Background and Technical Rationale for Introduction of One dose of Inactivated Polio Vaccine (IPV) in Routine Immunization Schedules

A handbook for training regional consultants and briefing NITAG members on technical aspects related to introduction of IPV as it relates to the Polio Eradication and Endgame Strategic Plan

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PAHO Note: This version includes recommendations from PAHO's Technical Advisory Group on Vaccine-preventable Diseases for the Region of the Americas. Parts of the original text of this document were eliminated or adjusted to align with TAG recommendations.

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ABBREVIATIONS & GLOSSARY OF TERMS

AFP	Acute Flaccid Paralysis
bOPV	Bivalent Oral Polio Vaccine containing serotypes 1 and 3
cVDPV	Circulating vaccine-derived poliovirus · cVDPV1 (type 1) · cVDPV2 (type 2) · cVDPV3 (type 3)
EPI	Expanded Program on Immunization
GAVI	Global Alliance for Vaccines and Immunization · GAVI Countries · NON-GAVI Countries
GPEI	Global Polio Eradication Initiative
IPV	Inactivated Polio Vaccine
iVDPV	Immunodeficiency-associated vaccine-derived poliovirus
mOPV	Monovalent Oral Polio Vaccine
OPV	Oral Polio Vaccine
PAHO	Pan American Health Organization
PIE	Post-Introduction Evaluation
PPS	Post-Polio Syndrome
PV1	Poliovirus type 1
RI	Routine Immunization
SAGE	Strategic Advisory Group of Experts on Immunization
TAG	Technical Advisory Group on Vaccine-preventable Diseases
tOPV	Trivalent Oral Polio Vaccine
VAPP	Vaccine-associated paralytic poliomyelitis
VDPV	Vaccine-derived poliovirus
VPD	Vaccine-preventable disease
WHA	World Health Assembly
WHO	World Health Organization
WPV	Wild poliovirus

EXECUTIVE SUMMARY

The *Polio Eradication and Endgame Strategic Plan 2013-2018* was drawn up in response to the May 2012 World Health Assembly declaring the completion of poliovirus eradication to be a programmatic emergency for global public health. Under this endgame plan to achieve and sustain a polio-free world, the use of oral polio vaccine (OPV) must eventually be stopped worldwide, starting with OPV that contains type 2 poliovirus (OPV type 2). At least one dose of inactivated polio vaccine (IPV) must be introduced as a risk mitigation measure before the withdrawal of type 2 OPV.

The steps involved are:

1. **By end 2015, introduce at least 1 dose of IPV into all routine immunization systems**, at least 6 months before the switch from trivalent oral polio vaccine (tOPV) to bivalent oral polio vaccine (bOPV, containing types 1 and 3 poliovirus).
2. **During 2016, switch from tOPV to bOPV, which does not contain type 2 virus, in routine immunization and polio campaigns.**
3. **Plan for the eventual withdrawal of all OPV.**

This manual will provide key technical information and up-to-date references to decision-makers and program managers and to train consultants who subsequently will be available to support country planning activities and training sessions for the introduction of IPV.

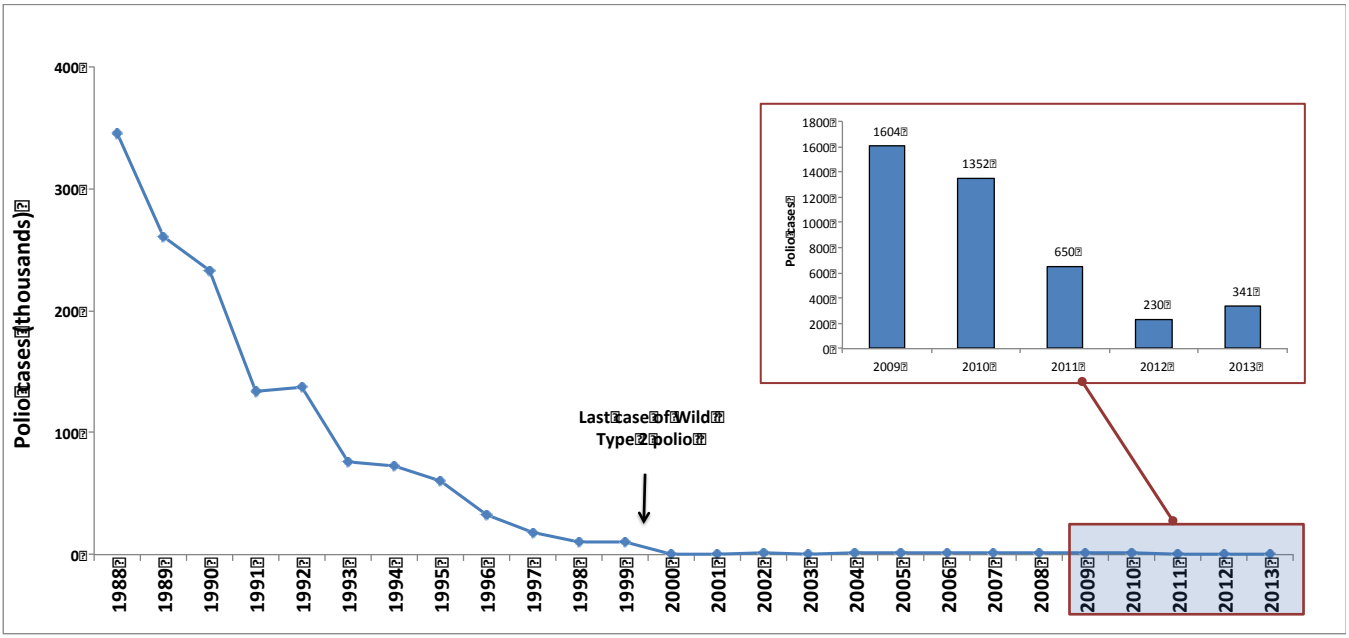
INTRODUCTION

The eradication of polio is a top global health priority. Since the World Health Assembly (WHA) announced a goal to eradicate polio in 1988, thereby creating the Global Polio Eradication Initiative (GPEI), the number of polio cases has drastically declined (Figure 1) from ~350,000 cases per year in 1988 to only 341 cases in 2013 (as of 20 Nov 2013).(1)

The key messages of this document include:

- SAGE has recommended that **all countries introduce at least one dose of IPV** into the **routine immunization schedule** before the end of 2015 and that all priority countries develop an introduction plan by June 2014 and all remaining OPV only countries develop a plan by end-2014
- Because OPV in rare cases can cause paralysis, **OPV cessation must occur for the world to be polio free.**
- OPV cessation will occur globally in 2 phases, with **removal of type 2 component in 2016 (global switch from trivalent OPV to bivalent OPV, containing types 1&3)** followed by bOPV withdrawal in 2018-2019.
- Introducing **IPV before the tOPV-bOPV switch** in 2016 will ensure that a substantial proportion of the **population is protected against type 2 polio** after the withdrawal of type 2 OPV.
- Introducing IPV will **mitigate risks of type 2 reintroduction** in association with the withdrawal of type 2 OPV and will **facilitate polio eradication** by boosting immunity to types 1 & 3.
- IPV introduction will happen through the routine immunization program. There is currently no plan to use IPV in mass immunization campaigns for catch up or other purposes. It is however possible that, in a few limited geographic areas of endemic countries, IPV could be used in combination with OPV for accelerating the eradication of the wild polio virus.

Figure 1: Clinical cases of polio related to wild polio virus globally (1988-2013, as of 20 Nov 2013)



To complete the final milestone, the WHA and countries endorsed *GPEI's Polio Eradication and Endgame Strategic Plan* in May 2013 which provides a detailed approach and concrete timeline for complete eradication of polio.(2) This plan is different from previous eradication plans because **it deals with the eradication and containment of polio caused not just by wild viruses but also paralytic cases associated with oral polio vaccine (OPV)**. To address risks associated with OPV use, the Plan calls for a phased withdrawal of OPV globally. This phased withdrawal would begin with removal of the type 2 component of OPV through a switch globally from trivalent OPV (tOPV) to bivalent OPV (bOPV, containing only types 1 and 3) in 2016. To manage risks associated with removal of the type 2 component of OPV, such as the emergence of circulating vaccine-derived poliovirus (cVDPV) or the re-introduction of the wild type 2 poliovirus, the World Health Organization's (WHO) Strategic Advisory Group of Experts (SAGE) has recommended that all OPV-using countries introduce at least one dose of IPV in their routine immunization programs before the end of 2015, prior to the tOPV-bOPV switch.(3-7)

The need to introduce IPV into all OPV-only using countries globally in a relatively short time represents a major and unprecedented challenge. However, it is also a timely opportunity to improve collaborations between global immunization partners and make efficient use of GPEI resources to strengthen routine immunization services, particularly in countries with the highest risk target populations and weak immunization systems.

The complete Endgame Plan and other resources related to GPEI can be found at http://www.polioeradication.org/resourcelibrary/strategyandwork.aspx

1. GPEI's Polio Eradication & Endgame Strategic Plan (the Plan)

1.1. Overview of the Plan and timeline

In May 2013, the WHA endorsed *The Polio Eradication & Endgame Strategic Plan* 2013-2018 (the Plan), developed by GPEI to complete the eradication and containment of all wild, vaccine-derived, and Sabin polioviruses.(2) It is important to note that this plan differs from previous plans to eradicate polio in that it comprehensively addresses strategies for both endemic and vaccine–related polio. The Plan also incorporates a strategy to contribute to the strengthening of Routine Immunization (RI) and to deliver other health services to the world's most vulnerable children in 10 focus countries (footnote countries[a]).

Key elements of the Plan

-End all types of polio disease

-Improve immunization systems

-Introduce IPV & withdraw OPV

-Mitigate risks of further outbreaks

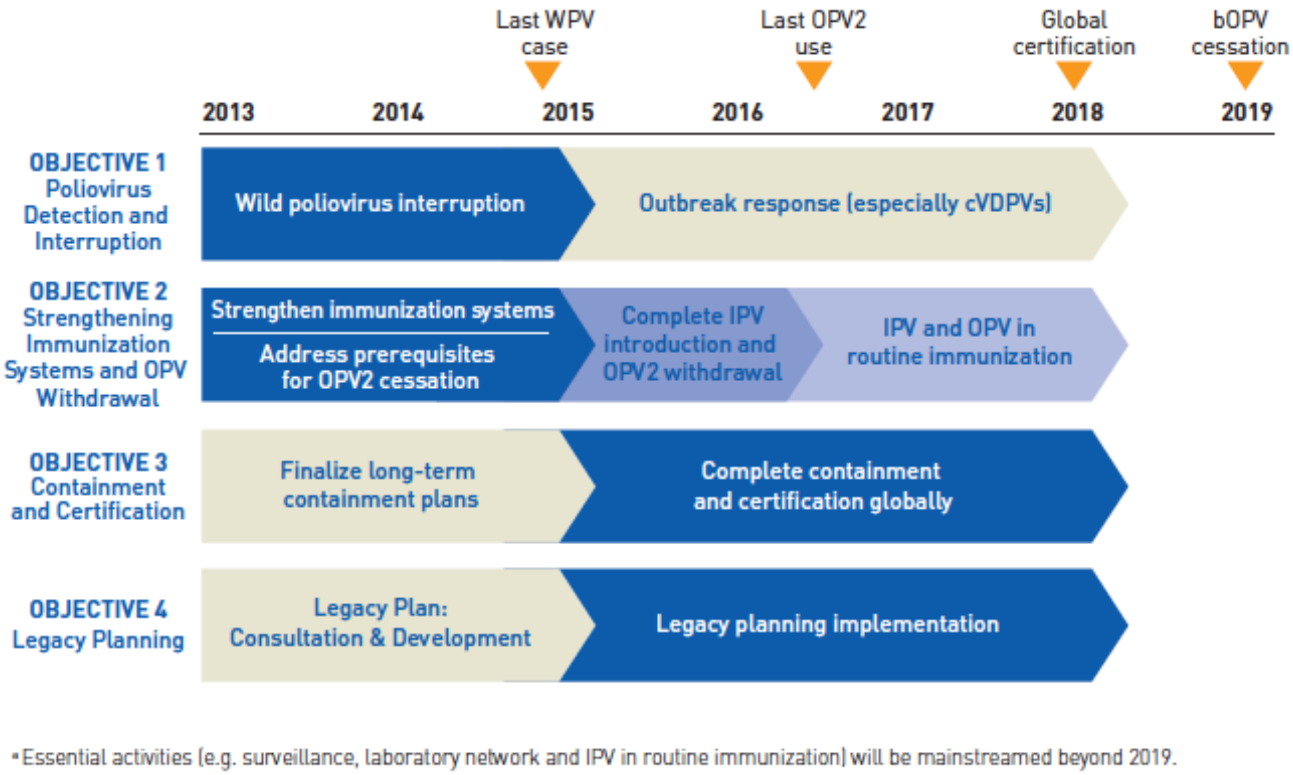
-Establish a concrete timeline

The Plan outlines four objectives (Figure 2). This manual provides the technical rationale for **Objective 2** which addresses the Endgame component of the Plan and calls for:

- strengthening routine immunization in 10 focus countries
- introducing at least one dose of IPV into the routine immunization schedule, and
- then replacing tOPV with bOPV (tOPV-bOPV switch) in 2016 in all OPV using countries – setting the stage for eventually ending bOPV use in 2019-2020.

[a] Focus countries have been identified by GPEI as representing areas still at considerable risk where GPEI has committed significant field assets. They include: Afghanistan, Angola, Chad, Democratic Republic of Congo (DRC), Ethiopia, India, Nigeria, Pakistan, Somalia, South Sudan

Figure 2: Polio Eradication and Endgame Strategic Plan (This figure shows that with full funding, the objectives can be pursued in parallel, with working target dates established for the completion of each.)



•Essential activities (e.g. surveillance, laboratory network and IPV in routine immunization) will be mainstreamed beyond 2019.

2. SAGE (WHO) and TAG (PAHO) recommendations

This manual relates to **Objective 2 of the Plan**, specifically the introduction of IPV into infant immunization schedules of all OPV using countries worldwide.

SAGE has recommended a global, coordinated withdrawal of the type 2 component of tOPV from immunization programs by April 2016. For countries which use only tOPV in their routine infant immunization programs, this will require switching from tOPV to bOPV (containing only types 1 and 3) for that purpose.(3-5, 8)

Prior to the tOPV-bOPV switch, SAGE recommends that all countries introduce at least one dose of IPV into their infant immunization schedules as a risk mitigation measure by providing immunity in case a type 2 poliovirus re-emerges or is reintroduced.(8) Countries have the flexibility to consider alternative schedules in accordance with local conditions, for example, documented risk of vaccine associated paralytic polio (VAPP) before 4 months of age.

Following the recommendations of WHO and SAGE, after analyzing the epidemiology of poliomyelitis in the Region, PAHO's Technical Advisory Group on Vaccine-preventable Diseases (TAG) issued the following recommendations for the Region of the Americas:

- When introducing IPV, countries should consider sequential schedules. Ideally, countries should consider two IPV doses followed by two OPV doses. However, if a country is considering only one IPV dose, this should be with the first DTP dose and followed by three OPV doses.

- Countries should not consider moving directly to an IPV only schedule at this time, unless they meet the criteria previously recommended by TAG and WHO (low risk of transmission and importation, high homogeneous coverage, and good sanitation).

Vaccination Schedule recommended for the introduction of inactivated poliovirus vaccine (IPV) in combination with the oral poliovirus vaccine (OPV).

Schedule	Basic			Booster	
	1st	2nd	3rd	1st	2nd
First option	IPV	IPV	OPV	OPV	OPV
Alternate option	IPV	OPV	OPV	OPV	OPV

This schedule, in addition to preparing the countries for the switch from tOPV to bOPV, has the additional advantage of lowering the incidence of VAPP cases, considering that in our Region, around 50% of VAPP cases are associated with the first dose of OPV.

- To accelerate eradication and reduce vulnerability, all endemic and high risk countries should develop an IPV introduction plan by the middle of 2014; all other countries that use OPV only should develop an introduction plan for IPV by the end of 2014.

- IPV introduction will happen through the routine immunization program. There is currently no plan to use IPV in mass immunization campaigns for catch up or other purposes. It is however possible that, in a few limited geographic areas of endemic countries, IPV could be used in combination with OPV for accelerating the eradication of the wild polio virus

- A catch-up strategy, where children born before the vaccine introduction date are immunized, is not recommended for IPV because these children will have been vaccinated with tOPV, and thus immunized against all three types of polio, particularly type 2.

3. Poliovirus vaccines: Role of IPV and OPV in The Endgame and Eradication Strategic Plan

The development of effective vaccines to prevent paralytic polio was one of the major medical breakthroughs of the 20th century. With the development and evaluation of bivalent oral polio vaccine in 2009, the Global Polio Eradication Initiative now has an armory of six different vaccines to stop polio transmission (Table 1).(9-12)

Table 1: Overview of available polio vaccines

Vaccine	*Wild Poliovirus (WPV) targeted*	*Description*
tOPV	All three types	Historically, the most common form of OPV used in the routine and supplementary immunization activities in low and middle-income countries globally, because of cost, ease of administration, and excellent oral and intestinal immunity
bOPV	Types 1 & 3	Licensed in 2009 after a clinical trial showed non-inferior immunogenicity to use of monovalent types 1 or 3
mOPV1, mOPV2, mOPV3	Either types 1, 2, or 3	mOPV1 and mOPV3 were introduced by GPEI in 2005 to improve OPV effectiveness in the last WPV reservoirs in Africa and Asia.
IPV	All three types	Currently used in most high-income countries due to its excellent safety profile and high efficacy; SAGE recommends introducing at least one dose in routine immunization schedules of all countries before beginning OPV2 cessation in 2016

3.1. Inactivated Polio Vaccine (IPV)

Key messages on IPV introduction

- The primary role of introducing **one dose of IPV into routine immunization programs** is to mitigate risks associated with OPV withdrawal and the potential reintroduction of polioviruses
- IPV will maintain type 2 poliovirus immunity during the tOPV-bOPV switch (removal of type 2 component of OPV) in 2016
- TAG recommends that IPV be administered in a sequential schedule (2IPV+2OPV or 1IPV+3OPV)
- Unlike OPV, IPV is not a "live" vaccine and thus carries no risk of vaccine-associated polio paralysis
- IPV induces humoral and oral immunity to polioviruses and boosts intestinal immunity in children previously vaccinated with OPV

3.1.1. Summary of IPV

IPV was developed in 1955 by Dr. Jonas Salk. Also called the "Salk vaccine," currently available IPV consists of inactivated (killed) wild-type poliovirus strains of all three poliovirus types.(12) The Salk IPV should be distinguished from the Sabin IPV that is still currently under development and is based on the Sabin OPV strains rather than wild virus strains. More information on Sabin OPV stains, OPV immunogenicity and rationale for OPV use can be found in Annex 3.

Because IPV is an inactivated vaccine and not a "live" attenuated vaccine, it carries no risk of vaccine-associated polio paralysis. However, in contrast to OPV, since it does not replicate in the gut, IPV induces substantially lower levels of intestinal immunity and does not confer protection to others through secondary spread. IPV is also less effective than OPV in reducing fecal-oral transmission. IPV is as effective as OPV in inducing oral immunity so it will be equivalent to OPV in preventing oral-oral transmission. Using both vaccines together provides the best form of protection.

The immune response to intramuscularly administered IPV varies based on the number of administered doses (higher with more doses) and the age at vaccination (higher with delayed immunization) (Table 2).(12-14) Unlike OPV, immune response does not vary substantially between industrialized and tropical developing country settings.

In the event of infection, the antibodies induced by IPV prevent the spread of the virus to the central nervous system and protect against paralysis.

Overview of IPV formulations: Currently licensed IPV formulations are given by intramuscular injection and administration requires sterile injection equipment and procedures by trained health workers. IPV is available as a:

- **stand-alone vaccine**, and
- **combination products** with diphtheria, tetanus, acellular pertussis, hepatitis B, or Hib antigens in tetravalent, pentavalent, or hexavalent formulations. Note that a combination product with whole-cell pertussis is not currently available

The combination products currently available are offered at a substantially higher cost than stand-alone IPV (at least $20-$40 per dose) as they use acellular pertussis, which is significantly more expensive to produce than whole cell pertussis.(15)

Note: Currently, only the stand-alone IPV is prequalified by WHO.

- It is available in fully liquid 1-dose, 5-dose, and 10-dose presentations

Stand-alone IPV is sensitive to heat and freezing and must be handled appropriately (see Operational Field Manual for additional information).(16) IPV has a shelf life of 24-36 months (depending on the brand) when stored in a refrigerator at 2°C - 8°C and protected from light. IPV is freeze sensitive and **should not be frozen**.

Note: IPV presented in 5 dose-vials, produced by Bilthoven Biologicals, has been prequalified and approved for use up to 28 days after opening, provided that the following WHO defined criteria are fully met.

1. **The vaccine is currently prequalified by WHO.** In order for a vaccine to be prequalified, WHO independently evaluates data on vaccine quality, safety and efficacy. This evaluation includes examining the effectiveness of preservatives, as well as the stability of the vaccine under different temperature conditions. In addition, the prequalification program assesses such things as the quality of vials, stoppers, caps and labels.

2. **The vaccine is approved for use for up to 28 days after opening the vial, as determined by WHO.** For injectable vaccines, this means that the vaccine contains appropriate type and amount of preservative.

3. **The expiration date of the vaccine has not passed.** This condition is part of immunization best practice and is included here to emphasize the importance of not using a vaccine vial after the product has expired. The expiration date may be reached over the course of the 28 days so, in line with good practice, the expiration dates of all opened vials should be checked prior to every use.

4. **The vaccine vial has been, and will continue to be, stored at WHO- or manufacturer-recommended temperatures.** All vaccines should be stored according to WHO or manufacturer recommended temperatures, normally between +2ºC to +8ºC, and should be protected from freezing and sunlight. If a vaccine vial is labelled as freeze-sensitive and is suspected of having been frozen, or a temperature alarm indicates exposure to sub-zero temperatures, the vaccine should be discarded.

Source: World Health Organization. Department of Immunization, vaccines, and biologicals. WHO Policy Statement: Multi-dose Vial Policy (MDVP). Handling of multi-dose vaccine vials after opening. Geneva: WHO; sept 2014. Disponible en: http://apps.who.int/iris/bitstream/10665/135972/1/WHO_IVB_14.07_eng.pdf.

Table 2: Comparison of characteristics of OPV and IPV

	Oral Polio Vaccines (OPV)	Inactivated Polio Vaccines (IPV)
Types	• Trivalent (tOPV): 1, 2, & 3 • Bivalent (bOPV): 1 & 3 • Monovalent (mOPV): 1, 2, or 3	Trivalent
Route	• Oral	Intramuscular (and sub cutaneous for some brands)
Immune response	• In industrialized settings, seroconversion is ~ 50% to all 3 serotypes for one dose, and > 95% after 3 doses with lifelong immunity • In tropical developing countries, lower immune response necessitates more than 3 doses and additional booster doses. After 3 doses of tOPV seroconverstion rates vary from: ○ 73% (range 36%-99%) for type 1 ○ 90% (range 71%-100%) for type 2 ○ 70% (range 40%-99%) for type 3 • Interference from type 2 vaccine virus is one reason for lower immune response to types 1 and 3	• Immune response similar between industrialized and tropical developing settings ○ 3 doses: nearly 100% seroconversion rates to all 3 serotypes ○ 2 doses: 40%-93% against the 3 serotypes, but exceeds 90% when vaccination is initiated after 8 weeks of age. ○ 1 dose: 19%-46% against Type 1, 32%-63% against Type 2, and 28%-54% against Type 3 poliovirus.
Pros	• Cheap • Easy to administer • Good oral and intestinal immunity • Confers transmission to contracts and secondary vaccination	• No risk of VAPP • Highly effective
Cons	▪ Causes paralysis in very rare cases (VAPP & cVDPVs)	• More costly than OPV • Cannot be administered by volunteers as it requires and injection • Does not confer transmission to contacts and thus provide secondary vaccination

3.1.2. Rationale for phased withdrawal of OPV

Although OPV is the appropriate vaccine until polio transmission is interrupted, with ongoing use of OPV and control of polio disease related to wild virus globally, the estimated number of polio cases related to OPV has exceeded those related to wild virus (Figure 4).

Because of this **very low but real risk of polio associated with OPV**, if the world is to remain free of polioviruses following eradication, then use of OPV ultimately will need to be stopped. To curtail the risk of polio associated with OPV (cVDPV and VAPP), the Endgame calls for a withdrawal of vaccine in two phases(2):

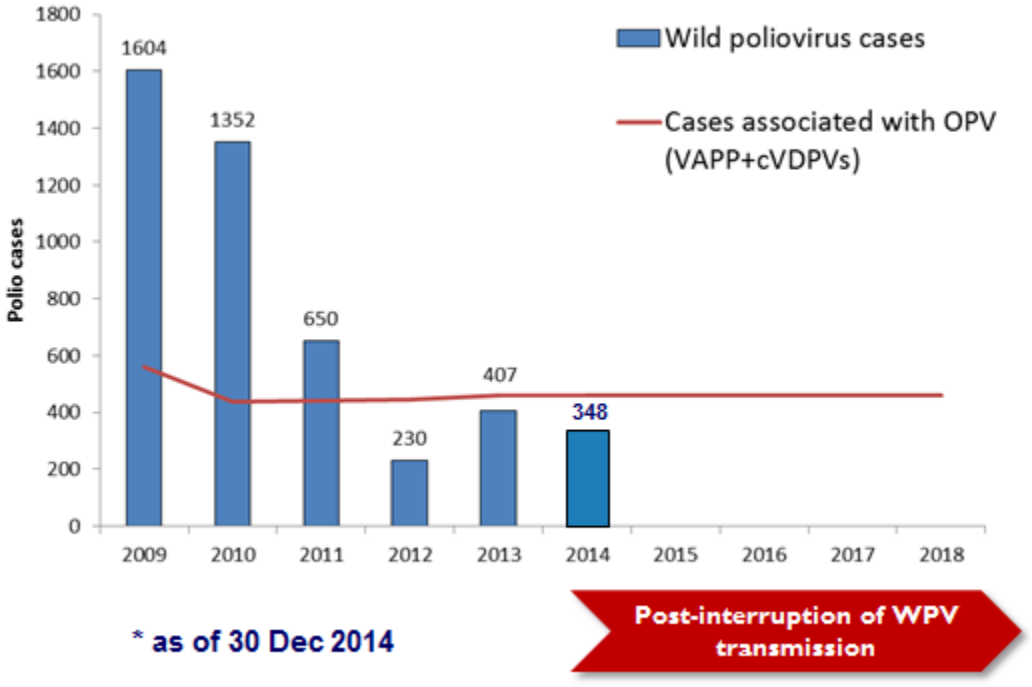
- **Phase 1**: removal of type 2 component of OPV, through a global switch from tOPV to bOPV
- **Phase 2**: withdrawal of bOPV after the certification of eradication of wild polioviruses

The phased withdrawal of OPV related to the epidemiology of WPV and vaccine-related cases of polio occurring globally in the past decade (Table 1). Removal of the type 2 component first is justified because:

- Type 2 WPV has not been circulating naturally since the last case was detected in 1999 in Aligarh, India thus obviating the need for the type 2 component of the vaccine
- Since 2009, 97% of all VDPVs have been due to Type 2 virus
- 40% of all VAPP cases are related to Type 2 component of OPV
- Presence of type 2 component in the vaccine impairs the immune response to types 1 and 3 poliovirus requiring more doses of tOPV to reach herd immunity thresholds for those types compared to the number of doses of bOPV to reach those same immunity thresholds.

Note that all cases of polio related to wild virus are now due to type 1 virus. Type 3 was last detected in November 2012, although absence of virus detection for one year is not sufficient for certifying eradication.

Figure 4: Reported paralytic cases of wild polio virus versus estimated cases of paralysis associated with OPV (VAPP and cVDPV) assuming ongoing use of OPV. Red bars depict WPV cases reported to GPEI as of 30 December 2014. Red line depicts cases of VAPP and cVDPVs estimated to occur based on midpoint of estimated cases of VAPP globally (250 to 500) and the average number of cVDPVs reported annually during 2008-2013.



3.1.3. Role of one dose of IPV in polio eradication and control

The primary role of introducing **one dose of IPV into routine immunization programs** is to mitigate risks associated with OPV withdrawal and possible reintroduction of polioviruses (Figure 5). The initial phase of OPV withdrawal – switch from tOPV to bOPV-- would lead to a gradual increase in the number of persons susceptible to type 2 poliovirus resulting in three main risks to the population.(6)

1. Immediate time-limited risk of cVDPV2 emergence;
2. Medium and long-term risks of type 2 poliovirus re-introduction from a vaccine manufacturing site, research facility, diagnostic laboratory, or a bioterrorism event.
3. Spread of virus from rare immune deficient individuals who are chronically infected with OPV2.

A reintroduction of poliovirus or cVDPV2 emergence could potentially result in a substantial polio outbreak or even re-establishment of global transmission.

There is precedent for type 2 wild polioviruses to be reintroduced into the population. During 2002-2003, a laboratory strain of type 2 wild poliovirus was introduced in India.(18) Fortunately, this outbreak was controlled, but it highlights the potential risk if the population is 100% susceptible, as would occur if all polio vaccination against type 2 viruses was stopped.

The introduction of at least one dose of IPV has an important supporting role in assuring complete global eradication of all polioviruses. SAGE has recommended the introduction of IPV in all OPV using countries worldwide by the end of 2015.(4, 17) The primary role for IPV introduction in 2015 is to maintain type 2 poliovirus immunity during the tOPV-bOPV switch (removal of type 2 component) in 2016. IPV introduction will also help interrupt transmission if an outbreak occurs and hasten the eradication of all polio diseases.

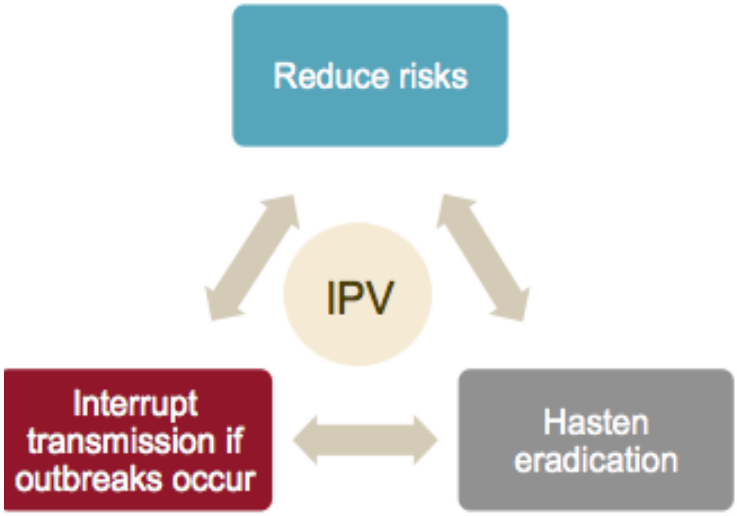


Figure 5: Schematic of rationale for introducing at least one dose of IPV

It is important to note that SAGE recommends IPV be introduced into the routine immunization programs. As indicated before and described in the subsequent sections, IPV is primarily intended to maintain type 2 poliovirus immunity while OPV2 cessation occurs globally. Thus, infants have to be vaccinated with at least one dose of IPV in addition to OPV during their routine EPI visit.

3.1.4. Reducing risks: individual protection from one dose of IPV

Evidence indicates that one dose of IPV may reduce risk by **protecting individuals against paralytic polio** should they be exposed to cVDPV2 or WPV2 or by **enhancing the population immunity that can be achieved through use of mOPV2 in** the setting of an outbreak of type 2 poliovirus post OPV2 cessation (Figure 6). Because a proportion of the population will already be immune as a result of having received IPV, the immunity levels reached after a dose of mOPV2 will be higher than the immunity levels reached with a single dose of mOPV2 in a completely susceptible population.

Immunologic response to mOPV2 after one dose of IPV

In the event that an outbreak of type 2 poliovirus does occur post OPV2 cessation, evidence indicates that the humoral and intestinal immunological response to mOPV2 or additional doses of IPV in individuals vaccinated with one dose of IPV would be substantially superior to those without prior IPV exposure.

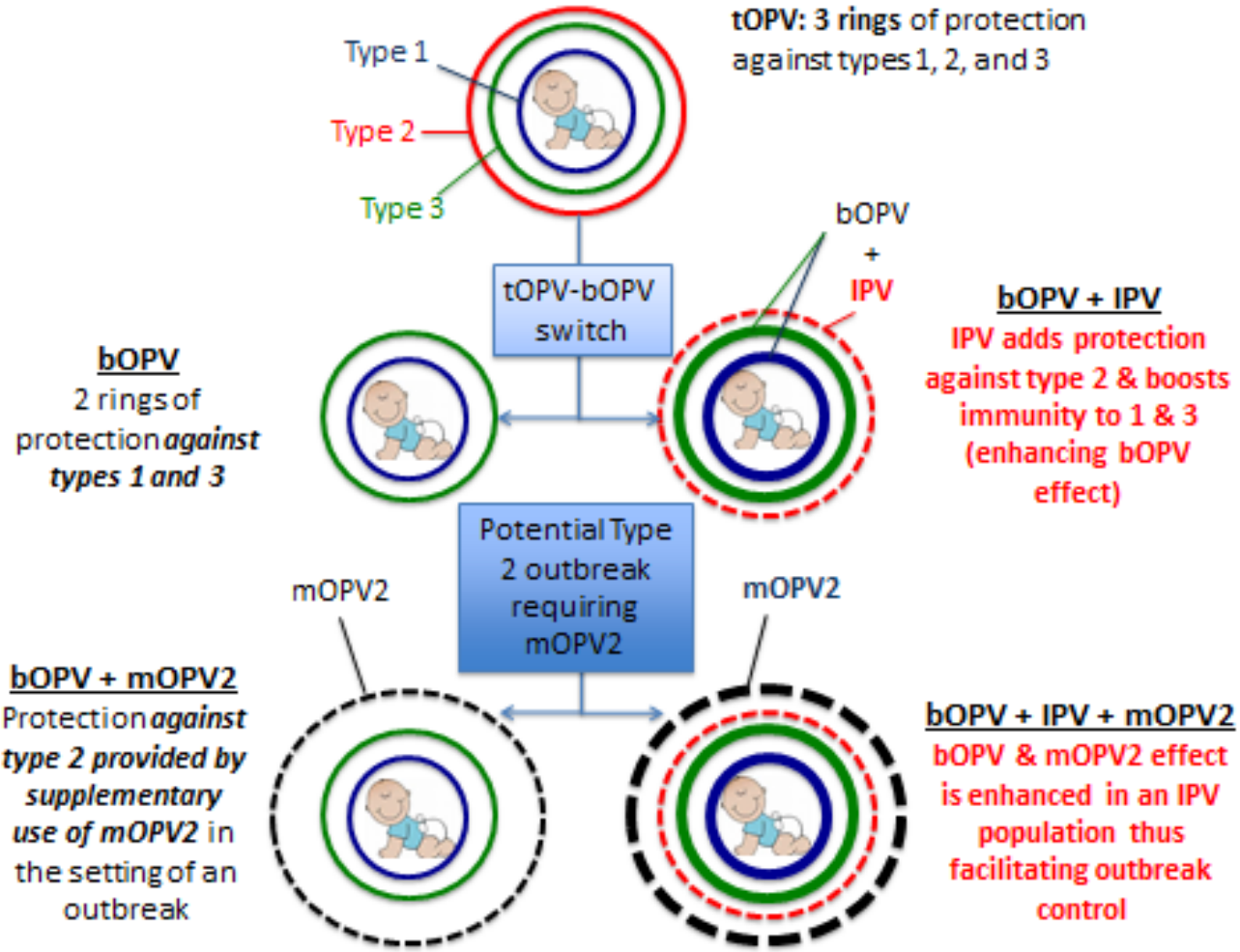
3.1.5. Transmission Interruption

Transmission of polio can either be oral-oral (more commonly in developed settings) or fecal oral (more commonly in high density, low sanitation settings). IPV is equally effective against oropharyngeal shedding as OPV—that is, oral shedding of poliovirus is rare after vaccination with either IPV or OPV.(27) With regard to fecal shedding, OPV is superior at reducing the prevalence of fecal excretion of poliovirus

However, IPV dose reduce the duration of shedding and the amount of virus in the stool. Thus, it is expected that prior receipt of IPV should contribute to curtailing transmission of poliovirus in the setting of an outbreak.

In summary, administration of one dose of IPV would induce immunity in a substantial proportion of the population and facilitate outbreak control with mOPV, should polioviruses be reintroduced. Faster outbreak control would be expected because the population immunity might already be close to herd immunity thresholds. Thus, a single dose of mOPV would be much more likely to induce the immunity levels needed to interrupt transmission than in a completely unvaccinated population.

Figure 6: Schematic description of technical rationale for use of at least one dose of IPV as part of the Endgame Strategy



Annex 1: Oral poliovirus vaccine (OPV)

A.3.1. Summary of OPV

OPV was developed in 1961 by Dr. Albert Sabin. OPV contains live-attenuated strains of poliovirus that are also referred to as the "Sabin strains."(10) Three forms of OPV are currently available--tOPV, bOPV, and mOPVs--with tOPV being the most commonly used form in routine and supplementary immunization activities in low and middle-income countries globally (Table 1).(9)

Live attenuated polioviruses replicate in the oral cavity, intestinal mucosa and lymphoid cells and in lymph nodes that drain those organs. Vaccine viruses are excreted in the stool of the vaccinated

person for up to 6 weeks after a dose, with maximum viral shedding occurs in the first 1–2 weeks after vaccination, particularly after the first dose.

OPV strains may spread from the recipient to contacts, who upon exposure may be infected with vaccine virus and thus protected.

Studies in temperate developed countries found that 3 doses of tOPV resulted in seroconversion of >95% of infants to all types and provided long-lasting immunity.(13) In developing countries, an average of 73%, 90%, and 70% of children seroconverted to poliovirus types 1, 2, and 3, respectively. Therefore, more than 3 doses and additional booster doses are required (through supplementary immunization activities) to improve seroconversion and achieve high levels of intestinal immunity.

The selection of the type of OPV for routine and supplementary immunization activities is evolving due to two factors:

1. Changing epidemiology of circulating polio strains: Since November 2012, **all cases of polio related to wild virus have been Type 1**. There has been no natural circulation of Type 2 WPV since 1999 when the last case was last detected in Aligarh, India. Type 3 WPV was last detected in November 2012, although absence of virus detection for one year is not sufficient for certifying eradication.[b]
2. Cases associated with OPV: although OPV offers effective protection against polio, it is a live attenuated vaccine and in very rare cases can lead to paralysis. There are two ways this can occur:
    a. Vaccine Associated Paralytic Poliomyelitis (VAPP): refers to spontaneous reversion to neurovirulence of one of the attenuated Sabin viruses in OPV. For every 2.4 million doses of OPV administered, one vaccine recipient or a close contact is paralyzed.[c] There are an estimated 250 – 500 VAPP cases globally per year.(10, 31) Of these, about **40% are caused by tOPV's type 2 component**.(32)
    b. Circulating Vaccine Derived Poliovirus (cVDPV) outbreaks: these rare outbreaks occur when a OPV strain is passed from person-to-person, mutating back to a neurovirulent and highly transmissible form.(33) **Almost all cVDPV outbreaks (97%) in recent years have been caused by a type 2 OPV-derived virus**.[d] Circulating VDPVs are widely transmitted in a community and are not likely to be related to contact with a recent vaccine recipient in contrast to VAPP which occurs in OPV recipients or their close contacts. Other very rare forms include VDPVs in persons with a primary immunodeficiency syndrome (iVDPVs) and ambiguous VDPVs where the virus is genetically different than the Sabin strains implying prolonged circulation allowing

[b] http://www.polioeradication.org/Dataandmonitoring/Poliothisweek.aspx

[c] http://www.who.int/ith/vaccines/polio/en/

[d] http://www.polioeradication.org/Dataandmonitoring/Poliothisweek/Circulatingvaccinederivedpoliovirus.aspx

those mutations to occur but is not known to be associated with an outbreak or immunodeficiency.

Note: For the world to be "polio-free," we must achieve complete eradication and containment of all polio disease related to 1) wild polioviruses; 2) VDPVs; and 3) VAPP

A.3.2. Rationale for ongoing use of OPV

OPV have been the primary vaccines of choice in the eradication effort because(9):

- OPV is inexpensive
- OPV can be easily administered orally without requiring trained health workers
- OPV not only induces humoral immunity to prevent infection of the nervous system but also produces oral and intestinal mucosal immunity thus reducing the amount of virus excreted leading to decreased transmission
- OPV can spread to close contacts through secondary spread thus immunizing them or boosting their immunity

Two important aspects of the current global situation of polio warrant ongoing use of OPV until polio transmission is interrupted.

1. First, WPV is still endemic in three countries (Pakistan, Afghanistan, and Nigeria) that continue to be reservoirs for re-infecting other countries worldwide
2. Second, in 2013, polio cases were also detected in five additional countries (Somalia, Kenya, Ethiopia, Cameroon, and Syria) that were previously polio free.

Until polio transmission is interrupted in all of these high transmission settings, OPV will be a critical component of the Eradication Plan.

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