Eradication of poliomyelitis will not be easy. Vacci es and vaccine manufacture are part of the solution ut part of the problem too.

Eradication of polio

For:

1. two good vaccines
2. no animal reservoir

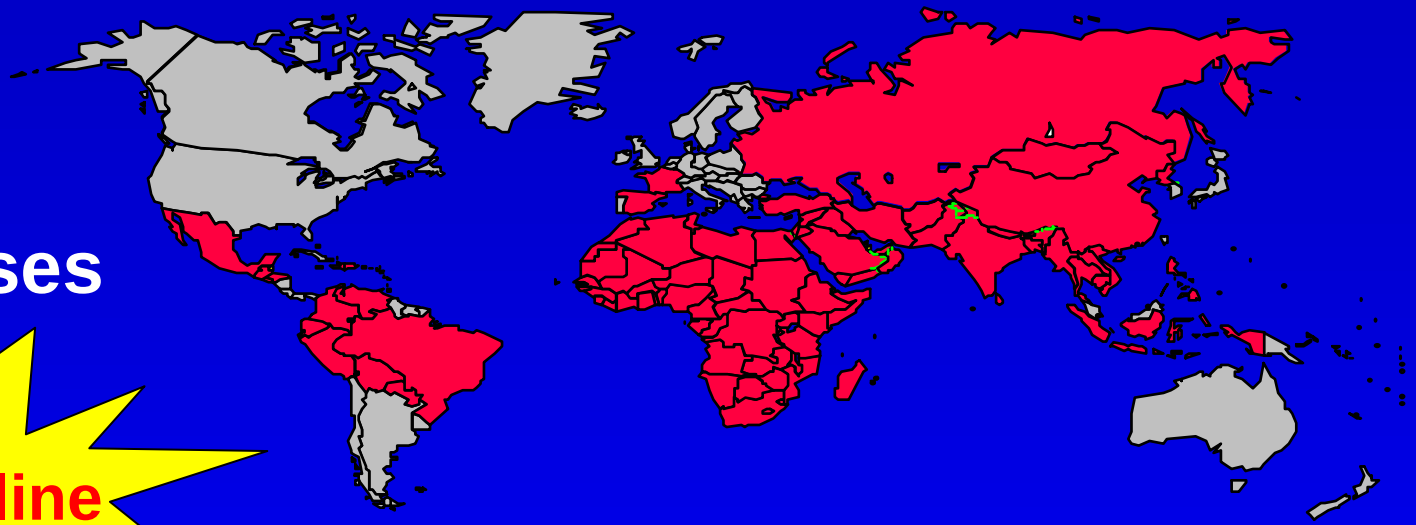
Against:

1. silent infections
2. vaccine issues
3. tropical countries
4. money, management, logistics, politics, sociology
5. What is eradication?

Progress 1988-2000

1988

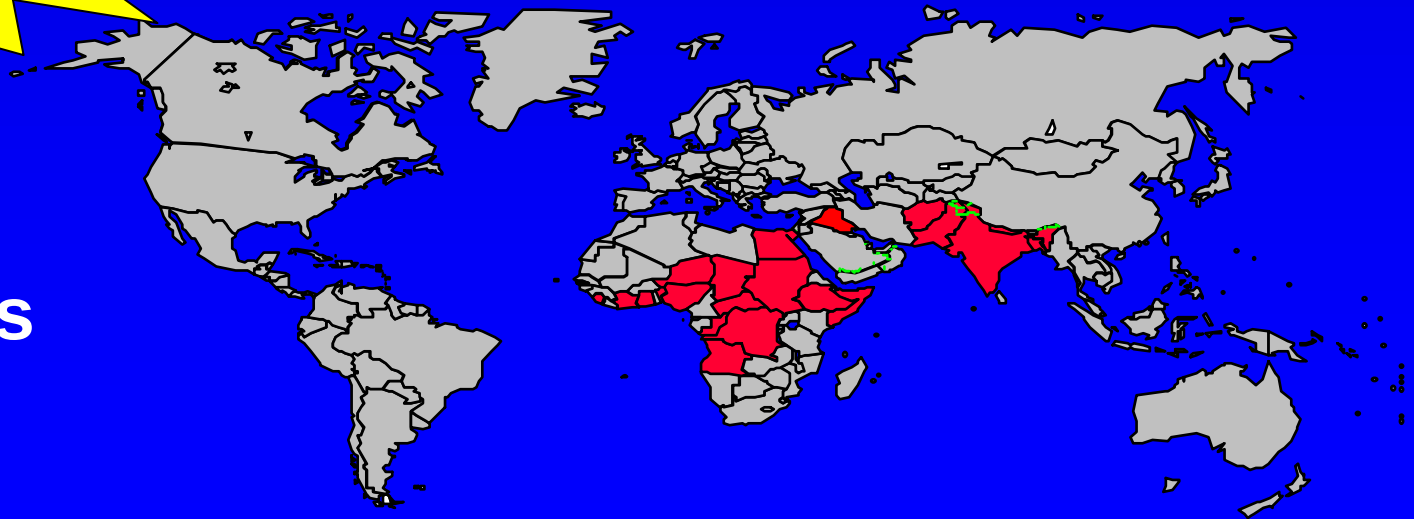
350 000 cases



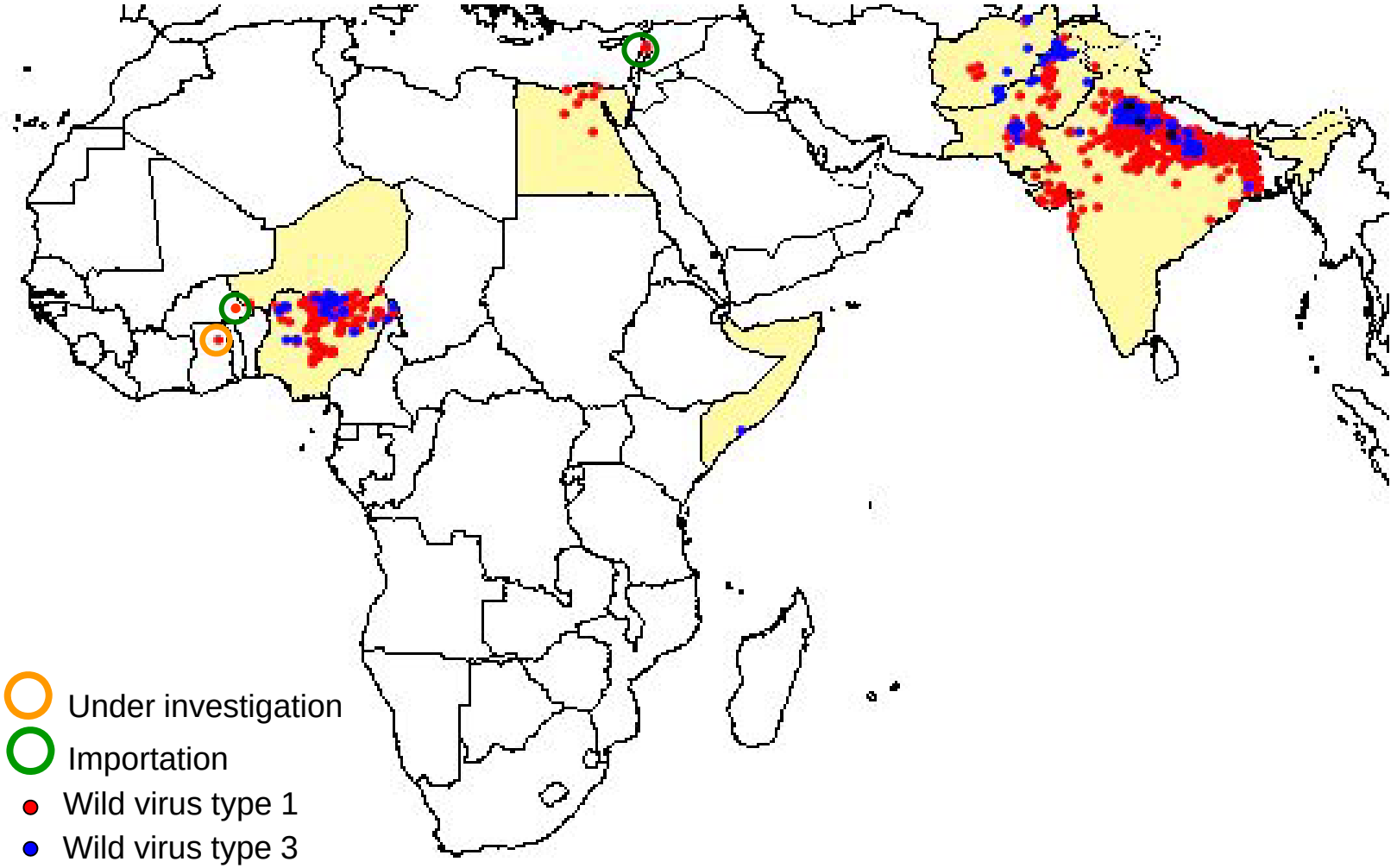
>99% decline in cases

2000

2797 cases



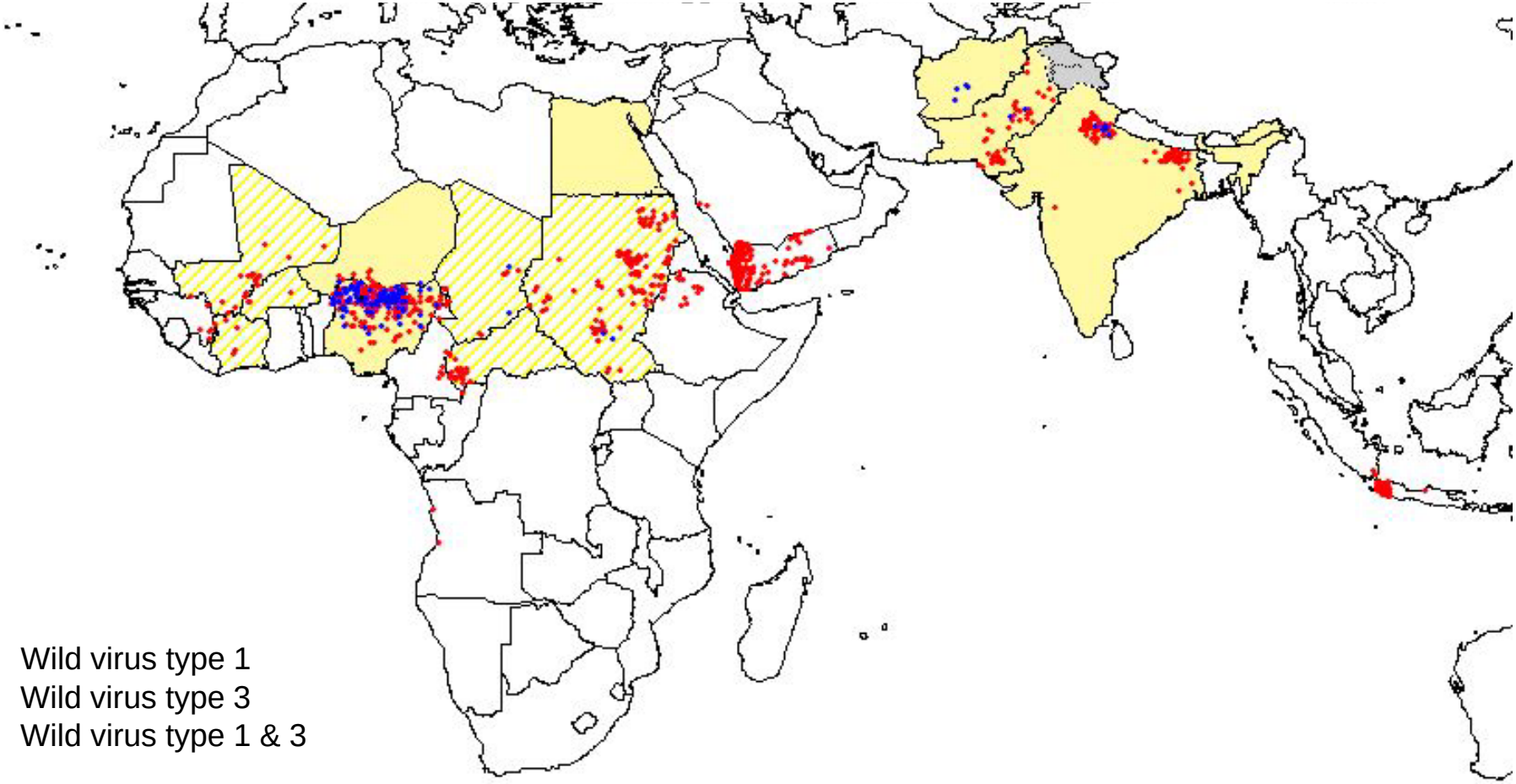
Wild Poliovirus*, 15 Apr 2002 to 14 Apr 2003



*Excludes viruses detected from environmental surveillance and vaccine derived polio viruses.

Data in WHO HQ as of 15 April 2003.

Wild Poliovirus*, 13 Jul 2004 to 12 Jul 2005



- Wild virus type 1
- Wild virus type 3
- Wild virus type 1 & 3

- Endemic countries
- Re-established transmission countries
- Case or outbreak following importation

*Excludes viruses detected from environmental surveillance and vaccine derived polio viruses.

Data in WHO HQ as of 12 Jul 2005

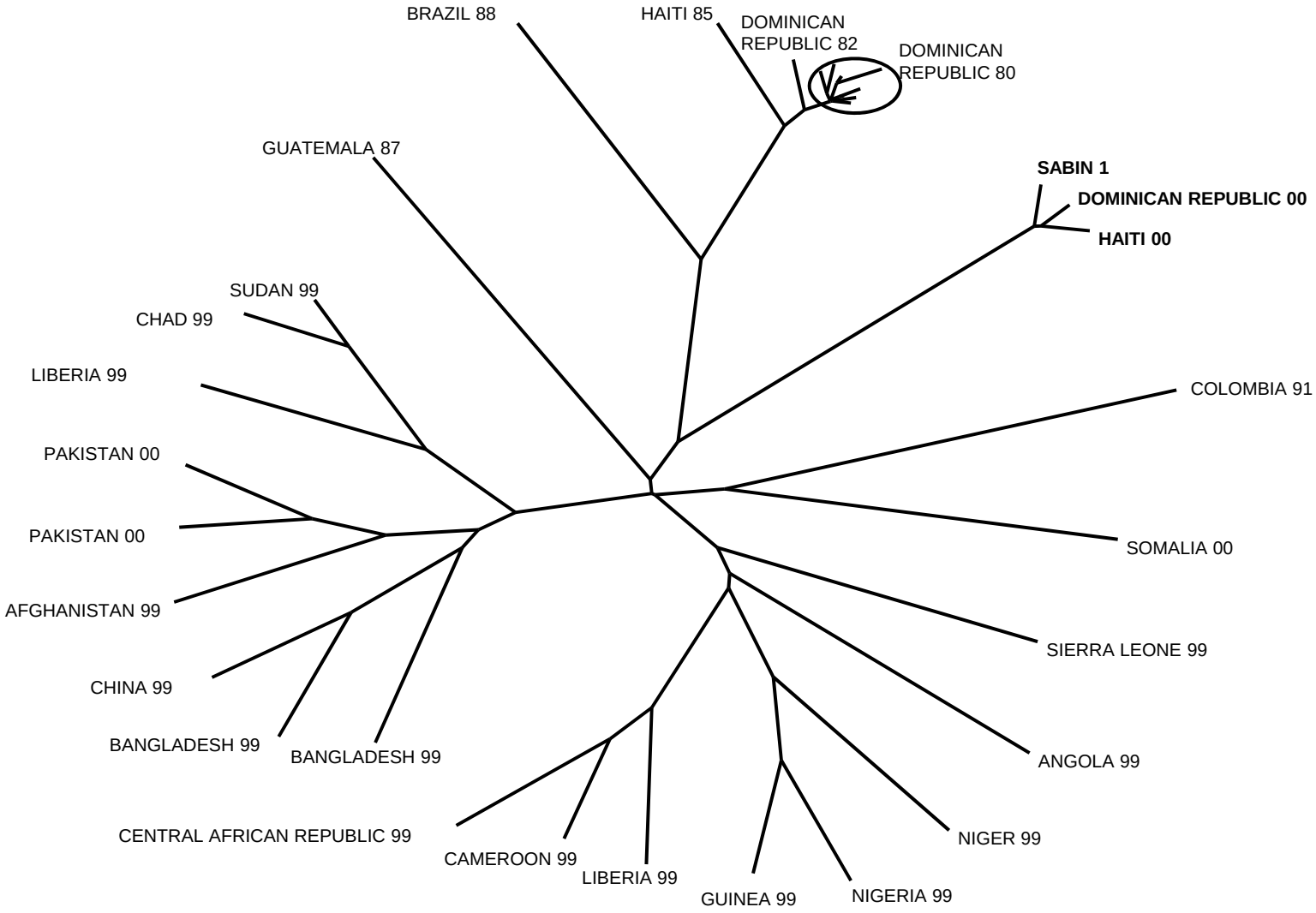
If one country has polio the world is at risk.

cVDPVs: circulating vaccine derived poliovirus strains which cause outbreaks

Arise where vaccine coverage is poor or patchy.

Outbreaks in Hispaniola, Egypt, Madagascar, Phillipines, China, Nigeria,etc

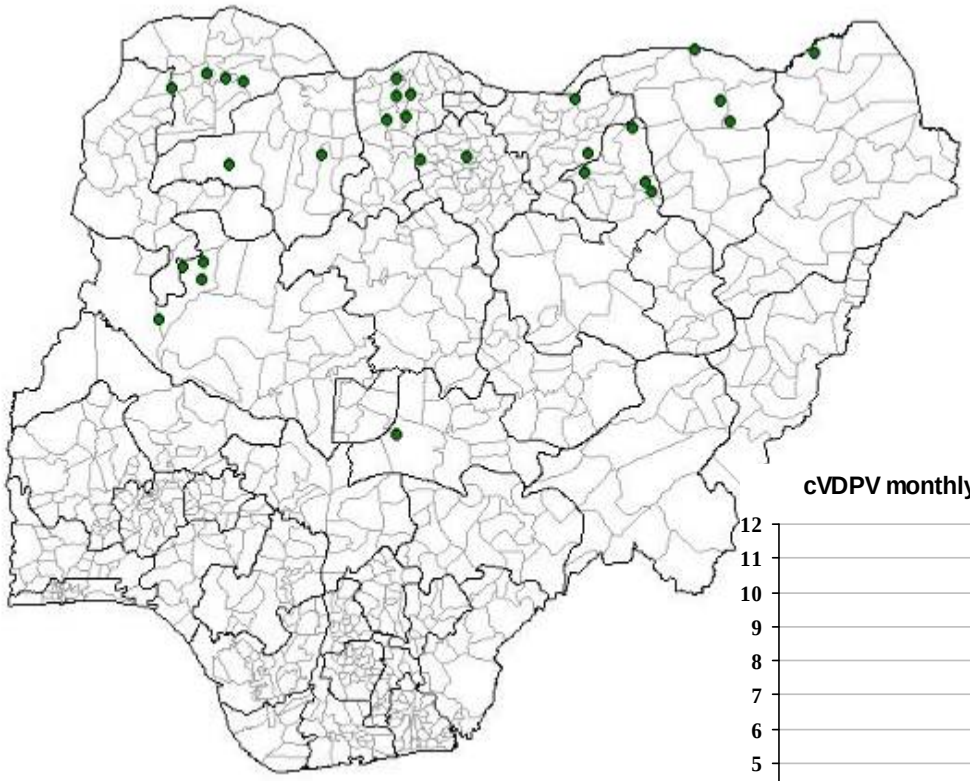
Relationship Between Sabin 1-Derived Isolates from Haiti and the Dominican Republic to Type 1 Wild Polioviruses



VP1 (906 nt)

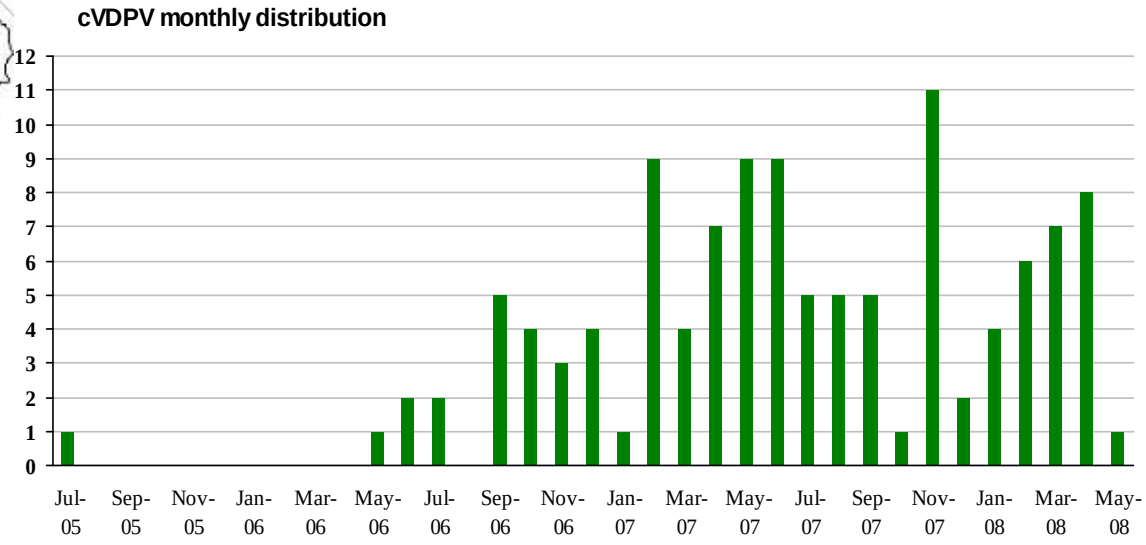
The Gravity of the Problem in Nigeria:

type 2 circulating Vaccine-derived Poliovirus (cVDPV)



Rolling 6 months map:
5 Dec 2007 – 4 Jun 2008

- cVDPV *(28 cases)*



dots are randomly placed within districts

Data in WHO HQ as of 04 Jun 2008

Hypogammaglobulinaemic patients can become chronic excreters of poliovirus after receiving OPV by mistake. The world record so far is over twenty five years.

Live oral polio vaccine can revert to circulating paralytic polio virus.

Prolonged excretion of poliovirus is possible.

Solution to the OPV issue

Stop using OPV to prevent new VDPVs.
Immunise with IPV to maintain protection.

IPV usage according to GPEI

Major uncertainty (in red)

Category of countries		Birth (Million, 2015)	Demand (Million, 2017)	Major countries	Potential IPV adoption scenario: Earliest Timing	Eradication dependent?	Duration	Type/Dose
Current users[1)]		20.0	74	• U.S., Mexico, Russia and others	n/a	No	Indefinite	Follow current policy
High income countries		0.1	0.3	• Singapore, Equatorial Guinea and others	2011	No	Indefinite	3 doses (Combo)
Self-producers	Eradication independent	19.6	70	• China, Japan	2013	No	Indefinite	3 doses (Combo)
	Eradication dependent	32.5	89	• India/Indonesia • Brazil	2015 or later	Yes or no	Indefinite	3 doses (Combo)
Upper middle-income countries[2)]	Eradication independent	2.1	6	• Algeria, Malaysia, Kazakhstan, Libya and Serbia[3)]	2013	No	Indefinite	3 doses (Combo)
	Eradication dependent	2.9	8	• Colombia, Argentina, Venezuela[4)]	2015 or later	Yes or no	Indefinite	3 doses (Combo)
Lower middle-income countries[2)]	2-4-6 month schedule	6.7	22	• Egypt, Iran, Iraq, Thai, Guatemala [5)]	2017	Yes	Indefinite or 5 years[7)]	3 (combo) or 2 (standalone)
	6-10-14 wk schedule	3.0	10	• Philippine, Morocco, Cape Verde and others	2017	Yes	5 years or indefinite	2 (standalone) or 3 (combo)
GAVI countries		50.3	96	• Nigeria, Pakistan, Bangladesh, Ethiopia, DR Congo [6)]	2017 or later	Yes or no	5 years or indefinite	2 (standalone) or 3 (combo)
	Total	137.3	375					

1)Include both standalone and Combo IPV use. Assumes non-Hexa IPV users will shift to Hexa in 2011
2)Excluding GAVI countries
3)Top 5 countries representing 87% of birth cohort
4)Top 3 countries representing 75% of birth cohort Top 5(plus Chile and Dominican Republic) represent 91% of birth cohort
5)Top 5 countries representing 87% of birth cohort
6)Top 5 representing 43% and top 10 (plus Tanzania, Uganda, Kenya, Serbia, Afghanistan, Vietnam) represent 61% of birth cohort
7)Represnting tentative use in post-eradication

IPV manufacture

Grow wild type virus
Treat with diluted formalin for twelve days
Use

The Cutter Incident (1955)

Poliomyelitis in 60 recipients and 89 contacts of vaccine.

Live virus isolated from vaccine.
Occurred within seven days of the licence being granted.

Founding of the Biologicals arm of FDA as we know it.

IPV production systems are the biggest single concentration of poliovirus on the planet.
Escapes have been documented in the past.
Although facilities have improved the entry of new manufacturers is possible.
This may be the most likely source of polio re-emergence if the wild type is truly eradicated.

At the moment there are four manufacturers of licensed IPV, all in Europe.

Reasons to use the Sabin strains

1. Safer than wild type
2. Provide a base for restarting OPV production in an emergency.

61st World Health Assembly resolution on longterm poliovirus risk management

Implications for GAPIII:

- Formally acknowledges goal of safer and more affordable IPV production
- Safeguards revised and re-organized
- Timing of safeguard implementation adjusted

Some issues

1. Assays.
2. Efficacy.
3. Yields and production.
4. Clinical trials.
5. Combination vaccines and interactions.
6. CONTAINMENT.

Developing country production

Interest by a number of vaccine manufacturers in the developing world to produce sIPV.

Large countries seem to be especially interested in producing sIPV, including China, India and others.

To produce sIPV safely, prospective manufacturer needs to make substantial capital and human resource investments to meet not only the GMP but also the containment requirements for sIPV.

Production in developing countries could lead to substantial reductions in cost of sIPV production.

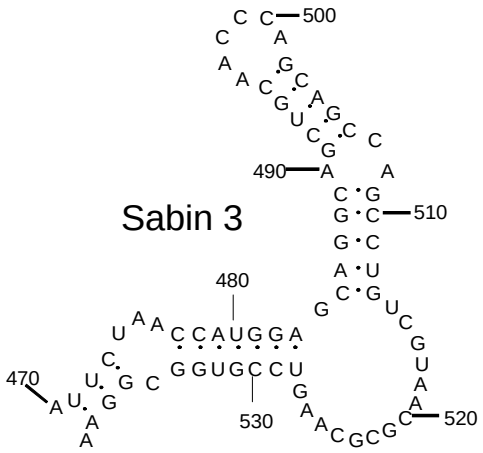
WHO/UNICEF Consultation meeting 2007

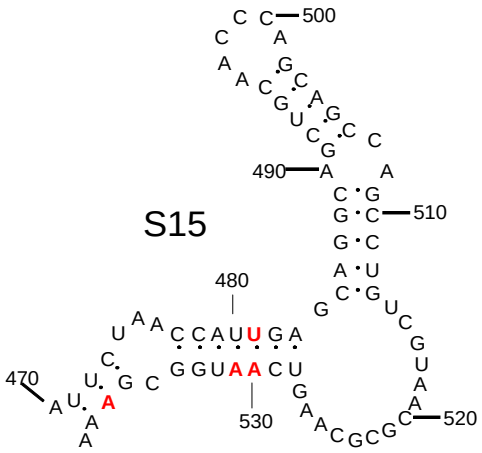
Prequalification (WHO)

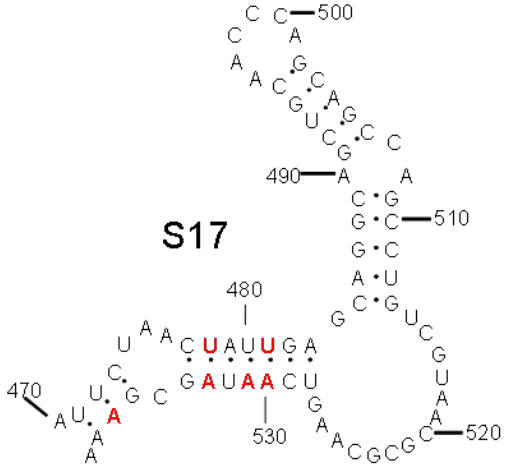
Six functions of the National Regulatory Authority:

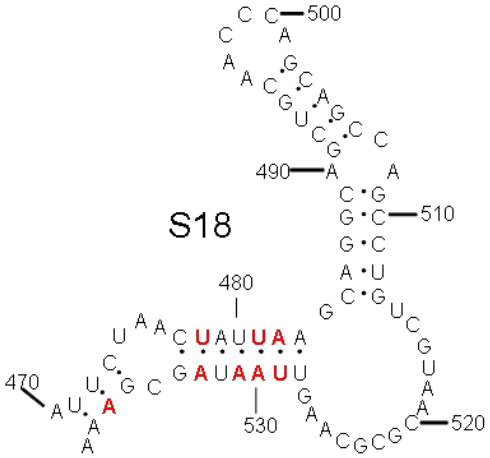
- Licensing
- Surveillance of vaccine performance
- Lot release
- Lab access
- GMP inspections
- Clinical evaluation

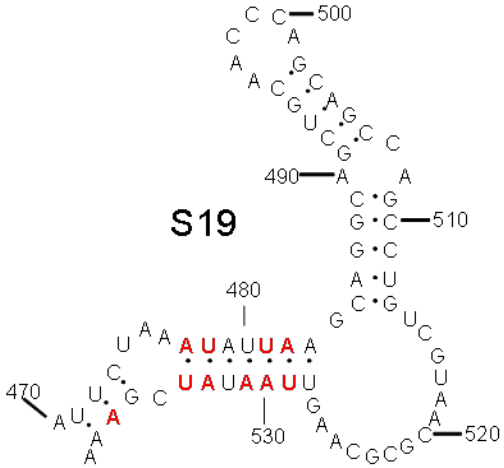
Design of mutilated strains











Summary

Polio is very nearly eradicated.

Vaccination will continue for some time, particularly with IPV.

It is unlikely that production will be confined to the existing manufacturers.

This has pluses and minuses which might be addressable.