

January 2021

Interim guidance on the use of trivalent oral polio vaccine for the response to circulating vaccine-derived poliovirus type 2

Addendum to Standard operating procedures: responding to a poliovirus event or outbreak, version 3.1

Acronyms and abbreviations

bOPV	Bivalent oral polio vaccine
cVDPV1	Circulating vaccine-derived poliovirus type 1
cVDPV2	Circulating vaccine-derived poliovirus type 2
cVDPV3	Circulating vaccine-derived poliovirus type 3
ECBS	Expert Committee on Biological Standardization
GPEI	Global Polio Eradication Initiative
mOPV2	Monovalent oral polio vaccine type 2
OPV	Oral polio vaccine
SIA	Supplementary immunization activity
SOP	Standard operating procedure
tOPV	Trivalent oral polio vaccine
VDPV2	Vaccine-derived poliovirus type 2
VVM	Vaccine vial monitor
WHO	World Health Organization
WPV1	Wild poliovirus type 1
WPV2	Wild poliovirus type 2

Context

Following the global certification of wild poliovirus type 2 (WPV2) eradication in 2015, the Global Polio Eradication Initiative (GPEI) planned and implemented the global withdrawal of trivalent oral polio vaccine (tOPV) and replacement with bivalent oral polio vaccine (bOPV) in April–May 2016. Termed “the switch”, this global effort impacted both country immunization systems and supplementary immunization activities (SIAs). The GPEI anticipated that a limited number of vaccine-derived poliovirus type 2 (VDPV2) outbreaks emerging in the post-switch period could be controlled through SIAs using Sabin oral polio vaccine (OPV) (e.g. monovalent oral polio vaccine type 2 [mOPV2]). However, inconsistent pre-switch intensification efforts to boost immunity against poliovirus type 2, a global inactivated polio vaccine shortage in 2016 and the uneven quality of outbreak response activities resulted in considerably more VDPV2 emergences and circulating vaccine-derived poliovirus type 2 (cVDPV2) outbreaks than predicted.

In addition to these cVDPV2 outbreaks, the continued transmission of wild poliovirus type 1 (WPV1) and the periodic emergence of circulating vaccine-derived poliovirus types 1 and 3 (cVDPV1 and cVDPV3) have led to concurrent circulation of different poliovirus types in several countries.

Therefore, in April 2020, the Strategic Advisory Group of Experts on immunization recommended the use of tOPV in areas of co-circulation of polioviruses types 1 and 2 or areas at high risk of co-circulation in order to avoid the need to conduct dual mOPV2 and bOPV SIAs.¹

Purpose and scope of this document

The purpose of this Interim guidance on the use of tOPV is to provide context and policy guidance on the use of tOPV in response to cVDPV2. Guidance in this document relies on scientific evidence and expert consensus, and considers epidemiology and operational realities, including vaccine supply, vaccine acceptance and country context.

This guide is for national governments and public health decision-makers who coordinate responses to poliovirus events and outbreaks, and their global, regional and country-level partners.

This document is an addendum to the *Standard operating procedures: responding to a poliovirus event or outbreak, version 3.1* (SOPs).² It provides interim guidance for the use of tOPV in line with the *Polio Endgame Strategy 2019–2023*³ and the addendum to the *Strategy for the Response to Type 2 Circulating Vaccine-Derived Poliovirus 2020–2021*.⁴ It should be used in conjunction with the comprehensive

¹ World Health Organization. Meeting of the Strategic Advisory Group of Experts on Immunization, 31 March–1 April 2020: conclusions and recommendations. *Weekly epidemiological record*. 2020;95(22):241-56. Available from: <https://apps.who.int/iris/bitstream/handle/10665/332218/WER9522-eng-fre.pdf?ua=1&ua=1> (accessed 1 August 2020).

² Global Polio Eradication Initiative. *Standard operating procedures: responding to a poliovirus event or outbreak, version 3.1*. Geneva: World Health Organization; 2020 Apr. Available from: <https://www.who.int/publications/i/item/9789240002999> (accessed 1 August 2020).

³ Global Polio Eradication Initiative. *Polio Endgame Strategy 2019–2023: Eradication, integration, certification and containment*. Geneva: World Health Organization; 2019. Available from: <http://polioeradication.org/wp-content/uploads/2019/06/english-polio-endgame-strategy.pdf> (accessed 13 August 2020).

⁴ Global Polio Eradication Initiative. *Strategy for the Response to Type 2 Circulating Vaccine-Derived Poliovirus 2020–2021: An addendum to the Polio Endgame Strategy 2019–2023*. Geneva: World Health Organization; 2020. Available from: <http://polioeradication.org/wp-content/uploads/2020/04/Strategy-for-the-response-to-type-2-circulating-Vaccine-Derived-Poliovirus-20200406.pdf> (accessed 13 August 2020).

operational guidance “tOPV management, monitoring, removal and disposal (without a vaccine vial monitor): Addendum to *mOPV2 management, monitoring, removal and disposal -Technical Guidance, version 2*”.⁵

Recommendation for the use of tOPV (strategy and scope)

tOPV can be made available to countries for cVDPV2 outbreak response in subnational areas where there is co-circulation or high risk of co-circulation of cVDPV2 with cVDPV1, cVDPV3 or WPV1 in order to avoid the need to conduct dual mOPV2 and bOPV campaigns.⁶

While this recommendation is made to ensure children are protected from both wild and vaccine-derived polioviruses of all three types, tOPV will only be used as an outbreak response tool in select countries that agree to its use, and not in routine immunization. tOPV should not replace bOPV use in routine Expanded Programme on Immunization schedules at this time.

Operational considerations – elements of the SOPs that remain the same

Definitions, outbreak response standards and protocols, including the response timing and scale of campaigns required for high-quality SIAs, remain the same as detailed in the outbreak response SOPs version 3.1.⁷

Since tOPV contains a live type 2 poliovirus, tOPV will be subject to the same usage controls that are currently followed for mOPV2 use before, during and after a campaign.⁶

The vaccine is manufactured to the same specifications as when the use of tOPV was stopped globally in 2016. However, the evaluation of vaccine vial monitor (VVM) compatibility for WHO prequalification has changed; this has no relationship to the safety, stability or immunogenicity of tOPV when kept at 2-8°C or at -20°C. The vaccine is stable for six months at 2-8°C and for two years at -20°C but is more sensitive to heat above 8°C. The fact that a VVM will not be included on the newly produced tOPV in no way affects the quality and safety of the vaccine itself.

Before the campaign

Requesting vaccine: The use of tOPV will require the same authorizations process and restrictions as required for the use of mOPV2.⁸ Countries must present a risk assessment and vaccine request form⁹ for consultation by the Advisory Group on mOPV2/tOPV Provision (Advisory Group). The Advisory Group will rapidly review the risk assessment and vaccine request and recommend a course of action to the WHO

⁵ Global Polio Eradication Initiative. tOPV management, monitoring, removal and disposal (without a vaccine vial monitor): Addendum to *mOPV2 management, monitoring, removal and disposal -Technical Guidance, version 2*. Geneva: World Health Organization; 2021. Available from: <https://polioeradication.org/wp-content/uploads/2021/04/tOPV-Technical-Guidance-tOPV-Management-Monitoring-Removal-and-Disposal-v1.0.pdf> (accessed 7 April 2021).

⁶ For further details, see Global Polio Eradication Initiative. tOPV management, monitoring, removal and disposal (without a vaccine vial monitor).

⁷ Global Polio Eradication Initiative. Standard operating procedures: responding to a poliovirus event or outbreak, version 3.1. Geneva: World Health Organization; 2020 Apr.

⁸ See “Requesting vaccine” (p. 35) in Standard operating procedures: responding to a poliovirus event or outbreak, version 3.1.

⁹ Global Polio Eradication Initiative. Sabin trivalent oral polio vaccine (tOPV) request form for the response to type 2 poliovirus. Geneva: World Health Organization; 2020. Available under: <http://polioeradication.org/tools-and-library/resources-for-polio-eradicators/gpei-tools-protocols-and-guidelines> (accessed 6 January 2021).

Director-General. Upon approval, the tOPV vaccine stock with the shortest shelf life will be released from the global stockpile for immediate use but would require:

- submitting a special request form to access the vaccine from a global stockpile, with release contingent on WHO Director-General approval (see below); and
- maintaining normal procedures for shipping and storage requirements (cold chain) as well as precise storage, temperature and transaction records at all supply chain levels (applied throughout the SIA).

During the campaign

- maintaining containment between SIA rounds.

After the campaign

- ensuring proper disposal after all immunization response rounds are completed as per GPEI recommendations.

Operational considerations – elements of the SOPs that are different

Before the campaign

- The heat sensitivity and absence of a VVM on the label of tOPV requires freezer storage space at the lowest possible level, closest to the vaccinator. Utilizing long-range passive cold-chain equipment and continuous temperature monitoring devices is also important to protect vaccine. The availability of this equipment should be verified during the cold-chain equipment inventory gap analysis before the outbreak response. Detailed operational guidance is available in “tOPV management, monitoring, removal and disposal (without a vaccine vial monitor): Addendum to *mOPV2 management, monitoring, removal and disposal - Technical Guidance, version 2*”.¹⁰
- An orientation session for front-line health workers on the use of tOPV (without VVMs) should take place prior to a campaign, particularly in the countries where public discourse around vaccine safety or hesitancy may present a risk to vaccine acceptance, to reassure front-line workers on the safety of tOPV in the absence of VVMs. These activities may be incorporated in the vaccinator and social mobilizer training, and include FAQs and training aides.
- Health journalists and public health establishments need to be aware of the rationale for tOPV use in outbreak response (i.e. not reversing “the switch”) and fully support it, resolving any potential concerns.

During the campaign

- As there is no VVM, implementing countries should follow strict temperature management procedures in addition to the usage protocols outlined in “tOPV management, monitoring, removal and disposal (without a vaccine vial monitor): Addendum to *mOPV2 management, monitoring, removal and disposal - Technical Guidance, version 2*”.¹⁰
- Although preventing vaccine wastage is important, due to the absence of VVM and the need to maintain full accountability for a vaccine under containment, the multi-dose vial policy is not recommended during tOPV campaigns.

¹⁰ Global Polio Eradication Initiative. tOPV management, monitoring, removal and disposal (without a vaccine vial monitor): Addendum to *mOPV2 management, monitoring, removal and disposal - Technical Guidance, version 2*. Geneva: World Health Organization; 2021. Available from: <https://polioeradication.org/wp-content/uploads/2021/04/tOPV-Technical-Guidance-tOPV-Management-Monitoring-Removal-and-Disposal-v1.0.pdf> (accessed 7 April January 2021).

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- Digital and social media spaces and communities need to be monitored for rumours linked to tOPV vaccine attributes and perceptions of safety.

After the campaign

- Reports on the quantities of all tOPV vials together with temperature data verification information should be sent to the next higher level.
- All unusable vials must be retrieved and disposed of at the regional or national level according to *mOPV2 management, monitoring, removal and disposal - Technical Guidance, version 2* **and to the local regulations for health waste disposal.**
- Support to front-line workers should be provided to resolve caregiver refusals due to the lack of confidence in tOPV.

Frequently asked questions

Q. tOPV was stopped globally during the switch, so why are we using it again?

In 2021, over four years after the global switch to bOPV, the world is facing increasing cVDPV2 outbreaks in parts of Africa, South-East Asia and the Middle East. mOPV2 has been the vaccine available to respond to these outbreaks. In some countries, the length and large scale of mOPV2 responses have displaced planned bOPV SIAs; in other countries, concurrent ongoing WPV1 circulation or concurrent cVDPV1, 2 or 3 circulations complicate response planning due to alternating bOPV and mOPV2 delivery. Furthermore, the cost of delivery of the cVDPV2 responses is considerable. For these reasons, tOPV, which protects against all three types of poliovirus, will be available for cVDPV2 response with only a modest price difference for the vaccine.

Q. Why did the VVM for tOPV not meet the requirements for tOPV?

In the context of tOPV prequalification, a review of the submitted stability data showed that the stability curve for tOPV did not match the curve of the VVM itself when tested at 37°C. The vaccine itself has not changed from production prior to 2016 and is manufactured to the same specifications as before the use of tOPV was stopped globally; instead, the evaluation of VVM compatibility for WHO prequalification has changed.

This has no relationship to the stability or immunogenicity of tOPV when kept at 2-8°C or at -20°C: the vaccine is stable for six months at 2-8°C and for two years at -20°C. Countries wishing to use tOPV should be assured that tOPV remains effective and immunogenic. tOPV from PT Bio Farma is a prequalified vaccine that complies with all requirements for safety, immunogenicity and stability.

Q. Is tOPV safe and effective, even without a VVM?

The tOPV vaccine itself has met all prequalification requirements. The prequalification process is based on specifications exacted by the Expert Committee on Biological Standardization (ECBS), an independent body that issues established, international norms and standards for the production and control of biological products. These norms and standards govern the contents used in the production of OPV and ensure that the purity of the vaccine meets all the technical criteria established by the ECBS, as verified through state-of-the-art technology. The fact that VVM will not be included on the newly produced tOPV in no way affects the quality and safety of the vaccine itself.

Q. How can vaccinators, health care providers and parents be assured of tOPV's efficacy, without a VVM?

Provided that recommended storage (cold-chain) procedures remain in place, i.e. that the vaccine is deep frozen in central/regional cold stores, that it is always kept at temperatures of 2-8°C in the health centre refrigerator or in vaccine carriers/cold boxes fitted with frozen ice packs, and that stated shelf life/expiration dates are adhered to, the vaccine remains potent, safe and efficacious.

It is important to note that even expired vaccine administered inadvertently would not present a safety issue to children. Only its efficacy would be affected, i.e. a non-effective dose would be administered, but one that is not harmful to children.

Q. Should anything be done differently while conducting tOPV SIAs with the VVM-less vaccine?

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Yes. The heat sensitivity and absence of a VVM on the label of tOPV requires freezer storage space at the lowest possible level, closest to the vaccinator. Utilizing only the long-range passive cold-chain equipment and continuous temperature monitoring devices are also important to protect tOPV.

References

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