious Materials	11

Numbers were consolidated for the CDC Polio and Picornavirus Laboratory Branch laboratories.
Numbers for universities reflect individual responding laboratories.
Apart from CDC, most WPV are Salk-Youngner IPV reference strains used in serologic studies.
WPV1 Mahoney is an IPV strain widely used in poliovirus research; Sabin 1 has been used as an alternative.
VDPVs are restricted to CDC and three other laboratories.
Several laboratories did not complete the section on disposition of stored materials, especially for poliovirus potentially infectious materials, pending clarification of the final classification of nucleic acids and respiratory specimens.

Data as of 06/22/16

Challenges (1)

- Some interpretations at WHO/HQ of GAPIII requirements are very prescriptive; may impede compliance
- High-risk infectious materials and low-risk potentially infectious materials (such as respiratory specimens, nucleic acids) are grouped together for containment in GAPIII
- WHO is aware of these challenges and has empaneled an Containment Advisory Group to help guide way forward
- Absence of statutory authority could limit compliance outside of Federal Government facilities
- Process for issuing Certificates to Poliovirus Essential Facilities incompletely defined
- Potentially infectious materials, especially of OPV/Sabin variety, present challenges for outreach

Challenges (2)

- 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
- Non-poliovirus labs, non-virus labs are not generally aware of poliovirus containment
  - Some may store potentially infectious materials
- Absolute poliovirus containment is not feasible
  - Undetected iVDPV excretion is likely to continue
  - Poliovirus can be easily prepared by synthetic biology
    - GenBank sequence data exists in perpetuity
- The goal is major reduction of risk, which is feasible, provided that colleagues are constructively engaged

Example of Impact of PV2 Containment on U.S. Vaccination Policy

- Poliovirus Vaccine: Current Guidance in General Recommendations for Persons Vaccinated Outside the U.S.

- General Recommendations included an alternative approach for children with no or questionable documentation of vaccination*
  - Serologic testing for neutralizing antibody to PV 1, 2, and 3 can be obtained commercially and at certain state health department laboratories (limited availability)
  - Persons with protective titers against all three types do not need to repeat doses but should complete the schedule as age appropriate.
- The alternative approach may no longer be feasible due to PV2 lab containment (*wording removed in the updated General Recommendations document*)
  - At least two commercial sources of antibody testing have indicated suspension of poliovirus PV2 antibody testing as a result of PV2 containment this year

**Source*: General Recommendations on Immunization: recommendations of ACIP. MMWR 2011:60(RR02);1-60

Slide courtesy Mona Marin and Manisha Patel DVD/NCIRD/CDC

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