SAGE Polio Working Group Report

Proposed policy for a switch from 'tOPV to bOPV' globally

April 10, 2012

Nov 2011: SAGE decisions

- phased rather than simultaneous removal of SABIN serotypes is desirable
- a pre-eradication switch from tOPV to bOPV for routine immunization is advantageous

Jan 2012: WHO Executive Board

'Requests…a comprehensive eradication & endgame strategy….inform Member States of the potential timing of a switch from tOPV to bOPV for all routine immunization programmes'.

EB Resolution 130/19

OPV2 cessation: rationale & context

High & increasing type 2 cVDPV burden

- cVDPV2 accounts for 83% of all cVDPV cases since 2000
- cVDPV2 found in 8 of 9 countries reporting a cVDPV in 2008-10
- 38% of annual VAPP cases globally are P2

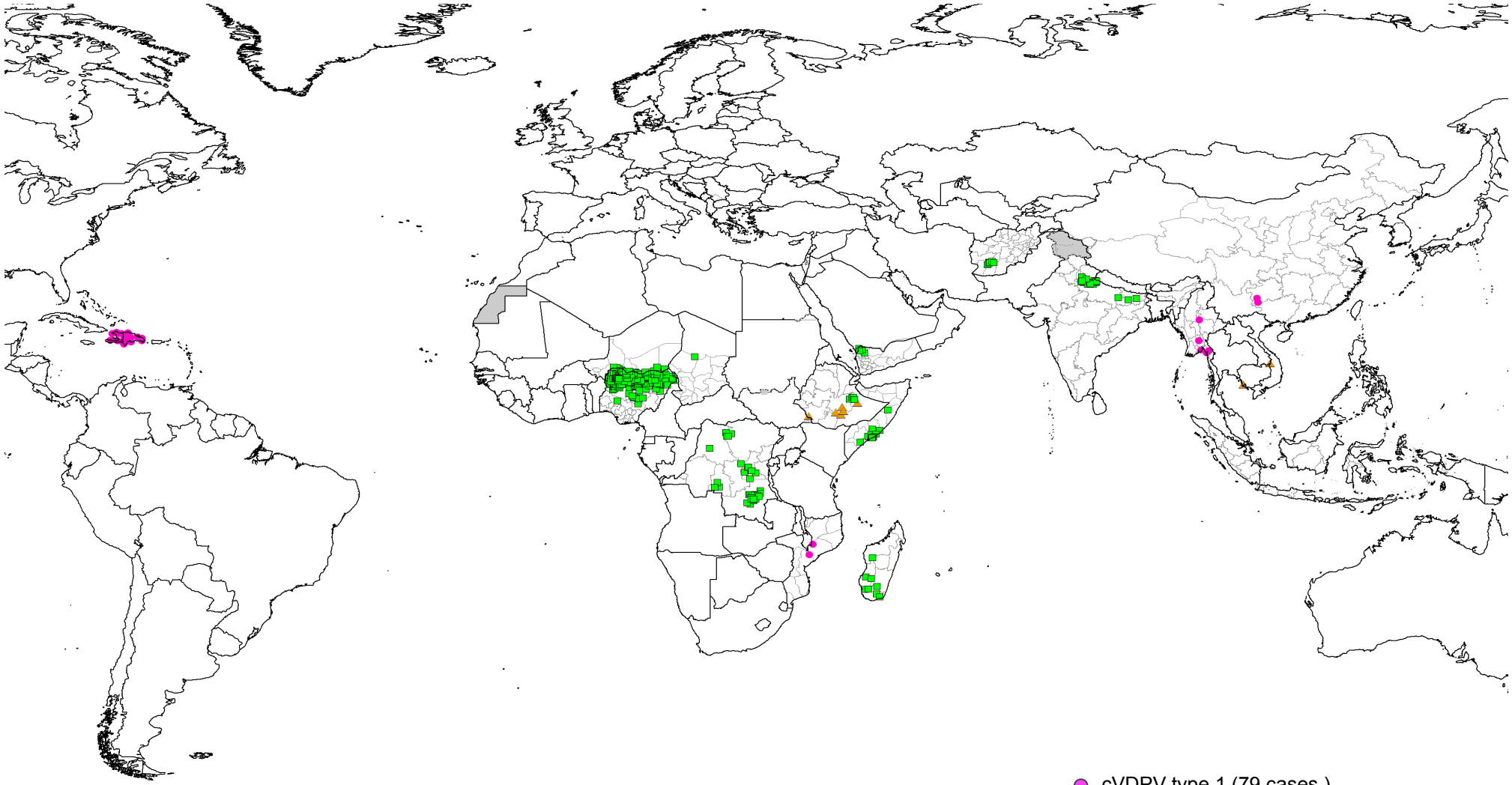
No WPV2 re-introduced since 2004, despite limited containment

Global surveillance & response nearly optimal & work is ongoing to address gaps

bOPV licensed & scaled up but some countries use a national tOPV

Low-cost IPV options, suggest <US$0.5/dose is currently feasible

circulating Vaccine-derived Poliovirus*, 2000 to 2011



*Circulating Vaccine-derived poliovirus (cVDPV) is associated with 2 or more cases of AFP. VDPV type 2 cases with greater than 5nt difference from sabin in VP1 and VDPV type 1 and 3 cases with greater than 9nt difference from sabin in VP1 are reported here. Figures exclude VDPV from non-AFP source. Figures may include different chains of transmission.

Data at HQ as of 06 Feb 2012

circulating vaccine-derived polioviruses*, 2000 to 2011

Country	cVDPV type 1*													First case	Most recent case
	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012		
Mozambique												2		10-Feb-11	02-Jun-11
Myanmar							1	4						09-Apr-06	06-Dec-07
Indonesia						46								09-Jun-05	26-Oct-05
China					2									13-Jun-04	11-Nov-04
Philippines		3												15-Mar-01	26-Jul-01
DOR/Haiti	12	9												12-Jul-00	12-Jul-01

Country	cVDPV type 2*													First case	Most recent case
	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012		
Niger							2			2	1	1		28-May-06	11-Nov-11
Nigeria						3	22	71	66	154	27	33		02-Jul-05	07-Nov-11
DRCongo									13	5	18	4		22-Mar-08	10-Nov-11
Yemen												5		09-Apr-11	29-Jul-11
Somalia									1	6	1	7		29-Jun-08	10-Jul-11
Afghanistan											5	1		10-Jun-10	20-Jan-11
Chad											1			10-Nov-10	10-Nov-10
India										15	2			14-Jun-09	18-Jan-10
Ethiopia									3	1				04-Oct-08	16-Feb-09
Madagascar		1	4			3								29-Oct-01	13-Jul-05

Predominance of cVDPV2 confirmed with new diagnostics

Country	cVDPV type 3*													First case	Most recent case
	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012		
Ethiopia										1	6			27-Apr-09	04-Nov-10
Cambodia						1	1							26-Nov-05	15-Jan-06

Data at HQ as of 15 Feb 2012

Prerequisites for a tOPV-bOPV switch I

Full cVDPV2 detection + control prior to OPV2 cessation

- interruption of all ‘persistent’ cVDPV2s ('persistence' defined as circulation for > 12 months)
- system for sensitive + timely cVDPV detection & response
- proven capacity to stop new cVDPV2 within 6 months

Laboratory containment

- Global Action Plan III adapted to reflect additional OPV2 cessation issues

Prerequisites for a tOPV-bOPV switch II

Vaccine availability (routine immunization)

- sufficient bOPV for tOPV/bOPV switch
- sufficient 'affordable' IPV to introduce at least 1 supplementary dose 6 months before bOPV-tOPV switch
- international agreement to stop delivery of tOPV formulations globally

Stockpile & outbreak response

- stockpiles of appropriate OPV2-containing vaccines (i.e. mOPV2)

Feb 2012: SAGE Key issues

- Nigeria urgently needs to stop the cVDPV2 that has been ongoing for > 5 years *(wild poliovirus type 2 was eradicated in 1999)*

- Intra-dermal administration of fractional (1/5th) dose IPV should undergo fast-track regulatory review given its potential role in a tOPV-bOPV switch

Evidence base & policy recommendations supporting SAGE recommendation for using IPV in the context of a tOPV-bOPV switch

Feb 2012: WG meeting on using IPV as part of a tOPV-bOPV switch

Key questions:

1. should routine IPV use be selective or universal ?

2. if universal, should minimum schedule be 1 or 2 doses?

3. can intramuscular & intradermal dosing (1/5th) with IPV be considered equivalent in context of a tOPV-bOPV switch?

4. optimal timing for a tOPV-bOPV switch? as part of the 'emergency plan' (e.g. late 2013/early 2014) or after?

1. Selective vs. universal IPV use?

Evidence base:

- as long as OPV use continues, cVDPVs pose a risk
- all countries are at risk of cVDPV2 exposure now
- IPV can reduce, but not eliminate, the already relatively small risk of cVDPV emergence*
- IPV can reduce the consequences of cVDPV emergence (fewer cases of paralytic polio in the event of a cVDPV2 outbreak)
- the risk of cVDPV emergence varies significantly by area, the schedule can be adapted to that risk

*Ref: *Duintjer Tebbens RJ, Pallansch MA, Kew OM, Cáceres VM, Jafari H, Cochi SL, Sutter RW, Aylward RB, Thompson KM. Risks of paralytic disease due to wild or vaccine-derived poliovirus after eradication. Risk Analysis 2006;26(6):1471-1505.*

1. Selective vs. universal IPV use?

WG recommendations:

- Given the availability of a low-cost IPV option, the introduction of IPV should be universal
  - all countries should switch from tOPV to bOPV and should, in advance, introduce a supplementary dose of IPV at the DPT3 contact
  - IPV will boost immunity to all serotypes in children with prior immunity & prime naïve children in case a 2nd IPV dose is required

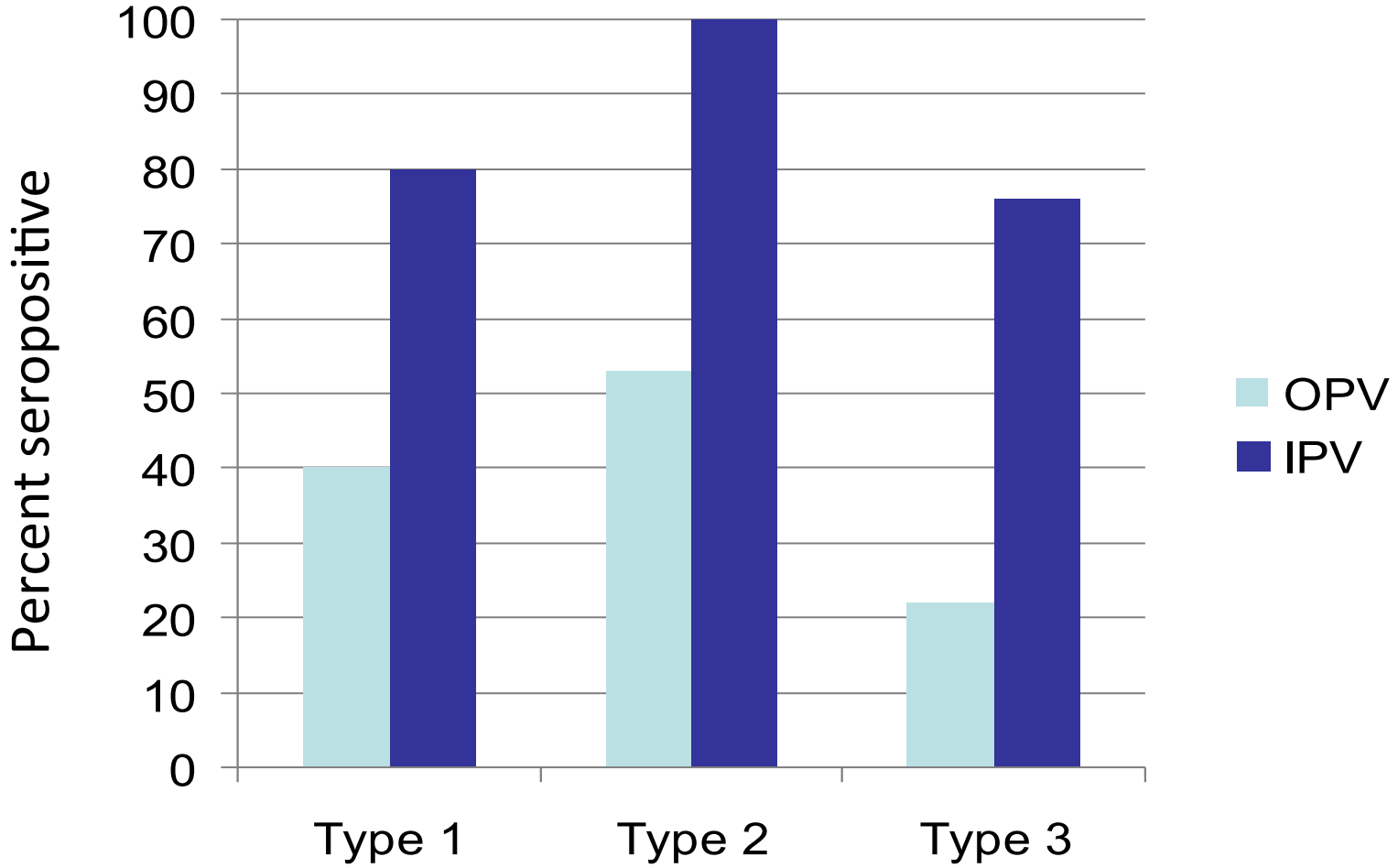
- This approach will reduce the risk of cVDPV2 emergence & in the event of a cVDPV2 outbreak the number of paralytic cases. It also provides a base for boosting immunity if needed.

2. One versus two IPV doses?

Evidence base:

- **In previously OPV-vaccinated children**
  - 1 dose of IPV significantly boosts humoral immunity
  - 1 dose of IPV could also boost mucosal immunity, thereby maximizing type 2 protection prior to a tOPV-bOPV switch
- 1 IPV dose appears to prime 95% of naïve children against PV2 (and, based on VAPP data, may provide protection against paralytic disease)
- in cVDPV high-risk & bordering areas, a 2nd IPV opportunity may consolidate type 2 immunity & potentially reduce consequences of a cVDPV2 emergence

Impact of a supplementary dose* of IPV vs. OPV in seronegative children who previously received 3 OPV doses, Côte d'Ivoire



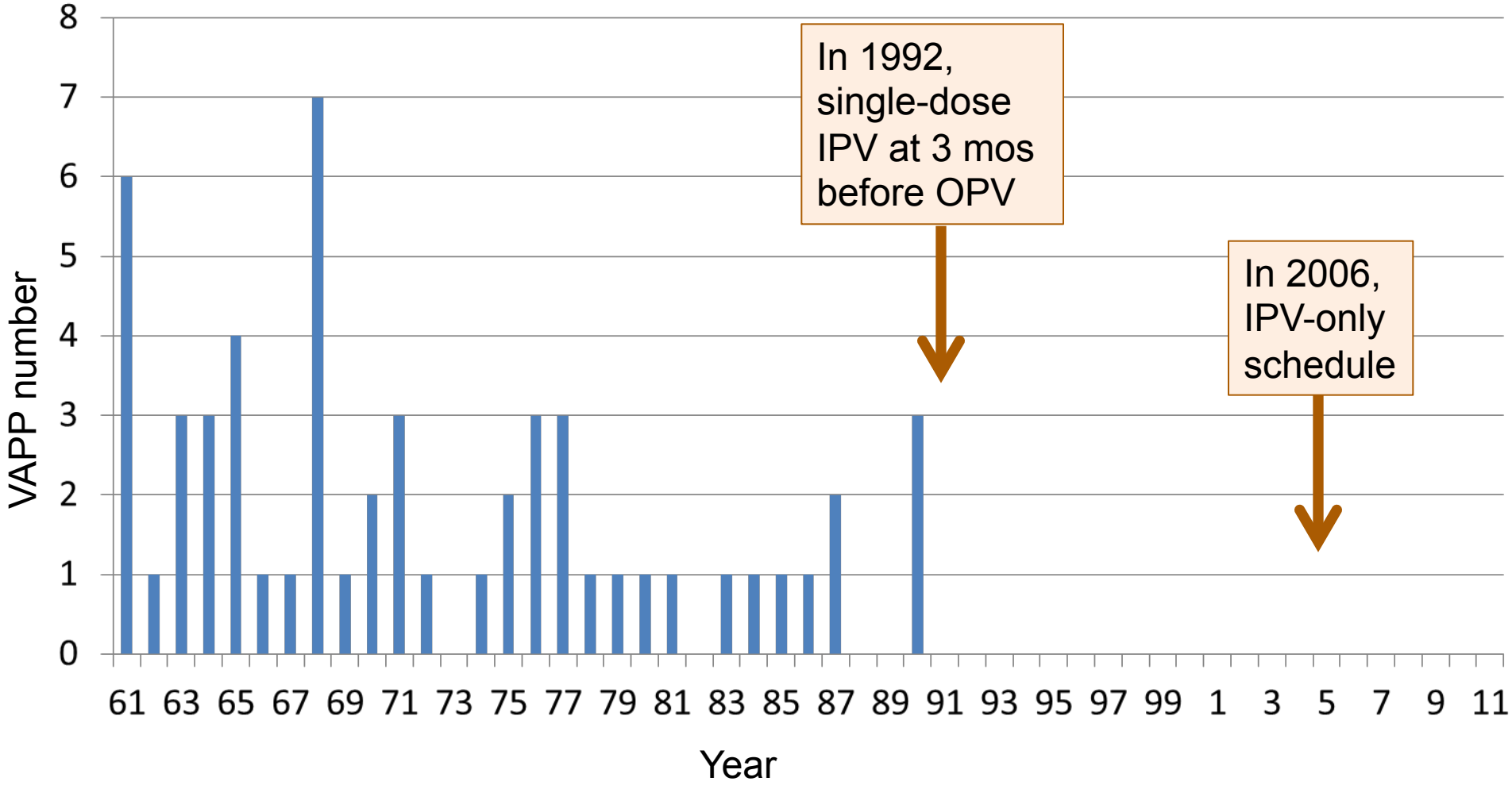
* supplementary doses given at 6 months of age

[Lancet 1993;341:1545-50]

Hungary Polio Vaccination Schedules

- *Before 1992*:
  - mOPV1, mOPV3 and mOPV2
- *In 1992*:
  - IPV at 3 mos (stand-alone vaccine), tOPV at 4, 5, 15 mos, 3 and 6-7 yrs
- *In 2006*:
  - IPV at 2, 3, 4, 18 mos and 6 yrs (pentavalent vaccine)

Vaccine-Associated Paralytic Poliomyelitis, Hungary, 1961-2011



2. One versus two IPV doses?

WG recommendations:

- Given the availability of a low-cost IPV option, all countries should introduce 1 IPV dose at least 6 months prior to a tOPV - bOPV switch, as part of the routine schedule at DPT3 contact

- Further work will need to clarify the need for and feasibility of offering a 2nd IPV opportunity for high-risk areas, including the development of clear criteria for defining high-risk areas

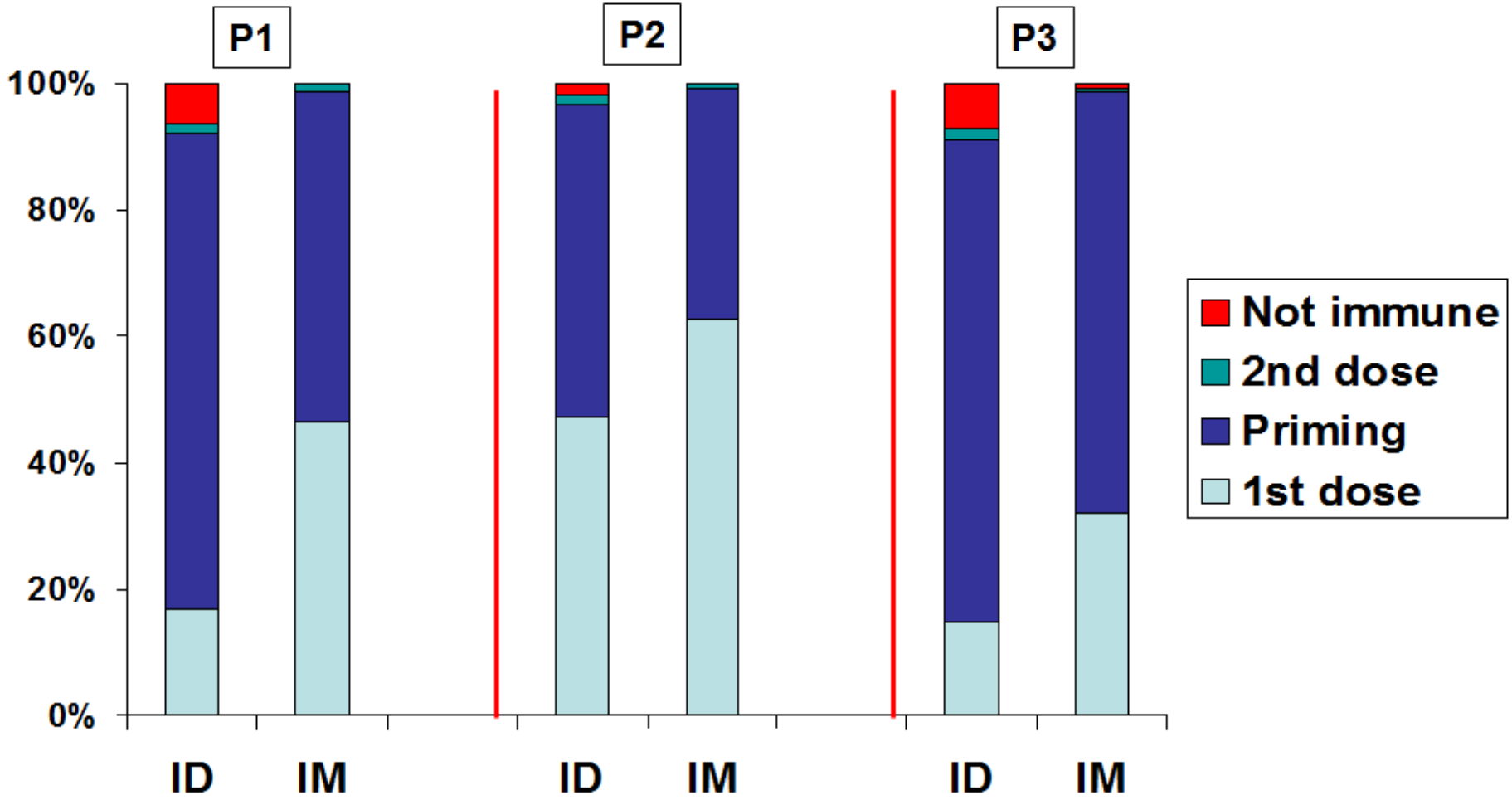
3. Is intradermal, fractional (1/5th) IPV dose an acceptable alternative to whole-dose IPV?

Evidence base:

- in naïve infants, intramuscular (IM) whole-dose IPV typically results in somewhat higher seroconversion rates & substantially higher titres
- however, in naïve infants, intradermal (ID) dosing appears to be nearly equivalent to IM for priming to type 2 if given at 4 months of age
- in previously OPV-vaccinated infants, ID dosing appears to be equivalent to IM dosing for immunity boosting
- some variability has been observed in ID studies, but this appears to be due to differences in the vaccines and devices used

IPV immunity contribution by dose & serotype

Cuba, 2009-10



** submitted for publication*

3. Is intradermal, fractional (1/5th) IPV dose an acceptable alternative to whole-dose IPV?

WG recommendations I:

Intradermal (ID) fractional (1/5th dose) IPV offers important potential advantages over intramuscular (IM) whole dose IPV in the context of a tOPV-bOPV switch

- lower production costs should lead to a substantially lower price than whole dose IPV, and represents the current leading opportunity to offer a low-cost, universal IPV option
- sufficient quantities should be available with current global IPV capacity, although use requires fast-tracking

3. Is an intradermal, fractional (1/5th) IPV dose an acceptable alternative to whole-dose IPV?

WG recommendations II:

- For the purposes of boosting immunity following OPV, ID IPV appears equivalent to IM IPV

- For the purposes of providing priming or protection against type 2 polio in the context of a tOPV-bOPV switch, ID IPV appears to provide an acceptable alternative to IM use

4. Timeline for a tOPV-bOPV switch?

Key Target Dates

- **by end-2012**: cessation of the ongoing cVDPV2 in Nigeria
- **by end-2013:** introduction of one supplementary IPV dose at the DPT3 contact in all OPV-using countries
- **by April 2014:** replacement of tOPV with bOPV for routine & supplementary immunization globally
  (possibly linked to Global Immunization Week)

Proposed SAGE recommendations:

(as per February 2012 SAGE meeting)

1. *The ongoing cVDPV2 in Nigeria must be treated as a public health emergency & stopped as rapidly as possible*

2. *Intradermal, fractional (1/5th dose) IPV should be submitted for regulatory review as rapidly as possible*

Proposed SAGE policy recommendations:

1. *By April 2014, tOPV should be replaced with bOPV for all routine & supplementary immunization, in a globally synchronized operation*

2. *Given the availability of a low-cost IPV option, by 6 months in advance of a global tOPV-bOPV switch, all OPV-using countries should have introduced 1 supplementary dose of IPV (e.g., at or after a vaccination contact at 14 weeks)*

3. *For the purpose of a tOPV-bOPV switch, IPV could be given either as full dose (IM) or fractional (1/5th) ID dose*

Next steps - SAGE Polio WG activities:

Jun 2012: *WG consideration of (a) criteria for defining high-risk areas for cVDPV emergence and (b) additional issues such as need/value of a 2nd IPV opportunity, outbreak response, surveillance & laboratory containment issues, and economics*

by Apr 2013: *WG further guidance on the routine use of IPV in the post-bOPV (post-bOPV) era based on additional information on costs & benefits, particularly for intradermal (ID) fractional dose IPV, that may become available (e.g. from ongoing trials in Cuba and India)*

Summary: Proposed SAGE Policy

1. The ongoing cVDPV2 in Nigeria must be treated as a public health emergency & stopped as rapidly as possible
2. Intradermal, fractional (1/5th dose) IPV should be submitted for regulatory review as rapidly as possible
3. By April 2014, bOPV should replaced tOPV for all routine & supplementary immunization, in a globally synchronized operation
4. By 6 months in advance of a global tOPV-bOPV switch, all OPV-using countries should have introduced 1 supplementary dose of IPV at or after a vaccination contact at 14 weeks, given the availability of a low-cost IPV option
5. For the purpose of a tOPV-bOPV switch, IPV could be given either as full dose (IM) or fractional (1/5th) ID dose

Extra slides

Context: SAGE Polio Working Group ToRs

- WHO Position Paper on Polio Immunization in the pre-eradication period: *published June 2010*
- Policy guidance on routine IPV use in low-income settings in post-eradication era: *from end-2013*
- Assess utility & feasibility of type 2 OPV cessation (tOPV-bOPV 'switch'): *target April 2012 for recommendations.*

Relevant studies planned for 2012

India:

- *Five-arm study*
- *bOPV at birth, 6, 10, 14 weeks (+/- IPV)*
- *3 IPV arms (full-dose IPV + 2 fractional dose IPV [needle & syringe & needle-free device]*

Cuba:

- *Five-arm study*
- *Comparative trial of 3 needle-free devices*
- *Single-dose IPV administered to infants with documented history of 2 doses of OPV*

EVERY LAST CHILD