Global Polio Endgame and tOPV to bOPV Switch

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POLIO GLOBAL ERADICATION INITIATIVE

Poliomyelitis

Photo Gallery, WHO

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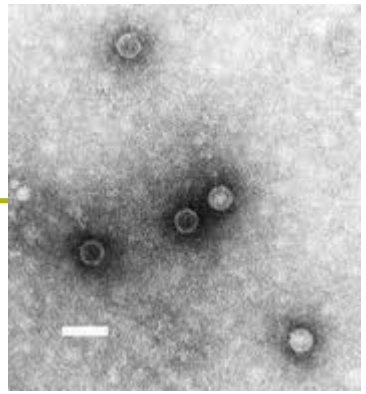
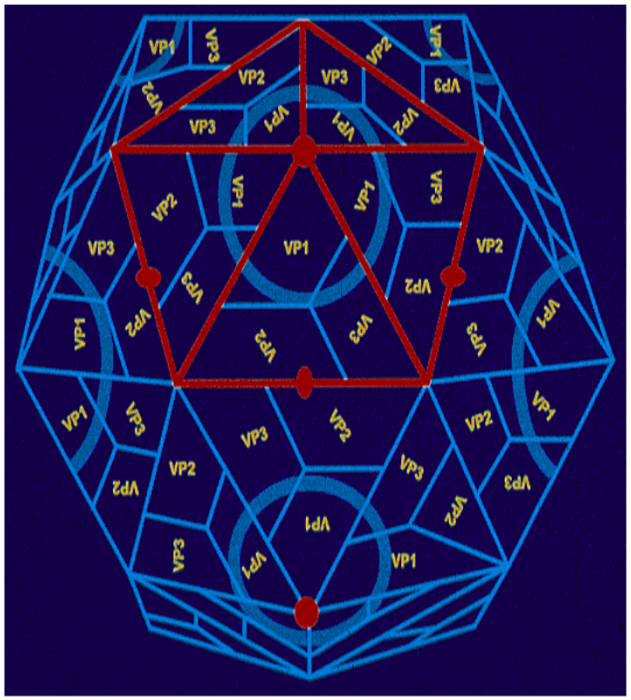
POLIOMYELITIS

Virology





- **Three serotypes:**
  Poliovirus types 1, 2, 3
- Family: Picornaviridae
  - **Genus:** ***Enterovirus***
  - ***Species:*** ***Poliovirus***

Melnick JL in Plotkin SA, Mortimer EA (eds) Vaccines 1994 (7) pp155-204c

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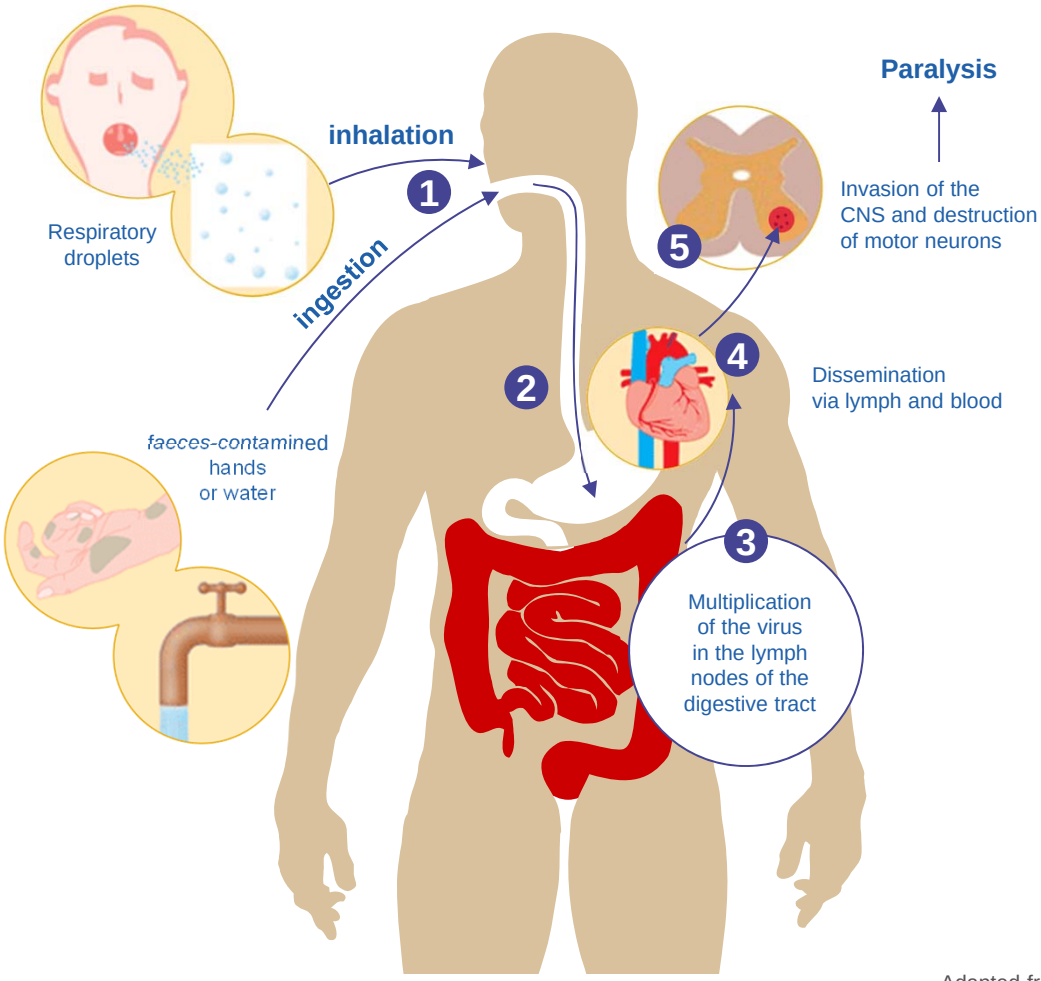
Poliomyelitis Pathogenesis
Infection may cause paralysis in a matter of hours



1. **Exposure** (ingestion, inhalation)[30]
2. **Adhesion/entry into gastrointestinal mucosa**[30]
3. **Local multiplication of poliovirus** (tonsils, peyer's patch of ileum, lymph nodes)
4. **Dissemination via lymph & blood**[30]
5. **Invasion of central nervous system**[30]
   → Destruction of motor neurons
   → Paralysis

Adapted from text in **[30]** Sutter. In:*Vaccines, 6th ed., 2012* **[32]** WHO. Online

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Clinical Aspects of Paralytic Disease

- **Incubation period 6-20 days (range 3-35 days)**
- **Prodrome [biphasic]**
  - Initial symptoms minor
  - Major symptoms evident 7 days later
    - Intense myalgia and hyper-reflexia of involved limbs
- **Paralytic symptoms begin 1-10 days after prodrome**
  - Asymmetric weakness, flaccid paralysis, diminished deep tendon reflexes
  - No sensory loss experienced
  - Proximal >> distal muscle involvement
  - Legs >> arms
- **Bulbar involvement in 5% to 35% of cases**
  - Dysphagia, difficulty with secretions
  - Anxiety

Types of polioviruses

Wild

- 99% reduction in cases of wild poliovirus since 1988
- Type 1 (359 cases in 2014)
- Type 2 (eliminated worldwide in 1999)
- Type 3 (none detected since November 2012)

OPV related

VAPP**

- Vaccine-associated paralytic poliomyelitis (VAPP)**
- Estimated ~250-500 globally per year
- Type 2 accounts for about 26-31%% of VAPP

VDPVs*

- Vaccine derived polioviruses (VDPV)
- Most are circulating VDPVs (cVDPVs)*
- ~54-185 per year from 2008 to 2014
- Type 2 cVDPVs account for 97% of cVDPVs

† More up-to-date numbers can be found at http://www.polioeradication.org/Dataandmonitoring/Poliothisweek.aspx

**Other extremely rare VDPVs include primary immunodeficiency VDPVs (iVDPVs) and ambiguous VDPVs (aVDPVs)*

***Refers to spontaneous reversion to neurovirulence of one of the attenuated viruses in OPV. VAPP occurs in OPV recipients or their close contacts in contrast to cVDPVs which are widely transmitted in a community and are not likely to be related to contact with a recent vaccine recipient.*

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POLIOMYELITIS

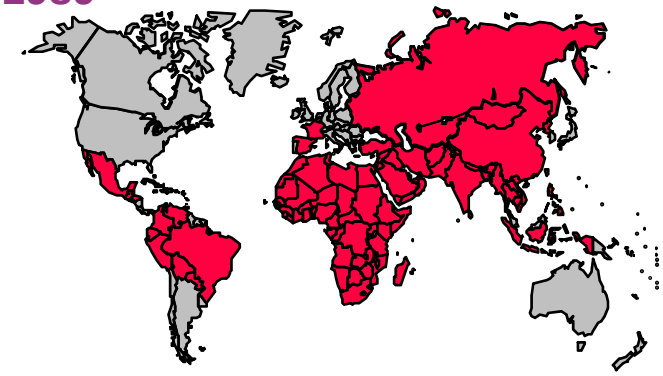
Epidemiology

1988

> 350 000 cases

> 125 endemic countries

Last polio case in South Africa in 1989



2012

205 cases (4 Dec)

3 endemic countries – Nigeria (114), Afghanistan (39), Pakistan (73)

Persistent Transmission Despite High Coverage

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Polio is getting closer to being « history »
2015 was a landmark year; 2016 off to a good start

- 2016 YTD: only 2 cases of Wild Polio Virus - Pakistan
  - 2 cases of cVDV1 – Lao

- Positive environmental samples still found both in Pakistan (Feb) and Afghanistan (Dec) = circulation ongoing

Polio Status in 2015

- **WPV cases in endemic countries**
  - Afghanistan 20
  - Pakistan 54

- **cVDPV identified**
  - Type 2: Guinea, Nigeria, Pakistan
  - Type 1: Ukraine, Madagascar, Laos

2015 Key milestones

Sept
- Global Certification Commission certified wild poliovirus (WPV) type 2 as eradicated

Sept
- World Health Organization removing Nigeria from the list of polio-endemic countries

Oct.
- 14 months after the last polio case was identified, Polio outbreak in Somalia officially declared over

Nov.
- 3 years with no wild poliovirus (WPV) type 3

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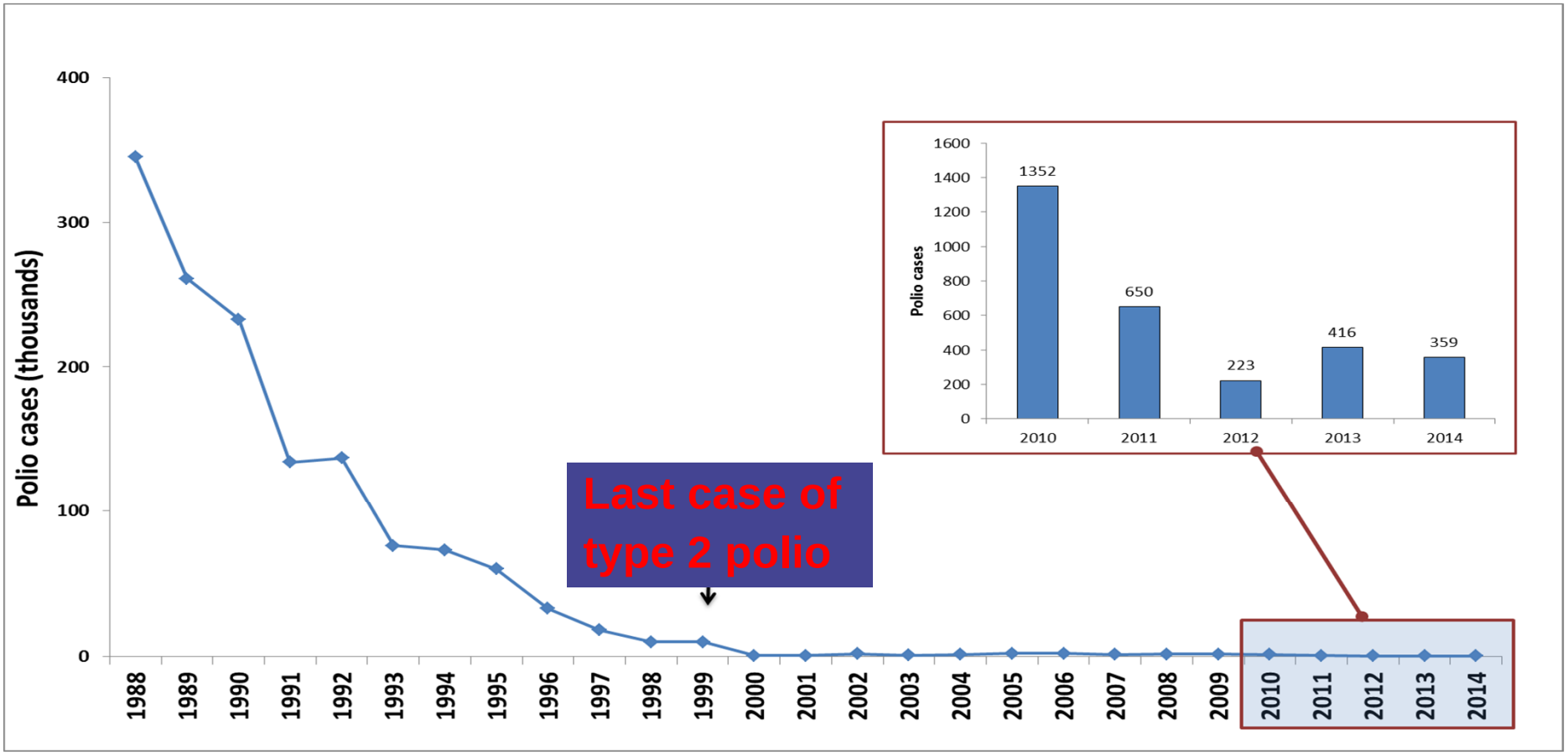
Type 2 *wild poliovirus*



*as of 31 Dec 2014; (*current numbers: http://www.polioeradication.org/Dataandmonitoring/Poliothisweek.aspx*

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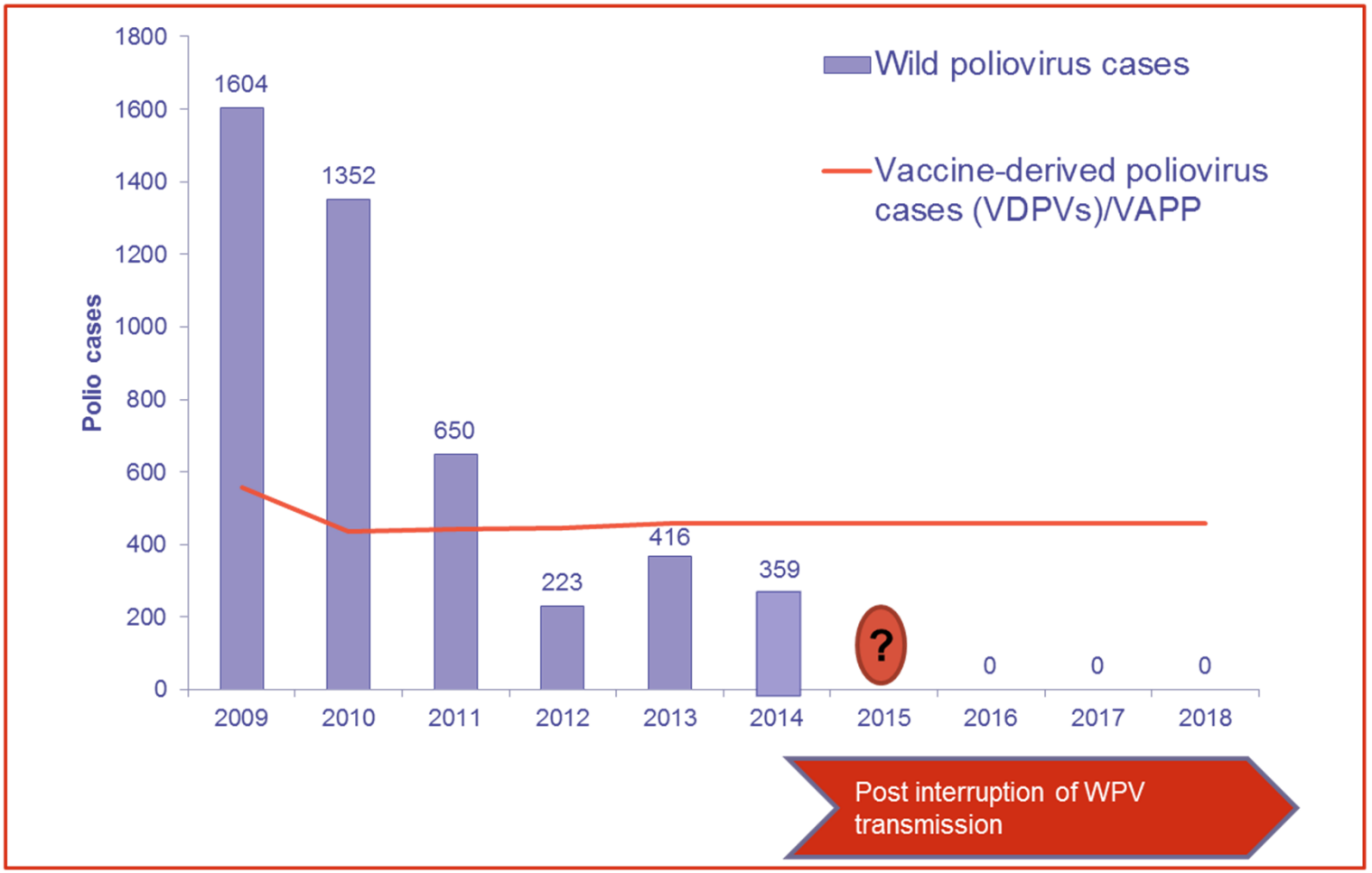
As wild polioviruses are eradicated, number of circulating vaccine-derived cases exceeds wild poliovirus cases



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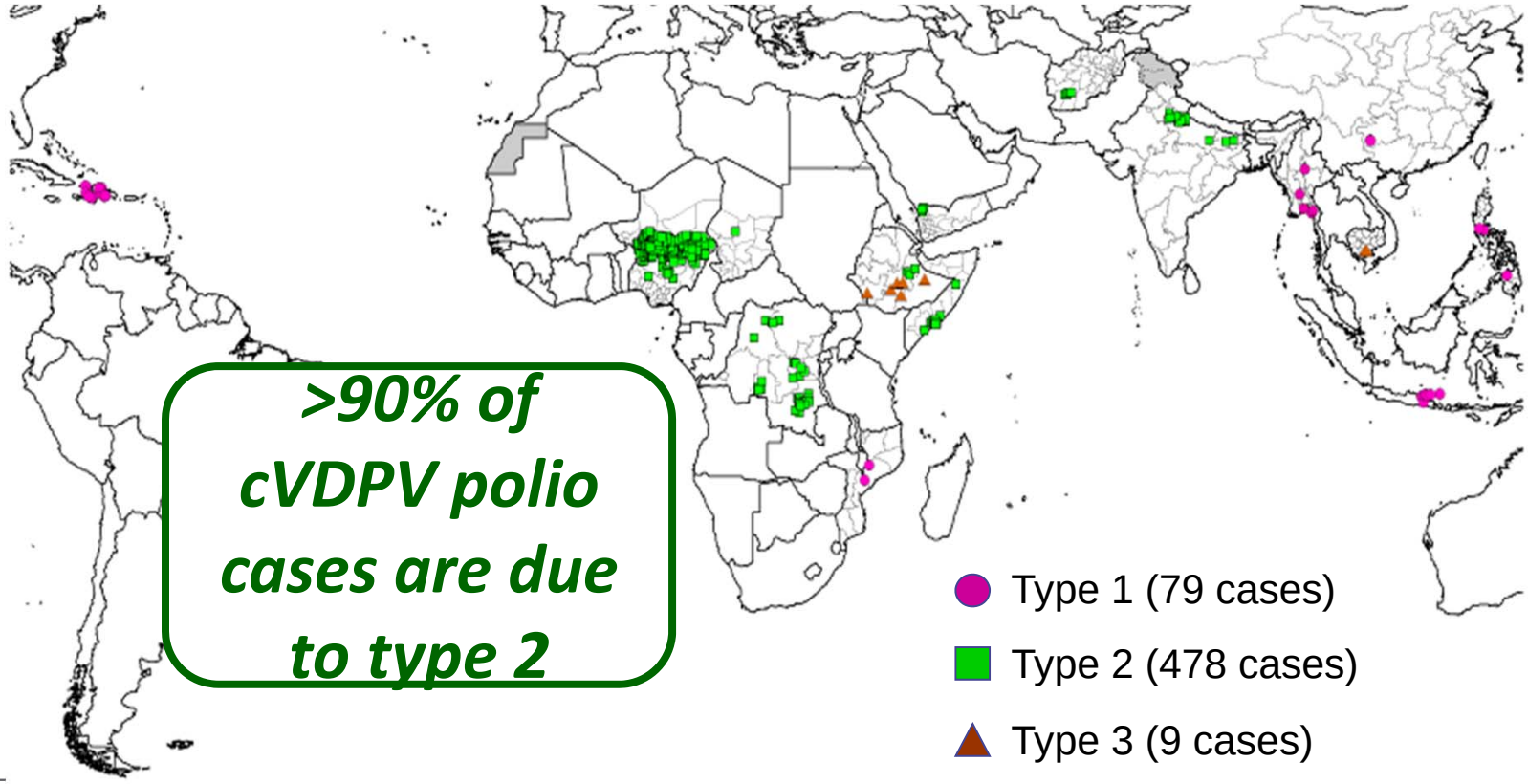
circulating Vaccine-Derived Poliovirus Outbreaks (cVDPVs), 2000-2011



>90% of cVDPV polio cases are due to type 2

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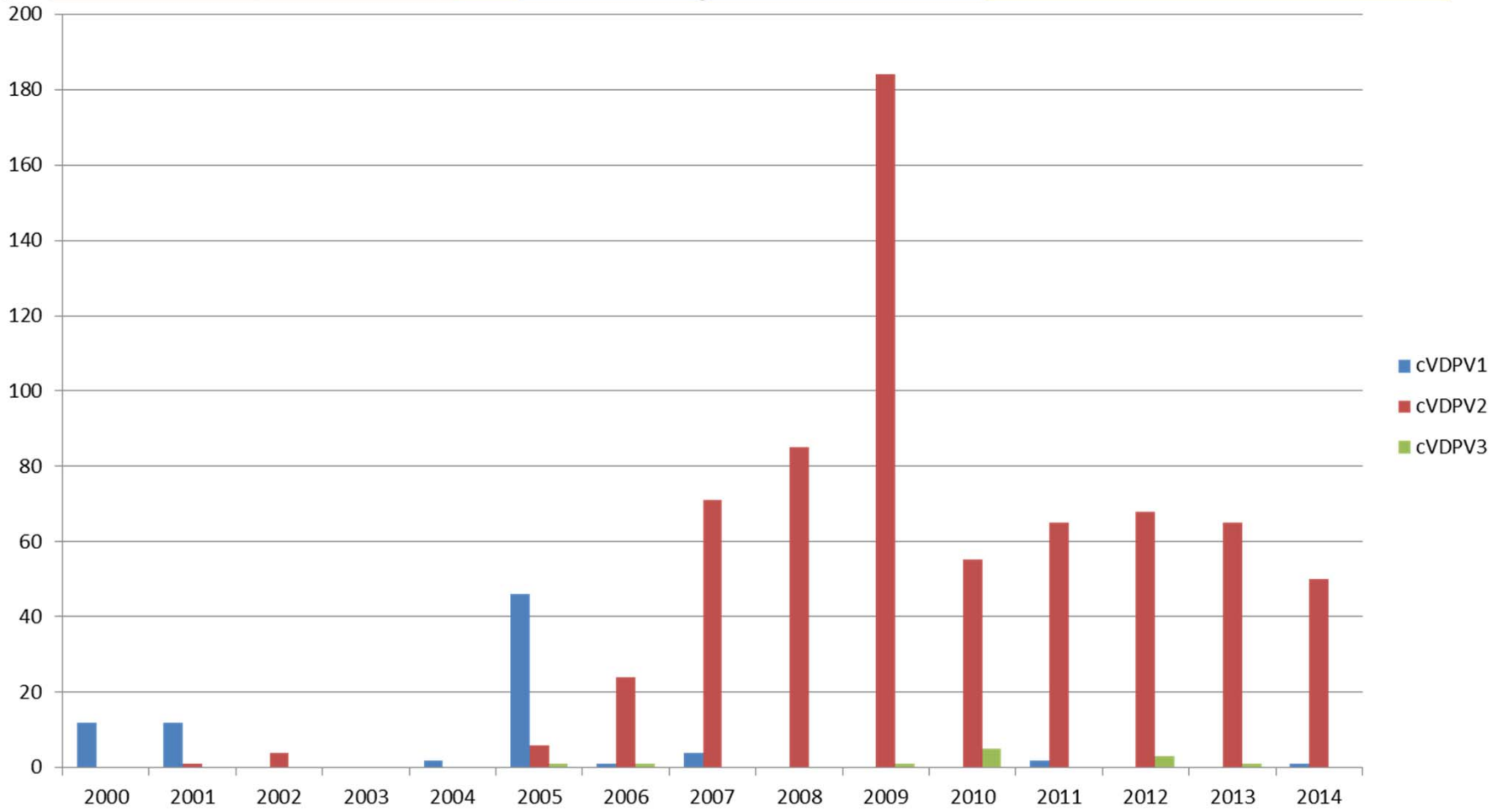
Type 2 component of tOPV has to be withdrawn because it is responsible for >97% of all *circulating vaccine derived poliovirus (cVDPV)* in recent years



*as of 31 December 2014; (*current numbers: http://www.polioeradication.org/Dataandmonitoring/Poliothisweek.aspx)

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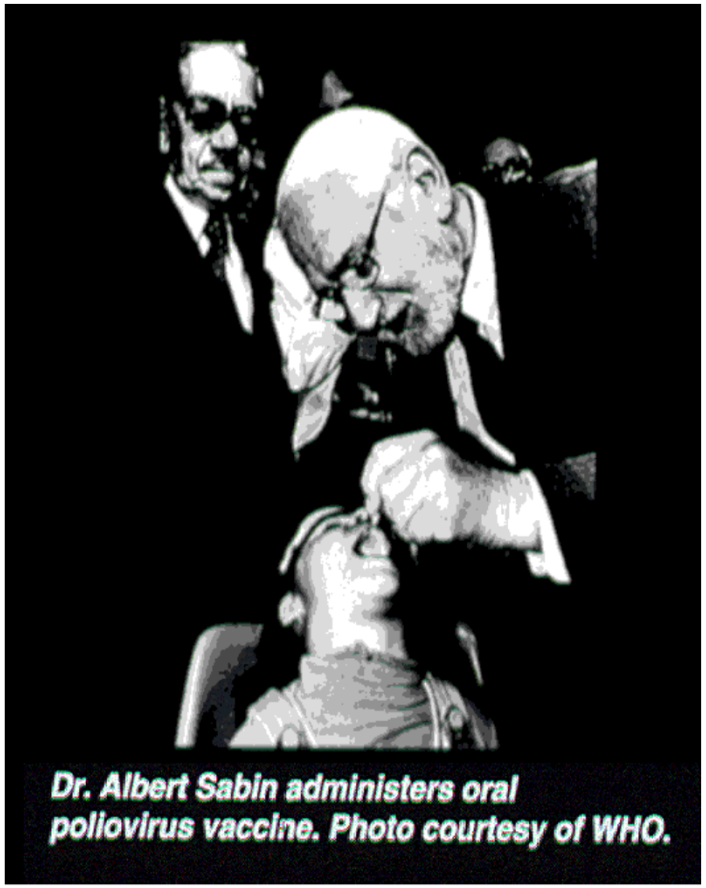
Oral Polio Vaccines (OPV) in routine and supplementary immunization activities globally

- Types of OPV
  - **Trivalent OPV (tOPV): types 1, 2, and 3**
  - **Bivalent OPV (bOPV): types 1 and 3**
  - **Monovalent OPV (mOPV): types 1 or 2 or 3**

- Currently, **TRIVALENT** is the most commonly used OPV in routine immunization globally, while **BIVALENT** is more commonly used in supplementary immunization activities.

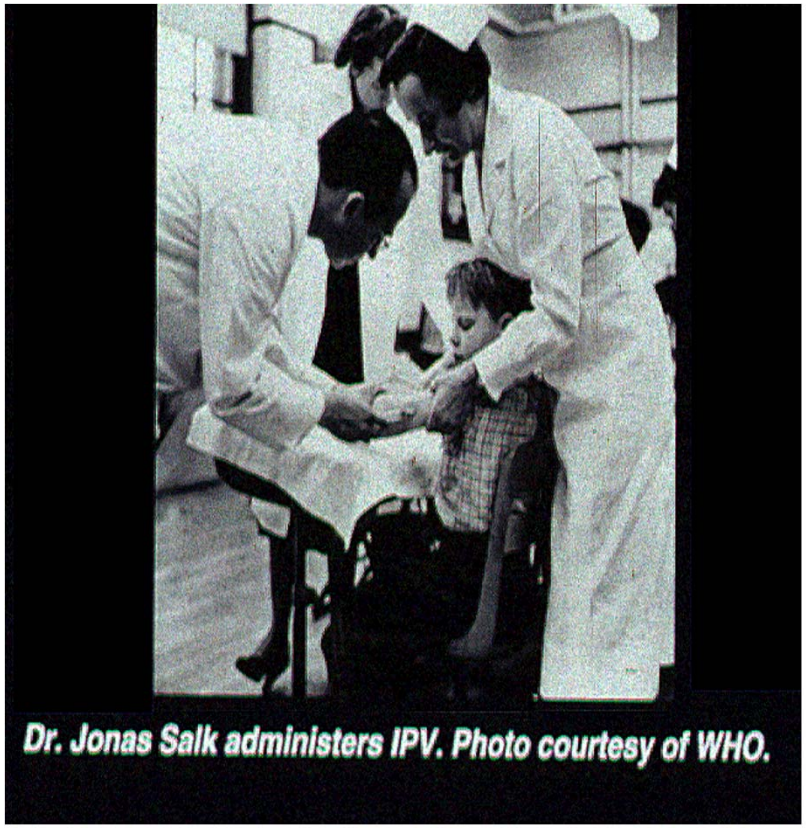
Live attenuated Poliovirus Vaccine (OPV)



Dr. Albert Sabin administers oral poliovirus vaccine. Photo courtesy of WHO.

- Developed by Sabin in 1961
- Attenuated and then produced in monkey kidney cell culture
- Minimum 3 doses for primary immunisation
- Immune response depends on replication of live attenuated viruses in the gut

Enhanced Inactivated Poliovirus Vaccine (eIPV)



Dr. Jonas Salk administers IPV. Photo courtesy of WHO.

- Inactivation of wild-type poliovirus strains
- New production techniques
- High potency
- Licensed in the US in 1987

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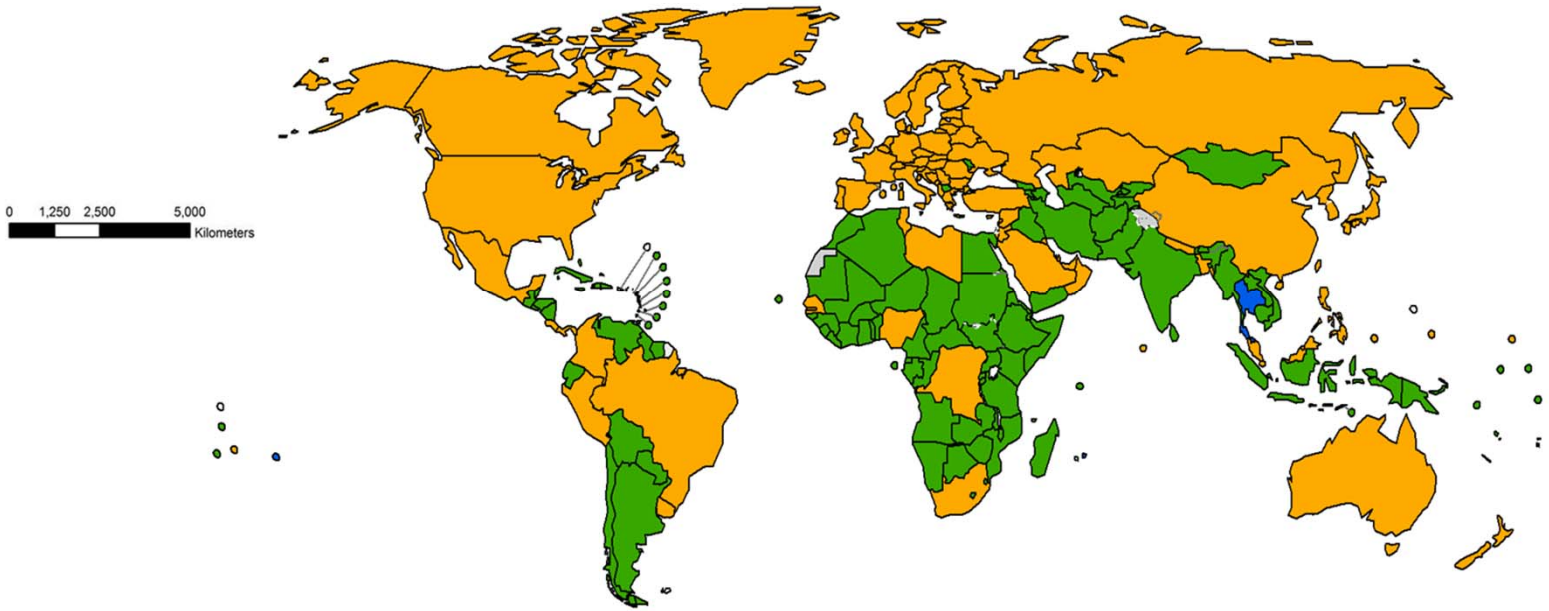
IPV Introduction status – May 2015

20 introductions
106 commitments to introduce



- **Introduced to date : 88 (45%)**
- **Formal commitment to introduce in 2015: 105 (54%)**
- **Intend to introduce in 2016: 1 (<1%) (Thailand)**
- ***Not applicable***

Since January 2013, the following countries have introduced IPV: Kazakhstan & Peru (July 2013); Libya (March 2014); Albania (May 2014); Panama (July 2014); Nepal & Tunisia (September 2014); Philippines (October 2014); China (December 2014); Comoros, Senegal & Serbia (January 2015); Colombia & ; Nigeria (February 2015); Bangladesh & Maldives (March 2015); DPR Korea, DR Congo and Gambia (April 2015); Madagascar (May 2015)

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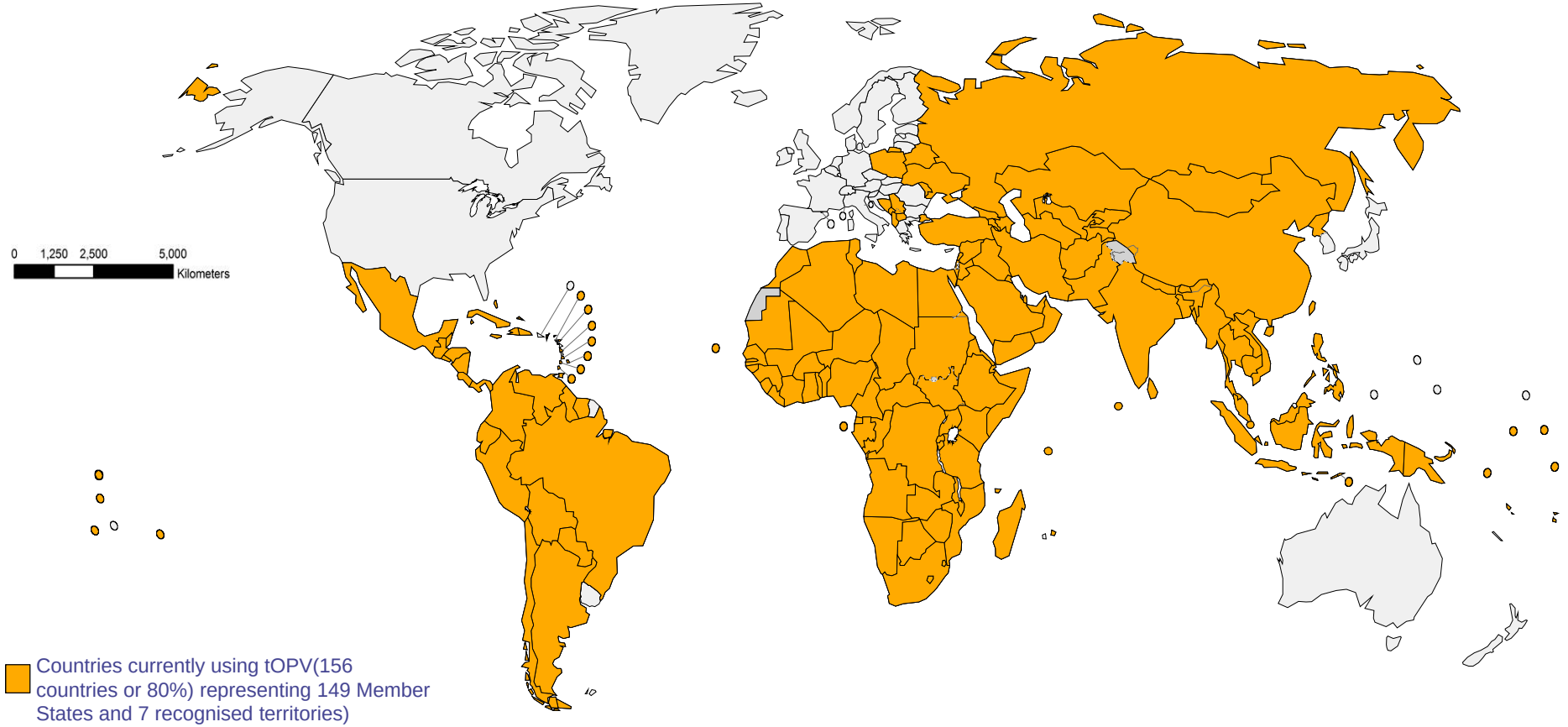
Member states and recognized territories using tOPV to date



Countries currently using tOPV(156 countries or 80%) representing 149 Member States and 7 recognised territories)

Countries not using tOPV (45 countries)

Not applicable

Data Source: WHO/IVB Database, as at 19 March 2015 Date of slide: 19 March 2015

Map production: Immunization, Vaccines and Biologicals (IVB), World Health Organization

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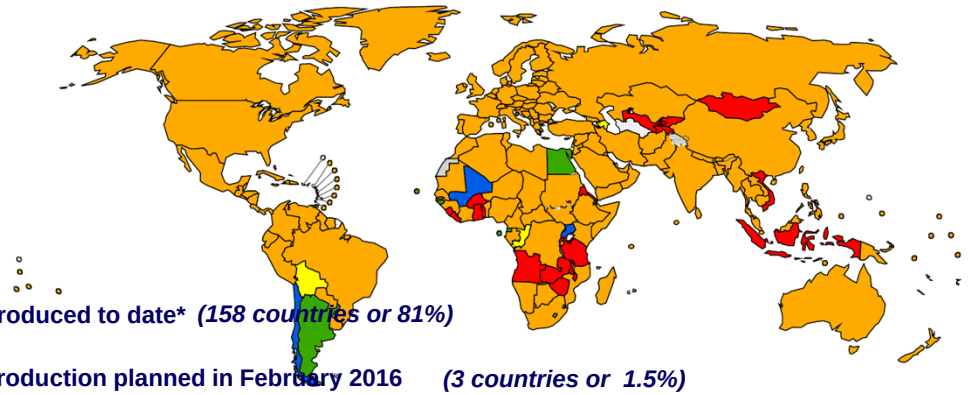
GPEI endgame is moving forward on April 2016 switch to bOPV

Global Polio Eradication Initiative timelines

"OPV switch confirmed"	SAGE recommendation implementation moves ahead
By July 2016	Introduction of at least 1 dose of IPV
April 2016	**Universal switch from tOPV to bOPV**
By 2020	Total OPV cessation & maintain IPV vaccination

IPV introduction* – Where do we stand?



Introduced to date* ***(158 countries or 81%)***

Introduction planned in February 2016 ***(3 countries or 1.5%)***

Introduction planned in March 2016 ***(3 countries or 1.5%)***

Introduction planned in April 2016 ***(9 countries or 5%)***

Introduction planned after April 2016 ***(21 countries or 11%)***

Not available

****Including partial introduction in Haiti, India & Venezuela***

Data source: WHO/IVB Database, as of February 2016

South African EPI schedule 2015

VACCINES	Birth	Dose1	Dose 2	Dose3	Booster 1	Booster 2
• BCG	0					
• tOPV	0	6w				
• DTaP-IPV-HB-Hib		6w	10w	14w	18m	
• RV		6w	14w			
• PCV		6w	14w		9m	
• Measles		6m	12m			
• Td					6y	12y

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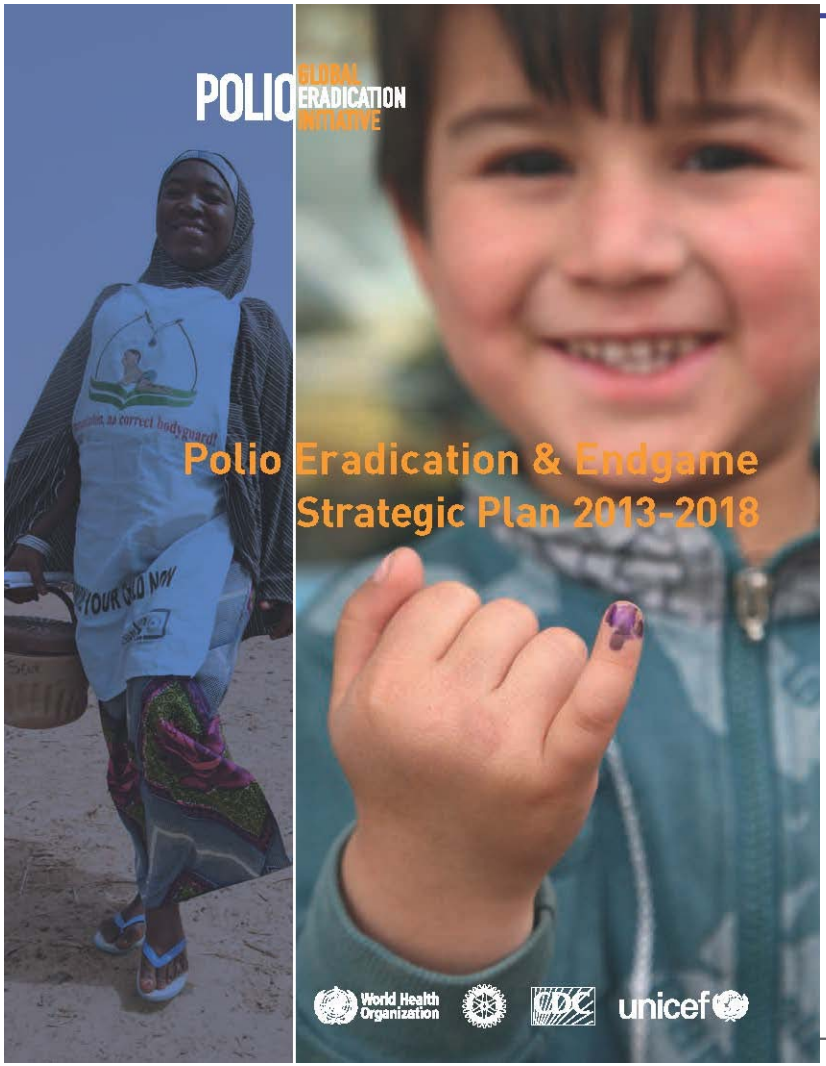
The Polio Eradication & Endgame Strategic Plan 2013-2018



The Plan differs from previous eradication plans because it addresses paralytic cases associated with both wild polioviruses and vaccine-derived poliovirus/VAPP

Eradication

- refers to **wild virus**

+

Endgame

- refers to management of **VDPVs and VAPP**

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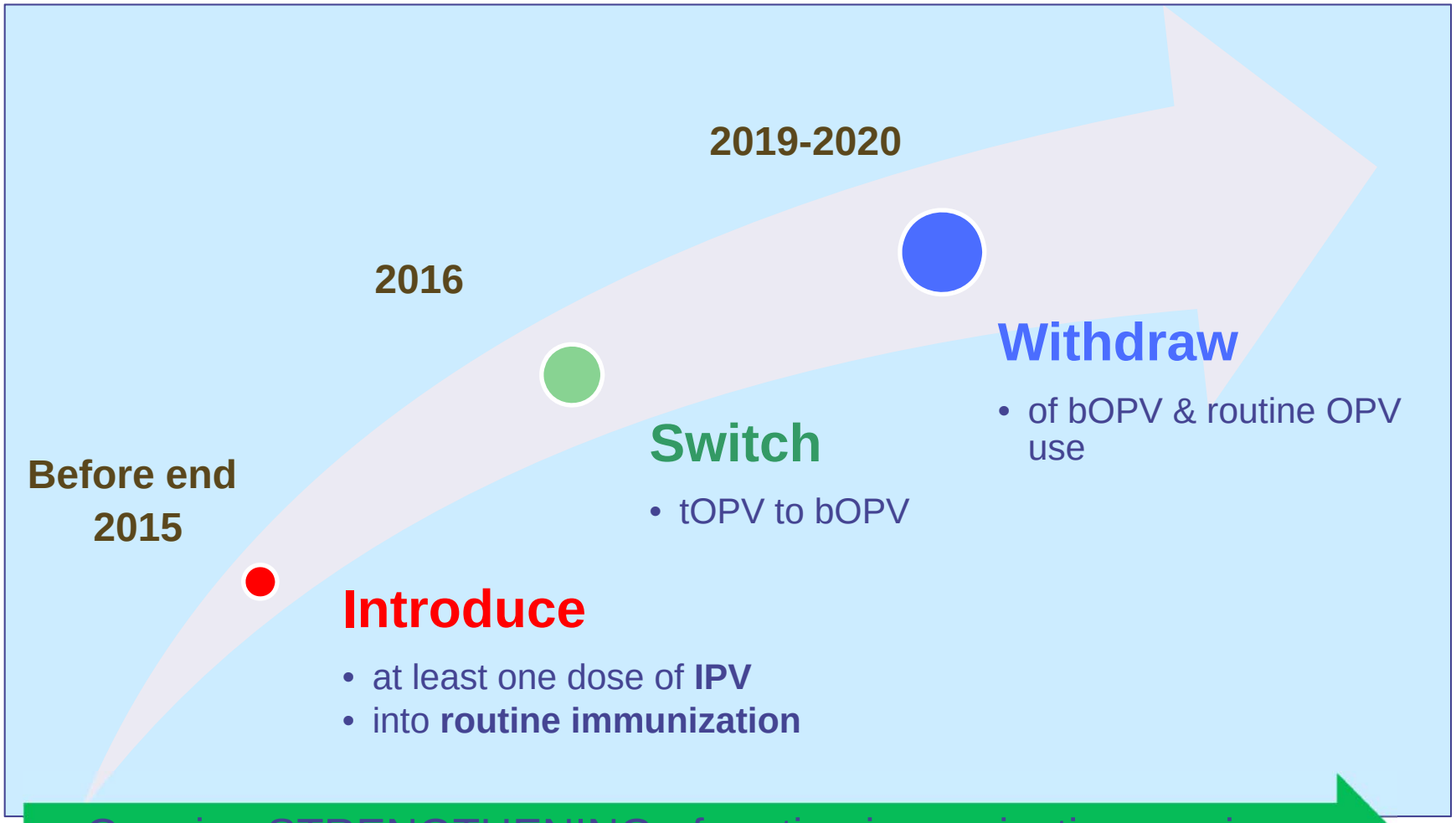
The Plan addresses the Endgame through three distinct stages



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The Endgame Plan calls for OPV cessation globally by 2018-2019

Endgame

- Plan refers to management of **VDPVs and VAPP**

- ***The world must ultimately stop using OPV to be polio free…but first***

Rationale for THE SWITCH from tOPV to bOPV in 2016

Currently, risks of type 2 component of tOPV outweigh the benefits

- Type 2 wild poliovirus **eradicated since 1999**
- New diagnostics and experience suggest **that type 2 component of tOPV causes >97% of VDPVs**
- Type 2 component of tOPV causes approximately 40% of VAPP today
- Type 2 component of tOPV interferes with immune response to types 1 and types 3
- Immunity against type 2 will be provided through **IPV introduction**

Rationale for introducing at least one dose of IPV prior to the tOPV-bOPV switch

IPV protects children against poliovirus types 1, 2 and 3. Introducing IPV prior to the tOPV-bOPV switch will maximize the proportion of the population protected against type 2 polio after OPV2 cessation. One dose of IPV will:

- **Reduce risks** associated with type 2 cessation
  - **Lower risk of re-emergence of type 2 polioviruses**
- **Facilitate interruption of transmission** with the use of monovalent OPV2 if type 2 outbreaks occur
- **Boost immunity** against types 1 & 3 thus hastening polio eradication

Rationale for continuing use of OPV until Polio Eradication & Global Certification

Wild poliovirus still circulating

- As long as there are susceptible persons in other countries, there is risk of export of the virus to these countries.
- **Endemic in 3 countries** – reservoirs for re-infecting others (Pakistan, Afghanistan, Nigeria)
- **In 2013, polio cases in 5 other countries** previously polio free countries (Somalia, Kenya, Ethiopia, Cameroon, Syria)

Eradication requires OPV

- **OPV is a critical component of the eradication strategy until polio transmission is interrupted** globally & the world is certified polio-free,
- **Risk of polio spread into other regions of the world is real** without the continued use of OPV

OPV is appropriate for eradication

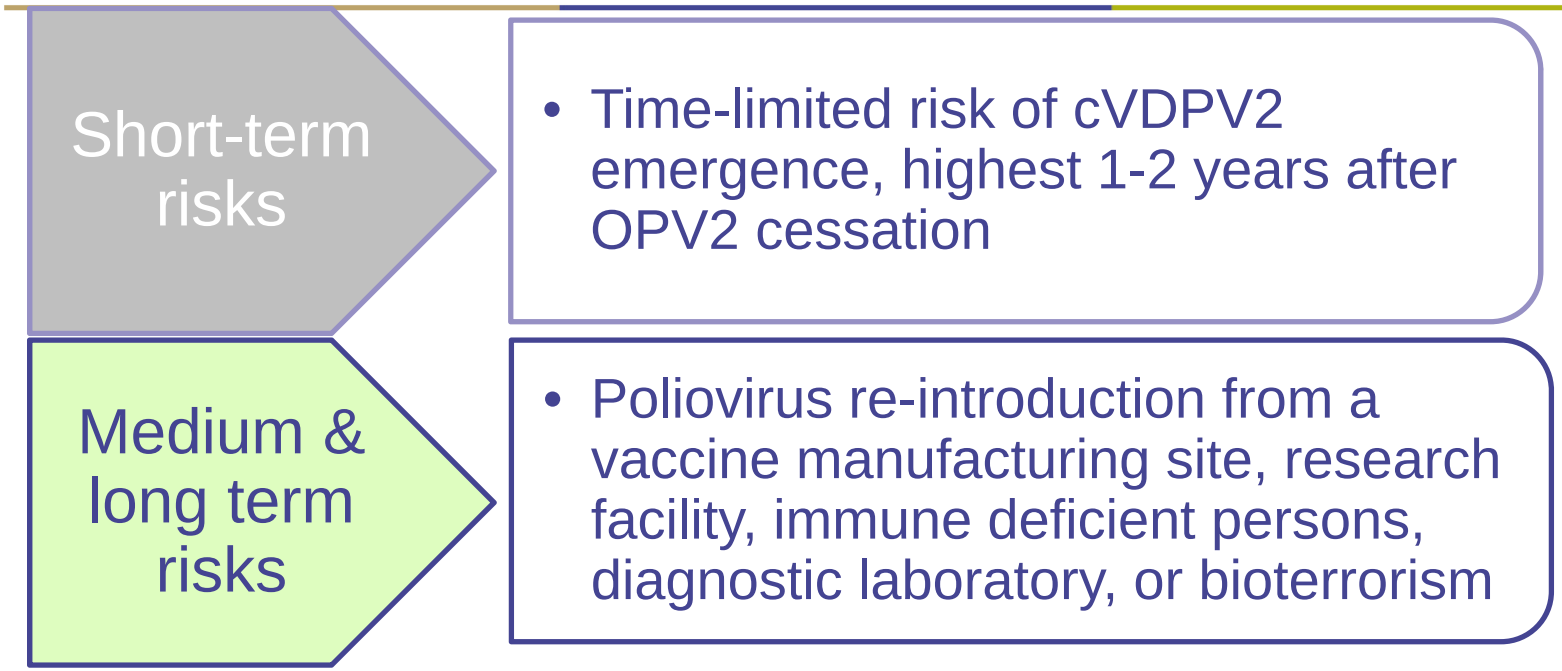
- Inexpensive
- Easy to administer
- Offers good oral and intestinal immunity—needed for interruption of person to person transmission

Rationale for retaining Types 1 & Types 3 components of OPV (bivalent OPV) until global certification of polio eradication

- Type 1 causes all polio cases related to wild virus today
  - **Few VDPV cases are type 1**
  - **Few VAPP cases in immunocompetent individuals**

- Type 3 last detected in November, 2012 (as of 20 November 2013)
  - **Few VDPV cases are type 3**
  - **Most VAPP cases (60%) in immunocompetent persons are type 3**
  - **While lack of detection since November 2012 is promising, the period without detection to date is not long enough to assume eradication—due to potential silent transmission, certification of eradication requires at least 3 years without detection of virus**
  - **Supply & licensing considerations of mOPV1**

Risks associated with OPV2 cessation



- These **risks are mitigated** by strengthening routine immunization and introduction of IPV

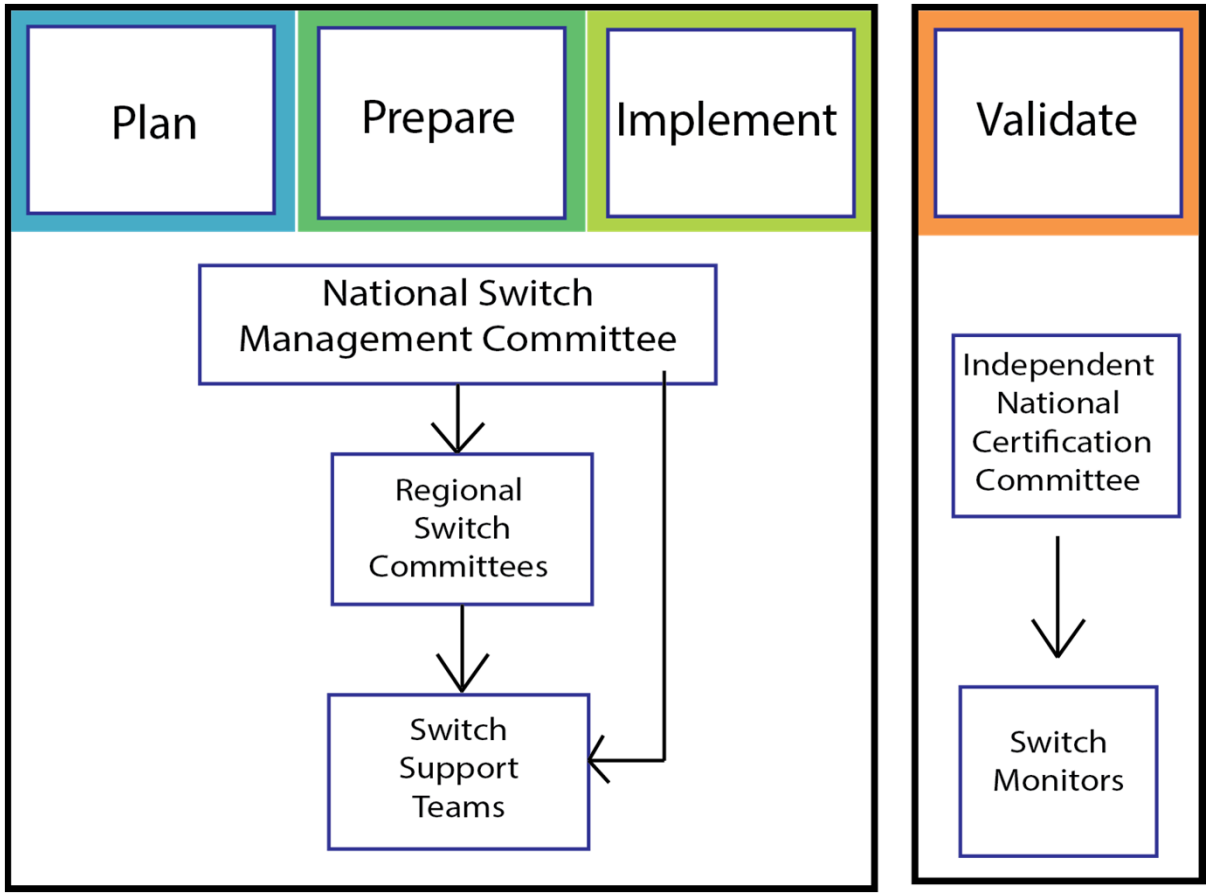
Mitigating the risks of OPV2 cessation

- High population immunity before switch
  - **higher risk countries to conduct tOPV SIAs in Q4 2015 and Q1 2016**
- Discontinuing tOPV production & distribution
- IPV introduction

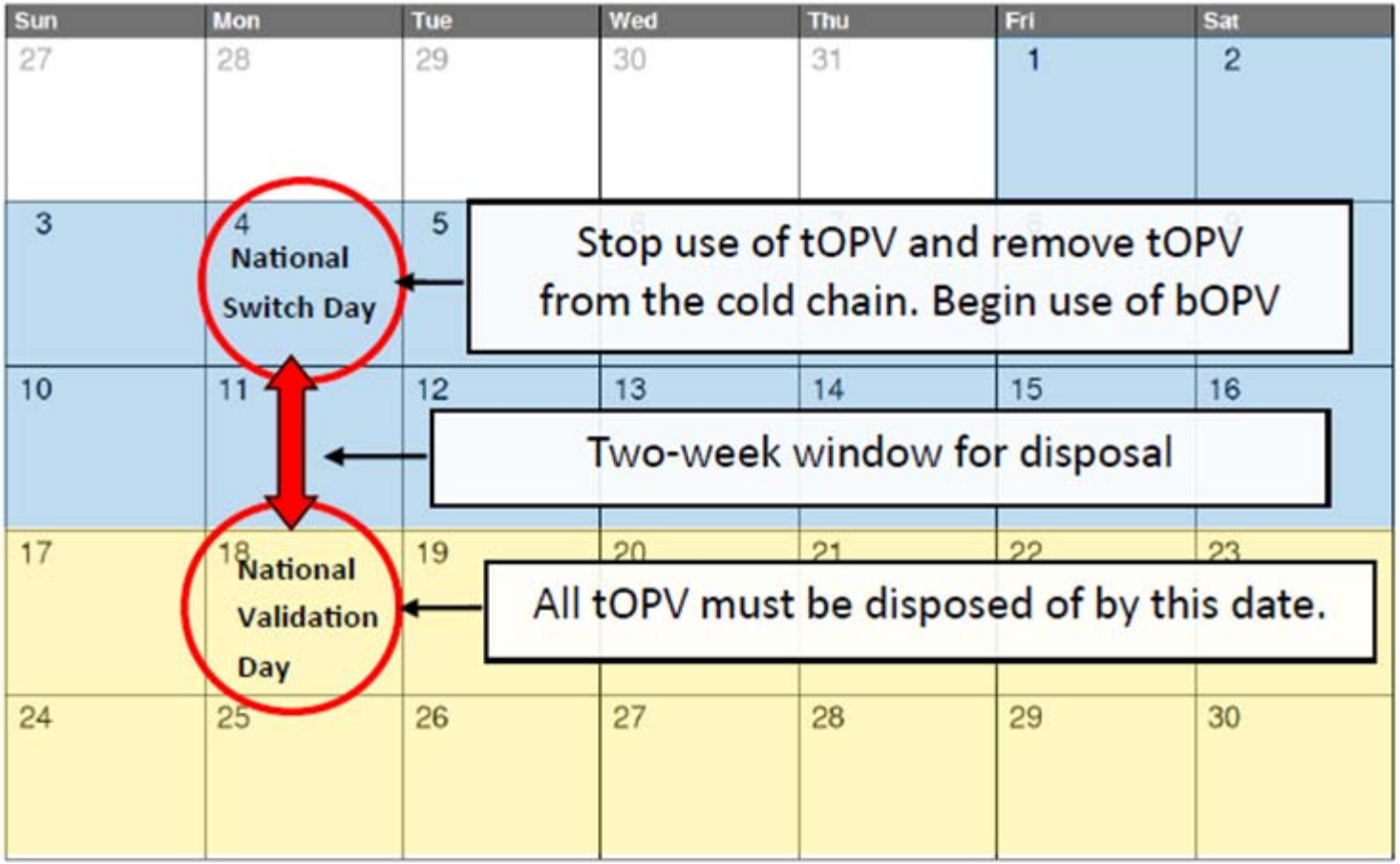
- **Switch in the month of April (2 weeks period) RSA-20 April 2016**
  - "low polio season" for countries with endemic polio or recent polio

- **Synchronizing switch globally**
  - **reduce risks of re-emergence and importation/exportation of type 2 cVDPVs from ongoing use of tOPV; the more simultaneous the switch across and within countries, the lower the risk of emergent cVDPV2s**

Management and Operational Oversight



Example of National Switch Process April 2016



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OPV Production Capacity

- Val de Reuil site: Sanofi Pasteur the main suppliers of oral polio vaccines (OPV)

SANOFI PASTEUR IPV CONTAINING VACCINES

Marcy l'Etoile and Toronto: IPV will be critical to eradication efforts, we have been investing for years to increase our production capacity in order to reach today's unmatched level

Already large capacity being ramped-up to support
IPV Expansion

In total, over 1 Billion doses of Sanofi Pasteur's IPV containing vaccines have been distributed worldwide since 1982

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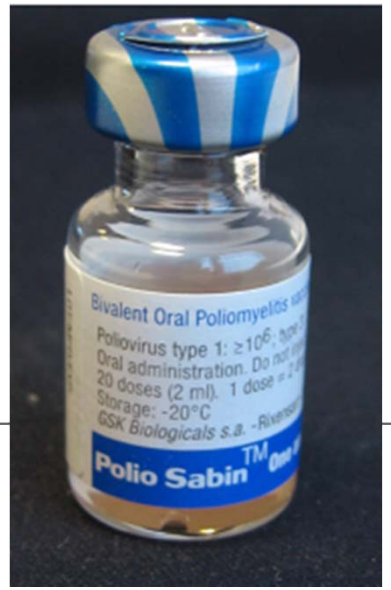
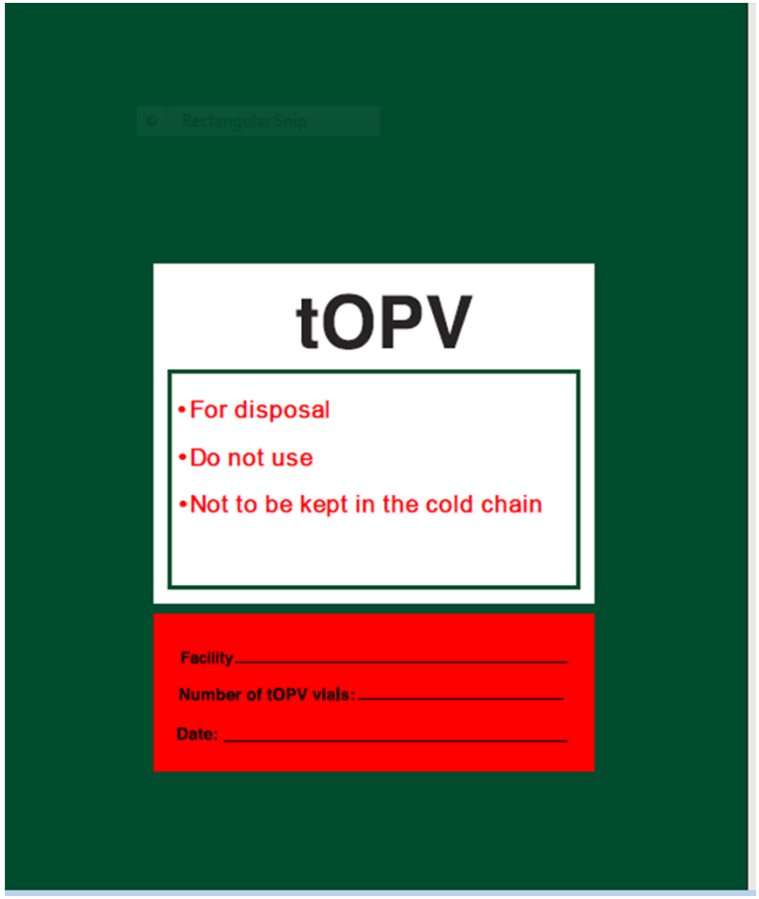
Sanofi Pasteur's Commitment

- Ensure adequate vaccines supply for routine Immunisation
- Support the tOPV to bOPV switch process
- Supply and Support SIAs, Immunisation Awareness campaigns
- Projects



tOPV removal bags



Without OPV, Polio Eradication is Impossible

Without IPV, Polio Eradication is Impossible

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