

Considerations for the introduction of a second dose of Inactivated polio vaccine (IPV2) in routine immunization programmes from 2021

This document is targeted to countries currently using 1 dose of standalone IPV (or 2 fractional doses) and bivalent oral polio vaccine (bOPV). This information is not applicable to countries using or planning to use combination IPV vaccines (i.e., hexavalent). Additional information on IPV can be found at https://www.who.int/immunization/diseases/poliomyelitis/endgame_objective2/inactivated_polio_vaccine/en/

Frequently asked questions (FAQs) 10 June 2020

Under the current Polio Endgame Strategy 2019-2023, oral polio vaccine (OPV) withdrawal remains one of the goals necessary for complete eradication of all polioviruses, wild as well as vaccine-derived polioviruses. To prepare towards complete OPV withdrawal, WHO recommended in 2013 that all countries should introduce at least 1 dose of IPV in their routine immunization schedule to provide an immunity base against paralysis caused by circulating vaccine-derived poliovirus type 2 (cVDPV2) and boost immunity against poliovirus types 1 and 3. By April 2019, this milestone was achieved by all 194 Member States.

The introduction of a second dose of IPV (IPV2) is recommended as the next step towards complete OPV withdrawal, while providing a higher protection against cVDPV2 which are currently circulating and represent a risk in many areas of the world. This interim document aims to aid countries in initiating decision making on introduction of IPV2 and early planning needed. Further detailed recommendations on polio vaccination schedules will be provided after the October 2020 meeting of the Strategic Advisory Group of Experts on Immunization (SAGE).

1. Why should countries introduce a second dose of IPV?

The addition of a second dose of IPV will increase protection against all polioviruses, including protection against paralysis caused by VDPV2. Once bOPV is removed after certification of eradication, two doses of IPV will ensure adequate protection against all poliovirus.

The initial introduction of one dose of IPV provided an immunity base against polio virus types 1, 2 and 3 (i.e. seroconversion and priming). In the context of the eradication of type 2 wild poliovirus and the subsequent withdrawal of type 2 oral polio vaccine, that immunity base produced by the first IPV dose could be rapidly boosted by a second dose of IPV, manifested by high antibody titers that would be expected to mitigate the consequences of cVDPV2 outbreak.^{1 2}

The WHO recommendation in 2013 for the introduction of a single IPV dose was mainly driven by supply availability. Now that IPV supply availability has improved and all countries have introduced the first IPV dose in vaccination schedules and considering the WHO recommendation of two IPV doses for the post-certification era³ schedules, countries are strongly encouraged to introduce a second dose of IPV. This recommendation concerns the period prior to bOPV withdrawal. During this period, we do not anticipate need for additional IPV doses in routine immunization. SAGE will in future meetings discuss the recommended IPV schedule during the post-OPV withdrawal period.

2. What are the current schedule options for planning the introduction of a second dose of IPV?

As a principle, the best final immunogenicity is achieved when the first IPV dose is administered at 14 weeks (with DTP3) or later, and the second IPV dose is administered at least four months after the first IPV dose; in most countries this coincides with measles-containing vaccine given at nine months of age. This schedule achieves best immunogenicity with 2 doses of IPV, however does not provide for early-in-life protection (i.e. meaning protection before or at three months of age).

As an alternative to the preferred option described above, countries may also opt for an early protection IPV schedule starting with first dose at 6 weeks of age and second dose at 14 weeks of age. While this schedule does not follow the four-month interval between doses described previously, it has an advantage of providing early protection as well as preventing vaccine-associated paralytic polio (VAPP) with the tradeoff being a decrease in final immunogenicity. This could be an option in countries with programmatic challenges of implementing IPV at the visit at 9 months of age.

Table 1 describes the seroconversion rates against poliovirus types 1, 2, 3 based on different schedules used for the 2-dose IPV regime.

¹ Sutter RW, Platt L, Mach O, Jafari H, Aylward RB. The new polio eradication end game: rationale and supporting evidence. *J Infect Dis* 2014; 210 Suppl 1: S434-8. DOI: 10.1093/infdis/jiu222

² Sutter RW, Bahl S, Deshpande JM, Verma H, Ahmad M, Venugopal P, et al. Immunogenicity of a new routine vaccination schedule for global poliomyelitis prevention: an open-label, randomised controlled trial. *Lancet* 2015; 386:2413-21. DOI: 10.1016/S0140-6736(15)00237-8

³ Weekly Epidemiological Record, No 22, 2 June 2017

Table 1: Summary of available studies on seroconversion against poliovirus types 1, 2, 3, after receiving 2 IPV doses according to different schedules.

2 IPV Dose Schedule			Final Seroconversion		
Study	Location	Schedule	Type 1	Type 2	Type 3
Unpublished (2020)	China	4m, ≥4 months after first dose (2 nd dose between 8-12 months) (Sabin)	100%	99%	98%
Resik (2019)	Cuba	4, 8 months	100%	100%	100%
Resik (2013)	Cuba	4, 8 months	100%	100%	99%
Cynthia (2019)	Bangladesh	14, 22 weeks	100%	99%	99%
Mohammed, A. J. (2010)	Oman	2, 4 months	88%	86%	92%
Cuba IPV group (2007)	Cuba	2, 4 months	90%	89%	90%
Anand, A (2015)	Bangladesh	6, 14 weeks	95%	91%	97%
Unpublished (2020)	Nigeria	6, 10 weeks	65%	67%	92%
Unpublished (2019)	India	6, 10 weeks	85%	70%	94%
WHO Collaborative Study (1996)	Oman	6, 10 weeks	71%	99%	91%
WHO Collaborative Study (1996)	Thailand	6, 10 weeks	94%	99%	93%

3. Can countries choose to provide the two doses of IPV as two fractional doses?

Yes. Countries can also achieve high levels of immunity against poliovirus types 1, 2, and 3 by providing two fractional intradermal IPV doses. A fractional intradermal IPV dose is 0.1 ml as opposed to 0.5 ml. This option should be considered after careful review of the programmatic feasibility, cost-effectiveness and regulatory implications.

Table 2: Summary of available studies on seroconversion against poliovirus types 1, 2, 3 after receiving 2 fractional IPV doses according to different schedules

2 fIPV dose schedule			Final Seroconversion		
Study	Location	Schedule	Type 1	Type 2	Type 3
Resik (2019)	Cuba	4, 8 months (ID)	89%	93%	82%
		4, 8 months (IM)	97%	99%	91%
Resik (2013)	Cuba	4, 8 months	94%	98%	93%
Mohammed, A. J. (2010)	Oman	2, 4 months	67%	67%	69%
Unpublished (2020)	India	10, 14 weeks	96%	77%	99%
Unpublished (2020)	India	6, 14 weeks	96%	87%	97%
Anand, A (2015)	Bangladesh	6, 14 weeks	88%	81%	89%
Cynthia (2019)	Bangladesh	6, 14 weeks	79%	64%	73%

4. Should countries already providing two fractional doses switch to a two full dose schedule?

No. Countries already providing 2 fractional doses do not need to change their schedule.

However, as global supply is adequate, countries could consider such a change if they prefer to give two full IPV doses.

In any case, countries should carefully consider any switch from fractional to full dose, or vice-versa, taking into account cost-effective, logistic and programmatic considerations.

5. How will these options apply to current polio schedules (primary series) based on one dose of IPV (or two fractional doses) and bOPV?

a. Countries using bOPV + IPV

	Birth (only in selected countries)	6 weeks (or 2 months)	10 weeks (or 3 months)	14 weeks (or 4 months)	9 months
Current schedule	bOPV	bOPV	bOPV	bOPV + IPV1	
NEW Option 1 IPV2 schedule	bOPV	bOPV	bOPV	bOPV + IPV1	IPV2
NEW Option 2 IPV2 schedule	bOPV	bOPV + IPV1	bOPV	bOPV + IPV2	

b. Countries using bOPV + fIPV

These countries do not need to change schedules if they continue administering two fractional doses.

c. Countries using a sequential schedule

A number of countries administer IPV in a sequential schedule without co-administration of IPV and bOPV at the same immunization contact. Generally, these countries have prioritized early-in-life protection and VAPP prevention.

For these countries, WHO recommends that IPV1 be given at 2 months of age and 3–4 months of age for the second dose.

Each of the doses in the primary series should be separated by 4–8 weeks depending on the risk of exposure to poliovirus in early childhood.

	2 months	4 months	6 months
Current schedule	IPV1	bOPV	bOPV
NEW Option 1 IPV2 schedule	IPV1	IPV2	bOPV
NEW Option 2 Fractional IPV2 schedule	fIPV1	fIPV2	bOPV

6. Do countries need to continue using bOPV in their routine immunization schedule when IPV2 is introduced?

Yes. The introduction of the second dose of IPV is an addition to the polio immunization schedule and it should not, at this time, replace the use of bOPV.

bOPV remains the vaccine of choice to interrupt poliovirus transmission and achieve the goal of polio eradication.

The SAGE, in its recent meeting of April 2020, concluded the following: “in the current epidemiological context, SAGE expressed caution over regions or countries moving from bOPV to an IPV-only schedule as a general principle and recommended that instead these regions or countries take a gradual approach, first introducing a second dose of IPV into routine immunization”.

Recommendation for the use of IPV in routine immunization schedules will be in place for the foreseeable future.⁴

7. Can IPV2 be given simultaneously with other vaccines (oral or injectable) in the immunization programmes?

Yes. IPV, whether is the first or second dose, is equally effective when given alone or with the other vaccines in childhood immunization schedules. IPV does not interfere with mounting a good immune response to the other vaccines and giving IPV simultaneously with other vaccines is as safe as giving the vaccines without IPV.⁵

Giving multiple injections at same visit is safe and encouraged. Health workers can be trained to feel confident to give multiple-injections in an immunization session. Delaying a scheduled vaccination would be a missed opportunity and should be avoided. No upper limit has been established regarding the number of vaccines that can be administered in one visit.⁶

8. With the introduction of the second dose, how do health workers proceed if a child presents at nine months and has not yet received the first IPV dose?

If a child comes in contact with immunization services for the measles vaccination and the first dose of IPV has not been given, the first dose should be given at that time and recorded under that immunization visit as IPV1. The second dose of IPV should be administered at least four weeks later or as soon as possible after the four-week interval has passed.

9. Is there enough supply to introduce a second dose of IPV in 2021?

Yes. However, should all eligible countries desire to introduce IPV2 in 2021, this could lead to a temporary global supply gap. In this instance, any global allocation of supply for the second dose of IPV would be guided by a risk prioritization process.

Gavi supported countries will receive specific information on the application timelines. For planning purposes, it is of upmost importance that interested countries indicate to GAVI -- or the appropriate procuring entity if not supported by Gavi -- of their interest in introducing a second dose of IPV, target date for introduction and demand estimates.

⁴ Full meeting report is available at: <https://www.who.int/wer/2020/wer9522/en/>

⁵ Additional information on multiple injections can be found at: https://www.who.int/immunization/programmes_systems/policies_strategies/multiple_injections/en/

⁶ <https://www.paho.org/hq/dmdocuments/2013/IM-JobAids-2010-08eng.pdf>

10. If a country had an IPV supply disruption because of the global shortage during 2015-2018 and has not yet been able to conduct catch up activities of the missed populations, should the country still consider introducing IPV2?

Yes. The introduction of a second dose of IPV is independent of the progress achieved on IPV catch-up activities. Despite the recent programme disruptions due to the Covid-19 pandemic, this situation should not prevent countries from future planning for the introduction of a second IPV dose.

Meanwhile, the SAGE has recently restated the importance of completing the catch ups of the missed cohorts due to past supply disruptions⁷. As supply has been already prioritized for these activities, countries which are yet to conduct the catch up are encouraged to do so as soon as possible.

11. What are the cold chain implications of introducing a second dose of IPV?

Currently, there are a number of different prequalified vaccine presentations⁸. It is expected that multidose presentation will not have or will have limited and manageable impact on cold chain capacity. Countries using single dose presentations could face some challenges and the introduction of second dose of IPV should take this in consideration.

⁷ Weekly Epidemiological Record, No 22, 29 May 2020

⁸ Inactivated Polio Vaccine. Supply Update. UNICEF Supply Division, August 2019 (<https://www.unicef.org/supply/reports/inactivated-polio-vaccine-ipv-market-update>)