

PLANNING FOR IPV INTRODUCTION

Implementation Facts

March 2014

Introduction

This booklet provides specific guidance on the introduction of inactivated polio vaccine IPV and the switch from trivalent OPV (tOPV) to bivalent OPV (bOPV). For more information on the rationale for IPV introduction, please see Planning for Introduction – Frequently Asked Questions and visit <http://tinyurl.com/ipv-intro>.

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IPV vs OPV

What is the difference between IPV and OPV?

IPV and OPV evoke different immune responses and therefore have distinct advantages and disadvantages. To complete eradication and get the benefits of both, **they should be used together.**

Figure 1: A comparison of advantages and disadvantages for OPV and IPV

	Advantages	Disadvantages
Oral Polio Vaccine (OPV)	<ul style="list-style-type: none">• Humoral (antibodies in the blood) immunity.• Gut/intestinal immunity.• Easy to administer via drops.• Inexpensive.	<ul style="list-style-type: none">• Vaccine-associated paralytic poliomyelitis (VAPP) occurs in rare cases (2-4 cases per 1 million children).• Rarely, through circulation in poorly immunized populations, the vaccine viruses mutate to circulating vaccine-derived polioviruses (cVDPVs) and can cause outbreaks of paralytic polio.
Inactivated Polio Vaccine (IPV)	<ul style="list-style-type: none">• Very good humoral immunity.• Equivalent to OPV in inducing immunity in the oral cavity thus is as effective as OPV in stopping oral – oral transmission of virus.	<ul style="list-style-type: none">• Insufficient to prevent wild polio virus (WPV) replication in guts of infected person and consequently poliovirus can still be transmitted by excretion in stool.• Requires injection.• More expensive than OPV.

What is meant by intestinal protection?

When a child ingests OPV, the vaccine virus enters the child's mouth and gut and replicates. The child then mounts immune responses in three places: (1) **antibody response in the blood** that protects against the virus invading the nervous system and causing paralysis, (2) **immune response in the mouth** which prevents shedding of virus in oral secretions and spread from those secretions and (3) **intestinal immunity** (also called gut or mucosal immunity), which prevents shedding of the virus in the stool. Thus, children vaccinated with OPV who come into contact with wild poliovirus are less likely to excrete poliovirus in their oral fluids or stool than unvaccinated persons. The predominant mode of transmission in the developing world is thought to be faecal-oral. Virus is shed in the faeces and, in poor sanitary conditions and with suboptimal hygiene measures, can infect other persons if transmitted by dirty hands or contaminated food and water. Therefore, strong intestinal immunity prevents transmission.

IPV is a killed vaccine that stimulates a very good humoral response (antibodies in the blood) in children after only 1 or 2 doses. IPV also prevents children from excreting virus in their mouths as effectively as OPV and hence to the extent that

polioviruses are transmitted through oral secretions, IPV is very effective at blocking that type of transmission. However, IPV alone does not induce the same level of intestinal immunity as OPV. Thus, while individuals vaccinated with IPV alone are protected against paralysis, they may excrete the virus and allow it to spread.

When IPV is administered after a few doses of OPV, the IPV not only enhances protection against paralytic disease but also boosts intestinal immunity, even more than an additional dose of OPV would provide. Thus, combining IPV with bOPV provides the advantages of both vaccines: strong intestinal immunity and antibody protection against the two serotypes in bOPV, types 1 and 3. This combination gives both the child and the child's community the best protection.

Planning

How does IPV introduction differ from other vaccines introduced in the past?

For the most part, IPV introduction will involve the same process as other new vaccine introductions. However, there are some notable differences:

- *Unprecedented timelines* - the urgency of eradication necessitates an accelerated introduction plan— all OPV-using countries should add at least one dose of IPV to routine immunization by end-2015;
- *Global scope* - its objective focuses on achieving a global good; and
- *Lack of direct impact indicators* - evaluation will be based on routine immunization coverage in contrast to indicators used to measure the impact of other vaccines (e.g., reduced mortality or disease rates at national level).

What steps will be necessary to introduce IPV?

Once the decision to introduce IPV has been made by the national authorities, the first step in IPV introduction will be to develop a plan for IPV introduction. This should be incorporated into the multi-annual integrated action plans¹ for strengthening immunization services at country level. The plan for IPV introduction should take into account the following:

- *IPV specific planning* - Ensuring the vaccine is licensed, training is scheduled with materials available, a communications plan is outlined, updated immunization registers and cards are developed and logistics are planned for.
- *Programme management* - including use of accountability frameworks, data management, evidence-based planning, training and supply management.
- *Microplanning* – for some regions this includes population mapping, harmonization of routine immunization microplans with polio SIA microplans to enable more complete session planning, vaccine supply management and cold-chain logistics.

¹ See WHO-UNICEF guidelines for developing a comprehensive multi-year plan (cMYP)

http://www.who.int/iris/bitstream/10665/100618/1/WHO_IVB_14.01_eng.pdf.

- *Advocacy and communication* - including top-level advocacy, engagement of local community leaders and household-level outreach.
- *Immunization delivery* - monitoring of immunization sessions, local community coverage and vaccine acceptance, social mobilization efforts, availability of health workers, vaccine delivery and other immunization session logistics and overall quality and impact of services.

Why are the timelines for IPV introduction so tight? How will countries achieve introduction targets in such a short period?

Wild polio cases are at the lowest level in history. With the prospect of eradicating wild poliovirus (WPV) transmission realistic and achievable in the near-term, aggressive timelines are required to avoid missing this window of opportunity.

Is there technical assistance available to support IPV introduction?

Support for IPV introduction is available from WHO and UNICEF regional office technical focal points as well as from NGOs and other immunization partners.

Technical assistance will be available to many countries from WHO and UNICEF regional office focal points, the GAVI Alliance, NGOs and other immunization partners. In particular, the *Polio Eradication and Endgame Strategic Plan* specifically calls for strengthening routine immunization, which will be supported by international partners and donors. This will facilitate the introduction of IPV according to the proposed timelines in close coordination with other routine immunization activities.

For more information visit <http://tinyurl.com/ipv-intro>.

Many countries are already planning to introduce other vaccines before 2016. How does IPV introduction affect these plans?

There are potential benefits to introducing IPV at the same time as other new vaccines. Studies in Ghana and Tanzania showed efficiencies in cost and time can be gained by introducing two new vaccines at once. Countries planning to introduce other new vaccine(s) in 2014 or 2015 may therefore wish to consider a joint introduction. This option should be discussed with regional immunization staff, National Immunization Technical Advisory Groups (NITAGs) and Ministers of Health as soon as possible in order to ensure adequate time for planning.

Is there enough IPV available globally?

Yes. There is enough production capacity for current IPV standalone products to meet the needs for all OPV-using countries to introduce one dose of IPV into their routine immunization programme.

However, to ensure sufficient IPV is available when countries are ready for its introduction, it is essential that all countries define their target introduction dates as

soon as possible (i.e., by the end of 2013 if possible, by mid to end of 2014 at the latest).

Schedule and presentation

What schedule should countries be using for IPV, and how many doses are recommended?

In November 2013, WHO's Strategic Advisory Group of Experts (SAGE) on Immunization recommended that countries add at least one dose of IPV to routine immunization, administered at 14 weeks of age or at the closest immunization visit following that age.

This recommendation is based on a detailed review of evidence in June 2013 that showed that the optimal timing for administering 1 dose of IPV in a routine immunization schedule in low and middle income countries is when the third dose of Diphtheria-tetanus-pertussis (DTP3) is given².

Further, a WHO Position Paper on polio vaccines published in February 2014 confirms that WHO no longer recommends an OPV-only vaccination schedule. For all countries using OPV only, at least 1 dose of IPV should be added to the schedule. The polio position paper is available online at:
<http://www.who.int/wer/2014/wer8909.pdf>

In countries with a 6, 10, and 14-week immunization schedule, this would mean that IPV would be administered at 14 weeks of age. For countries with a 2, 3, and 4-month schedule, the IPV dose would be administered at 4 months of age. In most cases IPV will be administered during the same visit as the third dose of OPV (4th dose of OPV if the country is giving a birth dose of OPV). National recommending bodies are responsible for evaluating country needs and in some cases, they may wish to follow an alternative schedule (e.g., go directly to an IPV-only schedule).

For the majority of countries, IPV should be introduced while continuing to provide OPV doses as done in the past. High OPV coverage, surveillance, and other existing polio eradication efforts remain critical components of the endgame plan.

Why is IPV administration recommended at 14 weeks of age?

IPV administration is recommended at 14 weeks of age because it provides the optimal balance between vaccine efficacy and early protection.

Administering IPV earlier than 14 weeks of age is not recommended because:

² The scientific rationale for administering IPV with DTP3 is that IPV performance is negatively affected by the higher levels of maternally-derived antibody at younger ages when DTP1 and 2 are typically administered, even after taking into account the potentially lower vaccine coverage due to drop-out rates between DTP1 and DTP3.

- *Immunogenicity is significantly higher after 14 weeks than at earlier age points.*
 - Studies have shown that IPV is substantially less effective against type 2 poliovirus when it is given to newborns and infants 6-10 weeks old. The current evidence suggests that a dose of IPV protects only 32-39% of infants aged 6-8 weeks against poliovirus type 2.^{3,4,5} In contrast, if the dose is given when the infant is 16 weeks old (4 months), it protects about 63% of infants.
- *The immunogenicity benefits outweigh the drop-out risks.*
 - The SAGE working group recognized that more children may be available for vaccination at DTP1 than DTP3, but decided that having more children available provided less of an advantage than the immunogenicity benefits of administering IPV at 14 weeks of age. WHO official estimates show that only three countries have massive drop-out rates (over 35%) between DTP1 and DTP3 (Chad, Equatorial Guinea & Gabon). The vast majority of countries have drop-out rates below 10%. The potential of reaching 10% more children at DTP1 does not outweigh the benefit of a 20-30% increase in vaccine efficacy gained by waiting until 14 weeks.
 - Studies to date and the pattern of VAPP in developing countries show that the majority of cases occur after this point. Thus, in most countries it is not necessary to give earlier doses than 14 weeks to have a substantial impact on VAPP.

Risks associated with introducing IPV later than at 14 weeks include:

- *Leaving more of the population at a greater risk should outbreaks occur.*
 - The purpose of IPV is to give infants protection against type 2 vaccine derived polioviruses (VDPVs) after the switch from tOPV to bOPV. This IPV dose will be the sole protection an infant will receive against type 2. He or she is therefore vulnerable until vaccinated. Waiting until 9 months to administer IPV would mean leaving a large pool of susceptible hosts (all children aged 0-8 months) to be infected by or to transmit type 2 vaccine derived polioviruses.
- *Reaching fewer children due to significant drop out rates between the 14 week visit and 36 week visit in some countries.*

What is the recommended schedule for children who do not receive routine immunization on time?

Children entering the routine immunization programme late should be given IPV at the first immunization contact after 14 weeks of age, or as per the national recommendation on children starting late for other vaccines. For children who are 12 months of age or older at the time of their first visit, there is likely to be only limited

³ Thompson KM, Pallansch MA, Duintjer Tebbens RJ, Wassilak SGF, Cochi SL. Pre-eradication national vaccine policy options for poliovirus infection and disease control. *Risk Analysis* 2013; 33(4):516-543.

⁴ Resik S, Tejeda A, Sutter RW, Díaz M, Sarmiento L, Alemañi N, García G, Fonseca M, Hung LH, Kahn A-L, Burton A, Landaverde M, Aylward RB. Priming after a fractional dose of inactivated poliovirus vaccine. *N Engl J Med* 2013;368:416-24.

⁵ Estivariz CF, Pallansch MA, Anand A, Wassilak SG, Sutter RW, Wenger JD, Orenstein WA. Polio vaccination strategies as we move towards poliovirus eradication. *Current Opinion in Virology* 2013 Online publication complete: 10-JUN-2013 DOI information: 10.1016/j.coviro.2013.05.007.

protection offered by a dose of IPV, however each country should develop its own guidelines for these situations.

Are there any special recommendations on schedule for children in high-risk communities?

No. The recommendation to immunize all children older than 14 weeks old with IPV if they have not yet received the vaccine is the same for all populations, but is especially important in high-risk communities where many children are under immunized.

For example, if a child 5 months old comes for immunization for the first time, he/she should receive the first doses of DPT1/Penta1/OPV1 and IPV.

In areas without an active routine immunization system where most immunization is accomplished through outreach activities, immunization programme managers may consider immunizing children older than 6 weeks with IPV. This is particularly relevant if immunization happens rarely (i.e., once every 6 months or once a year). In these situations, every opportunity to protect a child should be seized.

Children are already getting lots of shots at DTP3 visit. Why not give IPV at another time all together?

A key objective of the endgame is to incorporate IPV into the existing system. When introducing IPV, policy makers are advised against creating new immunization contacts, as this would have major implications for caretakers and health care workers in terms of organization and resources.

What IPV presentation options exist?

Currently, IPV is prequalified by WHO as a stand-alone vaccine in 1-dose, 2-dose and 10-dose presentations. WHO expects a 5-dose presentation to be available in 2014. These products are preserved with 2 phenoxy-ethanol, which does not meet WHO requirements for an effective preservative. Thus, IPV needs to be treated as if it does not contain a preservative, which means that any open vials of this vaccine must be discarded at the end of the immunization session or six hours after opening, whichever comes first. These vaccines are licensed for use as a 0.5 ml dose administered intramuscularly.

IPV-containing combination presentations with diphtheria, tetanus, acellular pertussis, hepatitis B, or Hib antigens in tetravalent, pentavalent, or hexavalent formulations are also available but at substantially higher cost than standalone IPV or currently used Pentavalent formulations. A combination product with whole-cell pertussis is not currently available.

IPV-combination vaccines are currently not available through UNICEF supply division. Countries interested in procuring combination vaccines will need to contact the manufacturer directly for further information on pricing and availability.

Routine immunization

Why is IPV not being delivered through campaigns?

As part of the endgame strategy, essential polio functions will need to be mainstreamed into ongoing organizational structures. Introducing IPV into routine immunization schedules is key to ensuring sustainability.

High immunization coverage is the best strategy for reducing the risk of cVDPV emergence before, during and after the withdrawal of OPV. In addition to reducing immediate and long-term polio risks, this establishes a significant opportunity for the polio eradication efforts to help strengthen immunization systems effectively.

Will the introduction of IPV interrupt routine immunization or take the focus away from it?

Objective 2 of the *Polio Eradication and Endgame Strategic Plan* aims to systematically use the GPEI infrastructure to more effectively strengthen immunization services. The key milestones on this objective's path include achieving at least a 10% year-on-year increase in DTP3 coverage in the majority of worst-performing districts in focus countries from 2014, thereby contributing to global immunization targets.

Financing

What will IPV cost?

UNICEF awarded a tender for IPV vaccines in February 2014, which makes sufficient quantities of affordable IPV available to support country introductions, in line with the Endgame Plan timeline. A multi-faceted IPV financing strategy is ongoing and further reductions in the cost of IPV are being pursued for the medium-term (i.e. post 2018) through continued efforts to develop and license new products.

Pricing for IPV is shown in the following table:

IPV pricing as of 28 February 2014			
	Ten-dose vials	Five-dose vials	Single-dose vials
GAVI-supported countries	EUR 0.75 per dose (approx. USD 1.00 per dose at current exchange rates)	USD 1.90 per dose	USD 2.80 per dose
Middle-income countries	EUR 1.49-2.40 (approx. USD 2.04-3.28 at current exchange rates)		

For more information on IPV pricing per type of presentation, including pricing tiers for middle-income countries, please see: <http://www.unicef.org/supply/files/IPV.pdf>

The current IPV-containing combination vaccines, which use an acellular pertussis component, are substantially more expensive (currently priced at US\$20-40/dose).

Is the vaccine's cost expected to drop over time?

Achieving an IPV price substantially below US\$ 1.00 per dose will require new products or delivery methods to be licensed. Possible options include the administration of a fractional dose (e.g., 1/5th of a full dose of IPV) through the intradermal (ID) route, or the intramuscular administration of a new IPV product containing a lower level of antigen with an adjuvant to enhance immune response. While one product may soon be licensed for intradermal administration, the adjuvanted products are unlikely to be licensed and accessible before 2015-2018.

However, intradermal administration of IPV brings additional programmatic complexities. Countries that wish to utilize intradermal IPV will need to ensure they have an appropriately trained workforce as well as equipment.

The development of an IPV-containing combination vaccine with whole-cell pertussis, which would be affordable for low and middle income country markets and could replace the currently used pentavalent (DTP-Hep B-Hib) vaccine, is not expected before 2020.

How do countries apply for financial support?

- **GAVI eligible and GAVI graduating countries**

Following a decision by the GAVI Alliance Board in November 2013, GAVI-eligible and GAVI-graduating countries will receive support until 2024, in a process similar to that followed for other new vaccines introduction support. GAVI eligible and GAVI graduating countries are now invited to submit applications for IPV.

What is the expected duration of GAVI support for IPV?

The GAVI board also approved a number of policy exceptions in relation to support for IPV. These include:

- co-financing is encouraged, but not required; and
- countries with DTP3 coverage less than 70% are eligible to apply.

In addition, a vaccine introduction grant is also available to support operational costs associated with IPV introduction. The GAVI application window is up to June 2015.

For further details on how to apply for GAVI support, including the application guidelines and form: <http://www.gavialliance.org/support/apply/>.

- **Other countries**

For other middle income countries, WHO and UNICEF are committed to helping all countries introduce IPV rapidly by providing technical assistance to develop IPV introduction plans, facilitating access to low cost IPV products through UNICEF-procurement processes and, if necessary, considering time-limited financial support to initiate procurement.

Contact your WHO or UNICEF country office for more information.