Strategic Planning for the Post-Eradication Era of Poliomyelitis

19 September 2007

World Health Organization

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In battle, no plan survives contact with the enemy.

von Moltke, the elder.

Presentation Outline

- Objective, background, vaccination options.
- Risks of paralytic poliomyelitis after eradication.
- Policy implications (work in progress).
- Prerequisites and contingency planning for stopping OPV.
- Research to refine policies & negotiating for OPV cessation.
- Implications for vaccination options & conclusions.

Objective of Post-Eradication Planning

To minimize the risk of paralytic disease due to poliovirus among current and future generations of children.

…. realizing that there are no risk-free options ….

The Polio Eradication Effort: Should Vaccine Eradication Be Next?

Alan W. Dove, Vincent R. Racaniello *

The authors are at the Department of Microbiology, Columbia University College of Physicians and Surgeons, New York, NY 10032, USA.

* To whom correspondence should be addressed. E-mail: vrr1@columbia.edu

1997

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

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MORBIDITY AND MORTALITY WEEKLY REPORT

637 Demographic Differences in Notifiable Infectious Disease Morbidity — U.S., 1992–1994
641 Prolonged Poliovirus Excretion in an Immunodeficient Person with Vaccine-Associated Paralytic Polio
643 Adult Blood Lead Epidemiology and Surveillance — U.S.
647 Community Report Cards — U.S.
655 Availability of Morbidity and Mortality Tables on the World-Wide Web

MICROBIOLOGY, Oct. 1998, p. 2893–2899
VOL. 36, NO. 10

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1998

Prolonged Replication of a Type 1 Vaccine-Derived Poliovirus in an Immunodeficient Patient

OLEN M. KEW,[1]* ROLAND W. SUTTER,[2] BALDEV K. NOTTAY,[1] MICHAEL J. McDONOUGH,[1] D. REBECCA PREVOTS,[3] LINDA QUICK,[2] AND MARK A. PALLANSCH[1]

Division of ... Eradication of Vac... Program.

Outbreak of Poliomyelitis in Hispaniola Associated with Circulating Type 1 Vaccine-Derived Poliovirus

Olen Kew,[1]* Victoria Morris-Glasgow,[2] Mauricio Landaverde,[3] Cara Burns,[1] Jing Shaw,[1] Zacarías Garib,[4] Jean André,[5] Elizabeth Blackman,[2] C. Jason Freeman,[1] Jaume Jorba,[1] Roland Sutter,[6] Gina Tambini,[3] Linda Venczel,[3] Cristina Pedreira,[7] Fernando Laender,[8] Hiroyuki Shimizu,[9] Tetsuo Yoneyama,[9] Tatsuo ... arrie van der Avoort,[10] M. Steven Oberste,[1] Da... [1] Stephen Cochi,[6] Mark Pallans... uadros[3]

2002

An outbreak of paralytic poliomyelitis occurred in the Dominican Republic (13 confirmed cases) and Haiti (8 confirmed cases, including 2 fatal cases) during 2000–2001. All but one of the patients were either unvaccinated or incom-

The world is using approximately 2 billion doses of OPV every year → thus, in this steady-state, massive quantities of Sabin viruses replicate and mutate constantly

Original Options for Longterm Polio Immunization Policy

- Stop all polio immunization.
- Stop all OPV; limited IPV use.
- Replace all OPV with IPV.
- Introduce new polio vaccines.

Technical Consultative Group to WHO on the Global Eradication of Poliomyelitis. "Endgame" issues for the global polio eradication initiative. Clin Infect Dis 2002;34:72-77.

Risks of Paralytic Poliomyelitis in the Post-Eradication Era

Risks of Polio After 'Eradication'
with Continued OPV Use

Risk	Frequency to date	Annual burden	Evolution over time
VAPP	**2-4/m birth cohort**	**250-500**	**stable**
iVDPV	**39 identified (since 1962)**	**~1**	**decreases**
cVDPV	**0-3* per year**	**~20**	**increases**
IPV sites	1 accident (1990s)	<1	decreases
Lab accident	1 investigation	NK	decreases
Deliberate	0	NK	unknown

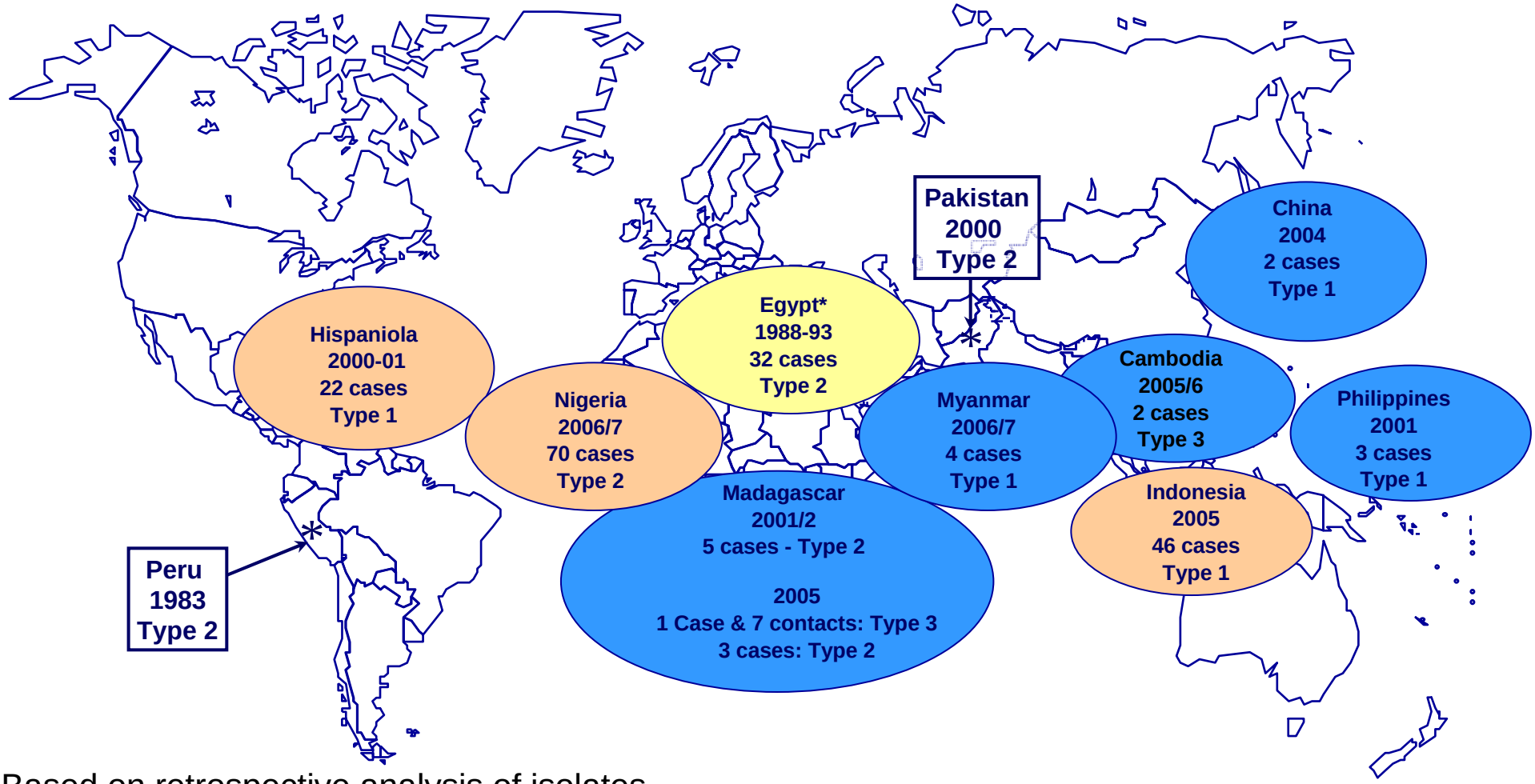
*based on current understanding

1º Risks Associated with Continued, Routine OPV Use

- *Vaccine-Associated Paralytic Poliomyelitis (VAPP):* paralytic polio occurring in vaccine recipients, or contacts of OPV recipients.

- *Circulating VDPV (cVDPV):* > 1 paralytic polio case with isolation of related but non-identical VDPV viruses (1 case if recombination present).

Outbreaks of circulating Vaccine-Derived Polioviruses (cVDPVs), 1988-2007



* Based on retrospective analysis of isolates.

Data reported to WHO as of 11 May 2007

Long-Term Poliovirus Excretors
(iVDPVs: 1º immunodeficiency-associated VDPVs)

39 iVDPVs (> 6 mos excretion)

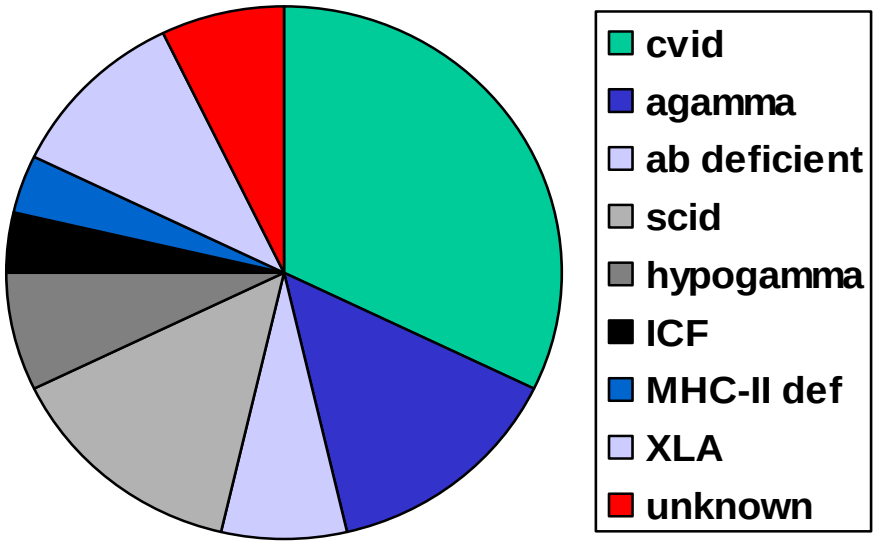
2 known to excrete >5 years.

Type 2 > Type 1 > Type 3

From:

- Industrialized countries (23)
- Middle income countries (15)
- Low income countries (1)

Immunodeficiencies linked to prolonged poliovirus excretion



Policy Implications (evolving area of work)

After interruption of wild poliovirus, continued use of OPV would compromise the goal of a polio-free world.

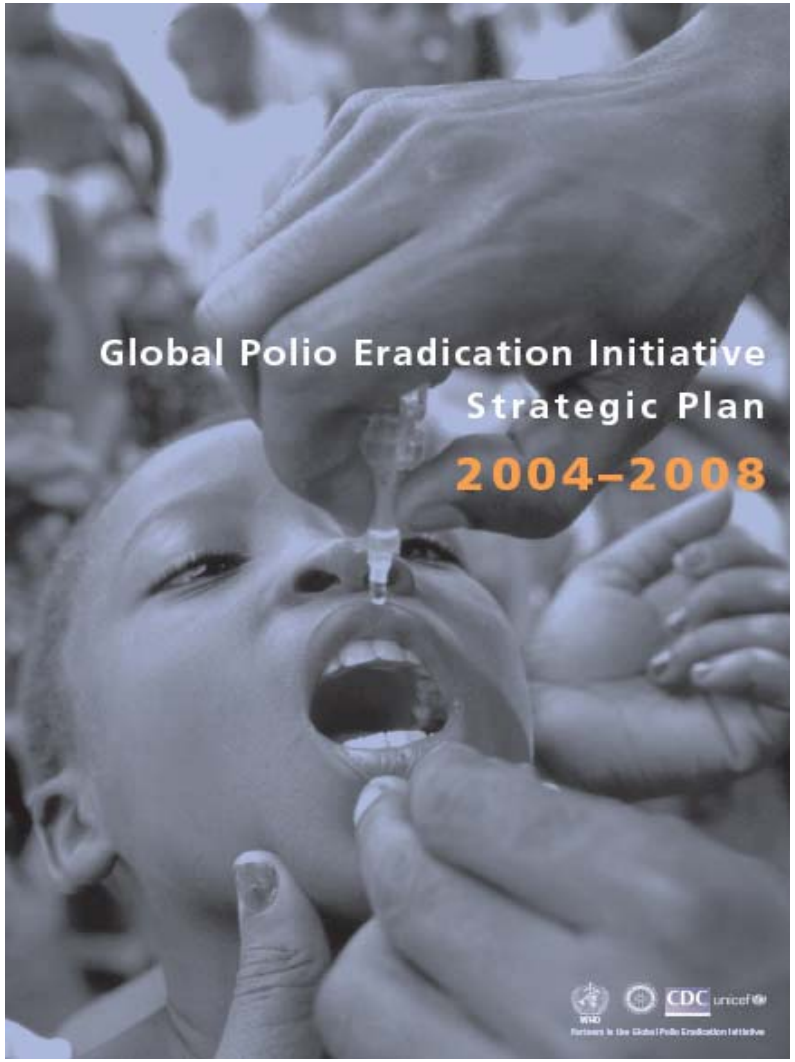
Expert Consultation on Vaccine-derived Polioviruses (VDPVs), Sept 2003, Geneva

Advisory Committee on Polio Eradication (ACPE), 2004

Policy Directive: after interruption of wild type poliovirus, continued OPV use would be incompatible with eradication.

Timing: cessation of routine OPV must occur while population immunity & surveillance sensitivity are high.

Strategic Plan 2004-2008



Direction & Objectives

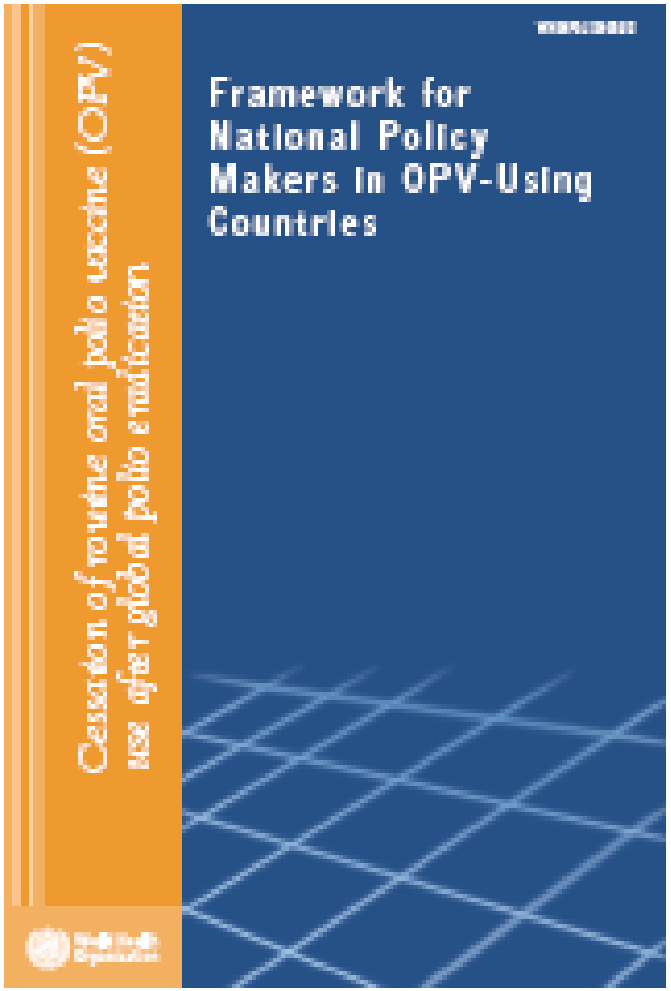
- Interrupt transmission of polioviruses.
- Achieve global certification of polio eradication.
- Establish policies & tools for OPV cessation.
- ‘Mainstream’ the polio eradication infrastructure

Prerequisites for OPV Cessation

Prerequisites for OPV Cessation

- Interrupt & contain wild polioviruses.
- Ensure global surveillance/notification capacity.
- Establish mOPV stockpile & response mechanism.
- Implement IPV requirements in biohazard settings.
- Synchronize cessation of trivalent OPV.
- Contain Sabin polioviruses.

Framework for Policy Makers, 2005



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1. Introduction
2. Rationale for eventual cessation of oral polio vaccine (OPV) use in routine immunization after eradication
3. Risks associated with OPV cessation
4. Risk management before, during and after OPV cessation: implementing the prerequisites for OPV cessation
   - Confirmation of interruption of wild poliovirus transmission globally
   - Appropriate biocontainment of all polioviruses
   - International stockpile of monovalent OPVs (mOPV)
   - Highly-sensitive surveillance for circulating polioviruses
   - Procedure for internationally-simultaneous OPV cessation
   - Long-term routine polio immunization policy
5. Timetable for OPV cessation
6. Glossary of terms

Major Developments in Past Two Years

Major Developments 2005-07

Surveillance

- Polio 'notifiable' in *International Health Regulations (2005).*
- New tools being developed (eg. Real-time PCR; IgM).

Response

- Stockpile *Standard Operating Procedures (SoPs)* draft.
- mOPV1 & mOPV3 licensed and in use.
- GAVI/iFF $190 million to initiate stockpile signed.

IPV

- Supplement to WHO IPV Position Paper (OPV cessation).
- IPV 2-dose & fractional dosing studies.

Longterm containment plan (GAP III)

Global Action Plan for Poliovirus Containment in the Post-OPV Era (3rd ed)

Longterm containment goal: <20 facilities worldwide.

For countries retaining viruses:

- 'Primary safeguards': longterm containment requirements.
- 'Secondary safeguards': low NPEV, sewage systems, high IPV.

Milestones, process and timeframes for OPV cessation, stock recall & destruction.

Draft document for public comment.

2006, 81, 137–144 No. 15

Weekly epidemiological record
Relevé épidémiologique hebdomadaire

14 APRIL 2006, 81st YEAR / 14 AVRIL 2006, 81e ANNEE
No. 15, 2006, 81, 137–144
http://www.who.int/wer

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Inactivated poliovirus vaccine following oral poliovirus vaccine cessation

Supplement to the WHO position paper

WHO issues a series of regularly updated position papers on vaccines and vaccine combinations against diseases that have an international public health impact. These papers are concerned primarily with the use of vaccines in large-scale immunization programmes; limited vaccination for individual protection, as executed mostly in the private sector, may be a valuable supplement to national programme but is not emphasized in these policy documents. Rather, the position papers summarize essential background information on the respective diseases and vaccines and conclude with the current WHO position concerning their use in the global context. The papers are reviewed by a number of experts within and outside WHO and are designed for use mainly by national public health officials and immunization programme managers. However, they may also be of interest to international funding agencies, the vaccine manufacturing industry, the medical community and the scientific media.

This document is a supplement to the WHO position paper on introduction of inactivated poliovirus vaccine (IPV) into countries using oral poliovirus vaccine (OPV).[1] It focuses on preparations for policy decisions on vaccination for the OPV cessation era, which is expected to begin approximately 3 years after confirmation of interruption of poliovirus transmission globally and appropriate containment of wild poliovirus mate-

[1] See No. 20, 2002, pp. 241–250.

Passage au vaccin antipoliomyélitique inactivé suite à l'abandon du vaccin antipoliomyélitique oral

Supplément à la note d'information de l'OMS

L'OMS publie une série de notes d'information régulièrement actualisées sur les vaccins et les associations vaccinales contre les maladies ayant une incidence sur la santé publique internationale. Ces notes d'information portent essentiellement sur l'utilisation des vaccins dans le cadre des programmes de vaccination à grande échelle; certaines vaccinations destinées à la protection individuelle, généralement effectuées dans le secteur privé, peuvent compléter utilement les programmes nationaux mais n'occupent pas une place importante dans ces documents d'orientation. Les notes résument plutôt les faits essentiels concernant les maladies et les vaccins correspondants et donnent en conclusion la position actuelle de l'OMS concernant leur utilisation dans le monde. Elles ont été revues par un certain nombre d'experts au sein même et en dehors de l'OMS et sont essentiellement destinées aux responsables nationaux de la santé publique et des programmes de vaccination. Toutefois, elles peuvent également être utiles aux organismes internationaux de financement, aux fabricants de vaccins, aux membres des professions médicales et aux médias scientifiques.

Le présent document est un supplément à la note d'information de l'OMS relative à l'adoption du vaccin antipoliomyélitique inactivé (VPI) par les pays utilisant le vaccin antipoliomyélitique oral (VPO).[1] Il s'intéresse aux dispositions à prendre concernant les décisions politiques de vaccination pour la période qui suivra l'abandon du VPO, qui devrait débuter près de 3 ans après confirmation de l'interruption de la transmission du poliovirus dans le monde et confinement

[1] Voir N° 20, 2002, pp. 241-250.

Inactivated poliovirus vaccine following oral poliovirus vaccine cessation

Supplement to the WHO position paper

Supplement to the WHO Position Paper on IPV Following OPV Cessation

Publication date: 14 April 2006 (WER)

Major Policy Implications:

- establishes IPV schedule & coverage requirements for countries holding poliovirus after OPV-cessation (i.e. longterm biohazards).
- introduces potential alternative IPV strategies for countries without poliovirus but which perceive themselves to be at risk (e.g. 2 dose schedules, fractional dosing).
- introduces the concept of 'consequence assessments' to guide decisions on sites for future IPV production facilities.

Stockpile *Standard Operating Procedures (SoPs) for monovalent OPVs*

1st Draft Circulated: 29 Sept 2006

Major Policy Implications:

- Proposes governance and ownership.
- Outlines release criteria & processes.
- Introduces target specifications for stockpiled mOPVs.
- Introduces containment conditions for stockpiled mOPV.

Timeline for Polio Eradication

	Eradication & Certification	OPV Cessation & Verification	'Post OPV' Era
Priority Activities	Stop wild virus. Certify eradication. Contain wild viruses. mOPV stockpile.	Stop trivalent OPV. Contain Sabin viruses. Verify cVDPV absence.	Surveillance. Stockpile. Containment.
Earliest Date	**2007 2008 2009 2010**	**2011 2012 2013**	**2014** →

Next Steps

Research for Safer and Affordable IPV

- Schedule
  - Routine schedule for IPV use in tropical areas (Cuba & Puerto Rico).
- Dose Reduction
  - Intradermal administration of 1/5 fractional IPV dose (Cuba & Oman).
- Schedule & Dose Reduction
  - 2-dose fractional schedule (DTP4 & measles)
- Adjuvants
  - Evaluate adjuvants for antigen reduction (S-IPV project).
- Seed strains for IPV production (Sabin & others)
  - Permit production of IPV in developing countries (S-IPV & NIBSC).
- Needle-free Device to Administer IPV Intradermally
  - Easier administration of fractional doses & use of volunteers.

Intradermal Immunization (≤0.2 ml)

NEW DEVICE

OLD DEVICE

Research for Outbreak Control

- **IPV**
  - **Mucosal immunity (Cuba).**
  - **Herd immunity for Sabin viruses (Indonesia).**
  - **Control of cVDPV (opportunity).**
- **Antiviral Agents**
  - **Development of two compounds (NAS meeting report).**
- **mOPV**
  - **Shorter interval between rounds (e.g., every 2 weeks – Somalia)**
- **Diagnostics**
  - **Direct detection without amplification.**
- **Stockpile**
  - **Composition.**

Negotiating OPV Cessation

'Binding' international consensus is required for:

- Destroying/containing *all* polioviruses (per GAP III),
- Synchronous cessation of all OPV & stock destruction.
- International oversight of the reintroduction of live attentuated viruses for outbreak response.

Process: Amendment to the Int'l Health Regs (2005).

Timeline: initiate intergovernmental process in 2007-8.

Requires a 36+ month process given the periods for (a) reservations & rejection and (b) Entry into Force (EIF).

Conclusion

Current Options for Longterm Polio Immunization Policy

Could inadvertantly *increase* longterm risks (due to lack of vaccines, bioterrorism, etc)

- ~~Stop all polio immunization.~~
- Stop all OPV; limited IPV use.
- Replace all OPV with IPV.
- ~~Introduce new polio vaccines.~~

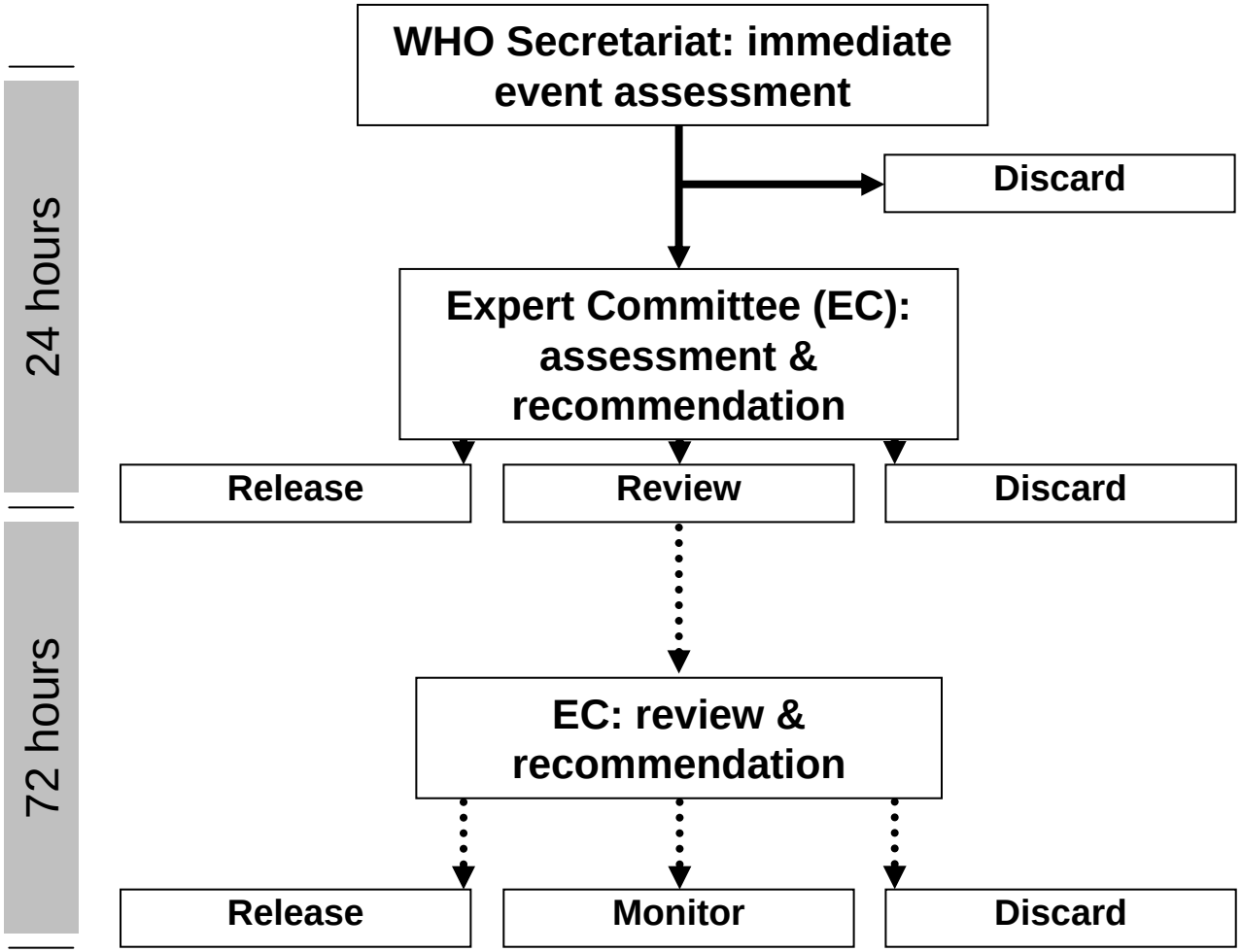
Not possible or realistic from regulatory, manufacturer & other perspectives

Conclusions

- "Without OPV cessation **no polio eradication**"
- **No risk-free option** to stop OPV (or to continue OPV).
- Strategies for stopping and preventing emergence of VDPVs are getting better defined (this is work in progress, integrating rapidly new scientific and programmtic data).
- Expanded use of IPV will make the world safer, but with current vaccine prices, there will be substantial costs and opportunity costs.
- Considerable research under way to promote **a safer and affordable IPV** for use in developing countries.
- Contingency planning assumes **cVDPV outbreaks** in the first 3 years after OPV cessation.

Thank you!

mOPV Stockpile Release & Use: Process



Screening for VPDVs
Summary data, 1999 to 2006

	AFP cases w. PVs	AFP cases w. Sabin-like viruses	Category VDPV (% of total SL)		
			cVDPV *	iVDPV	other VPDV
1999-2001	3423	3257	25 (0.76%)	3 (0.09%)	4 (0.12%)
2002	6294	2948	4 (0.13%)	0 (-)	4 (0.13%)
2003	3167	2451	0 (-)	2 (0.08%)	1 (0.0.04%)
2004	3689	2373	2 (0.08%)	0 (-)	3 (0.13 %)
2005	5393	4422	52 (1.2%)	4 (0.09%)	3 (0.07%)
2006	5301	3685	22 (0.60%)	3 (0.08%)	1 (0.03%)
Total	27,267	19,136	105 (0.55%)	12 (0.06%)	16 (0.08%)

Source of data: Reports from regions for lab quarterly newsletter

NB. Minnesota iVDPV of 2005 not included, because from non-AFP sample source

- **Approximately 0.7% of Sabin related strains classified as VDPV**
- **Only a subset (i.e. discordant in ITD tests) of SL strains sequenced**
- **Network's screening policy biased toward mutations in SL viruses that cause antigenic changes**
- **Some VDPVs not detected by network's screening policy**

Evolution of Poliomyelitis Risks Following Eradication

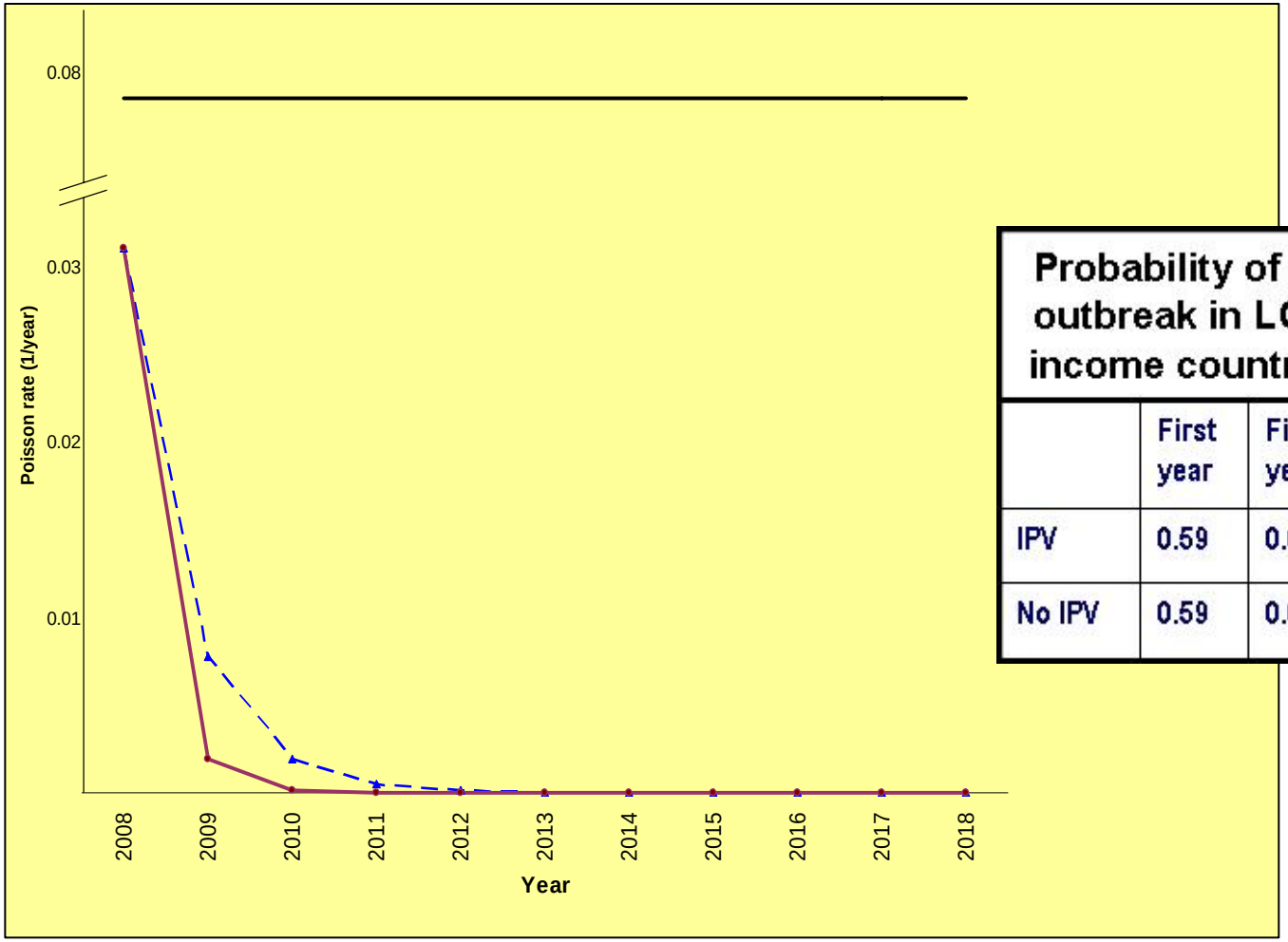
Polio Risks & OPV Cessation

(by income bracket* & immunization policy)

Timeline: years after cessation	Principle risks during OPV cessation phase (0–3)	Principle risks in the 'post-OPV' era (3–5)
Low income OPV-using countries	• circulating VDPVs • mishandled OPV stocks • iVDPVs (short term excretors)	• negligible risks (contingent on high income countries)
High income IPV-using countries	• negligible risks	• laboratory accident • IPV production accident • iVDPVs (chronic excretors) • intentional use

* in upper-middle income countries, risks & policies may reflect high income; low-middle income countries may reflect low income countries.

Global Risk of cVDPV Emergence after Synchronous OPV Cessation



Probability of ≥ 1 outbreak in LOW income countries

	First year	First 3 years
IPV	0.59	0.61
No IPV	0.59	0.69

*Duintjer-Tebbens RJ et al. Risks of Paralytic Disease due to Wild or Vaccine-derived Poliovirus after Eradication. Risk Analysis 2006;26:1471-505.