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)
Update 14 April 2021

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 inactivated polio vaccine (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.

SAGE recommended that a second IPV dose be introduced by all countries that currently administer one IPV dose and bOPV in their routine immunization schedule. Regardless of the 2 dose IPV schedule used, introduction of the second IPV dose would not reduce the number of bivalent OPV (bOPV) doses used in the routine immunization schedule[1].

[1] Weekly epidemiological record, No 48, 27 November 2020

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. [2] [3]

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 era[4] 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?

The preferred schedule is to administer the first IPV dose at 14 weeks of age (with DTP3/Penta3), and to administer the second IPV dose at least 4 months later (possibly coinciding with other vaccines administered at 9 months of age). This schedule provides the highest immunogenicity and may be carried out using full dose IPV or fractional intradermal IPV (fIPV) without loss of immunogenicity. SAGE added that countries may consider alternative schedules based on local epidemiology, programmatic implications and feasibility of delivery.

As an alternative to the preferred schedule, countries may choose an early IPV schedule starting with the first dose at 6 weeks of age (with DTP1/Penta1) and the second dose at 14 weeks (with DTP3/Penta3). This alternative schedule offers the advantage of providing early-in-life protection; however, there is a lower total immunogenicity achieved. If this schedule is chosen, full dose IPV should be used rather than fIPV due to lower immunogenicity of fIPV at early ages.

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

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[2] 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

[3] 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

[4] 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 (2nd 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. An intradermal fIPV 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, keeping in mind that early-in-life protection schedules should not be based on fIPV, due to lower immunogenicity of fIPV at early ages.

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 October 2020 meeting, concluded the following: "Regardless of the 2 dose IPV schedule used, introduction of the second IPV dose would not reduce the number of bivalent OPV (bOPV) doses used in the routine immunization schedule".

Recommendation for the use of IPV in routine immunization schedules will be in place for the foreseeable future.[5]

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.[6]

Giving multiple injections at same visit is safe and encouraged. Heath 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.[7]

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.

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[5] Full meeting report is available at: https://www.who.int/wer/2020/wer9522/en/

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

[7] 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 disruptions[8]. 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 presentations[9]. 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.

[8] Weekly Epidemiological Record, No 22, 29 May 2020

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