IPV and the OPV switch: risk mitigation

18 March 2016

Background

- In March 2014, UNICEF issued awards to two manufacturers for the supply of IPV in 1, 5 and 10 dose vials and long term supply agreements were established through to 2018
- Due to technical challenges in scaling up IPV bulk production and the associated quality control testing and releases, there is now reduced availability from both manufacturers for all presentations
- The IPV supply constraints are expected to remain dynamic until 2018 and will continue to be closely monitored
- All possible steps are being taken in order to limit the number of countries impacted by the delays and minimise the consequences of this unforeseen situation

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Recap on the role of IPV

- One dose of IPV will induce an immunity base (sero-conversion and/or priming) to poliovirus type 2, and boost immunity against types 1 and 3
- This immunity base is expected to reduce the risk of paralytic disease following poliovirus type 2 exposure
- In case of epidemic transmission of poliovirus type 2, a second dose of polio vaccine (mOPV2 or IPV) should rapidly close any remaining immunity gaps and induce mucosal immunity (reducing the risk of community transmission)
- Therefore IPV primarily serves as a risk mitigation tool

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Review by SAGE in October 2015

- SAGE reaffirmed its recommendation that the globally synchronized switch should take place in April 2016, and confirmed the switch window **from 17 April to 1 May 2016**
- **SAGE concluded that the risks of continued use of tOPV is greater than the risks of switching to bOPV** in multiple respects: epidemiological, programmatic, political, and financial
- SAGE emphasized that even in the event of further changes in IPV supply, the switch date will not be changed
- **SAGE also confirmed that all countries must implement the OPV switch in April 2016, even in instances where IPV introduction had not occurred prior to the switch**

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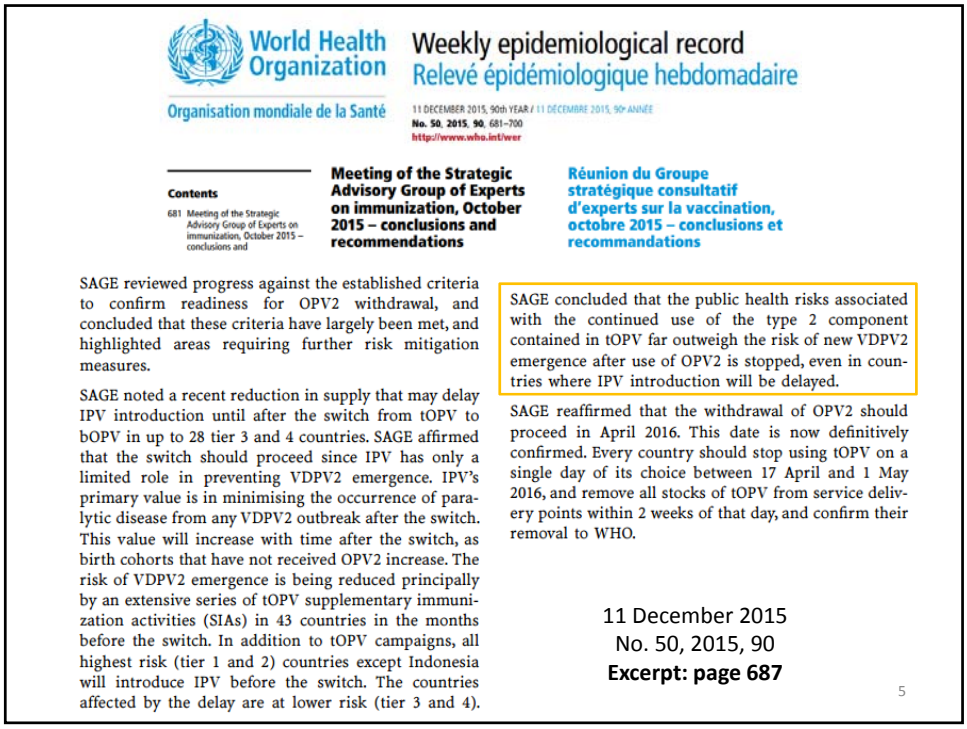

World Health Organization
Organisation mondiale de la Santé

Weekly epidemiological record
Relevé épidémiologique hebdomadaire

11 DECEMBER 2015, 90th YEAR / 11 DÉCEMBRE 2015, 90e ANNÉE
No. 50, 2015, 90, 681–700
http://www.who.int/wer

Contents

Meeting of the Strategic Advisory Group of Experts on immunization, October 2015 – conclusions and recommendations

Réunion du Groupe stratégique consultatif d'experts sur la vaccination, octobre 2015 – conclusions et recommandations

SAGE reviewed progress against the established criteria to confirm readiness for OPV2 withdrawal, and concluded that these criteria have largely been met, and highlighted areas requiring further risk mitigation measures.

SAGE noted a recent reduction in supply that may delay IPV introduction until after the switch from tOPV to bOPV in up to 28 tier 3 and 4 countries. SAGE affirmed that the switch should proceed since IPV has only a limited role in preventing VDPV2 emergence. IPV's primary value is in minimising the occurrence of paralytic disease from any VDPV2 outbreak after the switch. This value will increase with time after the switch, as birth cohorts that have not received OPV2 increase. The risk of VDPV2 emergence is being reduced principally by an extensive series of tOPV supplementary immunization activities (SIAs) in 43 countries in the months before the switch. In addition to tOPV campaigns, all highest risk (tier 1 and 2) countries except Indonesia will introduce IPV before the switch. The countries affected by the delay are at lower risk (tier 3 and 4).

SAGE concluded that the public health risks associated with the continued use of the type 2 component contained in tOPV far outweigh the risk of new VDPV2 emergence after use of OPV2 is stopped, even in countries where IPV introduction will be delayed.

SAGE reaffirmed that the withdrawal of OPV2 should proceed in April 2016. This date is now definitively confirmed. Every country should stop using tOPV on a single day of its choice between 17 April and 1 May 2016, and remove all stocks of tOPV from service delivery points within 2 weeks of that day, and confirm their removal to WHO.

11 December 2015
No. 50, 2015, 90
Excerpt: page 687

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Risk management rationale

(endorsed by SAGE in October 2015)

- **IPV has only a limited role in preventing the emergence of type 2 vaccine-derived polioviruses** (VDPV2). IPV's primary value is in minimizing the occurrence of paralytic disease from any VDPV 2 after the switch
- The majority of countries affected by the delay are in low risk tiers 3 and 4. **Population immunity against type 2 is high in these countries** (due to consistently high routine immunisation coverage) so the risk of VDPV2 emergence and spread is minimal
- The risk of VDPV2 emergence is **principally reduced by ensuring high coverage, and may include high quality tOPV SIAs** before the switch in countries or communities with immunity gaps
- In addition to tOPV SIAs, almost all **highest risk (tier 1 and tier 2) countries will have introduced IPV** in routine immunization before the switch
- **A global stockpile of mOPV2 (which is WHO prequalified) and IPV** is available for outbreak response in the event of VDPV2 detection in any country after the switch. Countries should have a mechanism in place for emergency authorization of mOPV use in an outbreak

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Allocation of available supply

(endorsed by SAGE in October 2015)

There are four criteria used to determine the classification of each country, and therefore its prioritization for the allocation of IPV.

Countries are considered to be in a higher risk tier if:

- The transmission of wild poliovirus has not yet been interrupted
- The country has a history of cVDPV outbreaks
- There are consistently low levels of routine immunization coverage (and therefore population immunity to type 2)
- The country shares borders with higher risk countries

→ Based on these criteria, countries considered as low risk may see delays in **IPV introductions** or **resupply shipments** for routine programmes.

If IPV introduction is delayed

- **Optimize type 2 immunity through tOPV SIAs** in locations with sub-optimum routine coverage, in the lead-up to the switch (advisable to all countries)
- **Coordinate switch implementation in a highly effective and timely manner,** to ensure no tOPV is used after the switch window
- **Enhance** AFP surveillance and environmental sampling
- **Ensure that preparations for IPV introduction are completed in advance**, so that IPV roll out can start as soon as the vaccine becomes available
- **Plan for the vaccination of any eligible infants who missed a scheduled dose of IPV after the OPV switch in April 2016**, e.g. came for DTP3 after switch, but IPV was not available
- **Prepare a response plan** so that in the unlikely situation that a type 2 cVDPV outbreak occurs, it can be addressed and ended as soon as possible

If IPV stock-outs may be expected

- **Closely monitor IPV stocks at all levels**, to balance stocks effectively to help prevent stock-outs, e.g. smaller and more frequent deliveries to lower levels to help with effective distribution of available supply
- **Ensure strict adherence to vaccinating children only in the target group**, e.g. one full dose of IPV at 14 weeks of age or the nearest following visit
- **Prioritize available supply to at-risk populations**, in the case of a potential IPV stock out
- **Apply the multi-dose vial policy**, to enable use of IPV with the vaccine vial monitor on the label up to 28 days after opening, to minimize wastage
- **Use vaccination cards and registers effectively** to record a missed dose of IPV, to facilitate later tracking and follow up

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The option of a fractional dose of IPV

As an alternative to the intramuscular injection of a full IPV dose, **countries may choose the implementation of a two-dose fractional dose schedule** (using 1/5 of a full dose), via the intradermal route.

This may require:

- A review of clinical data at national level, by the NITAG or equivalent
- An assessment of the implications of the introduction of a fractional dose schedule from a programmatic perspective (e.g. supply of syringes, added training, time to roll-out, changes to the schedule, etc.)
- A decision by the NITAG and NRA to move to an off label use of IPV

For outbreak response, a fractional dose of IPV has been endorsed for use in conjunction with mOPV.

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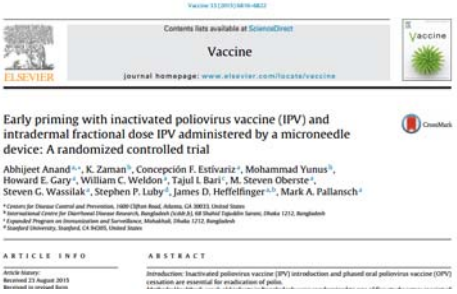
Two fractional doses versus one full dose


Vaccine

Early priming with inactivated poliovirus vaccine (IPV) and intradermal fractional dose IPV administered by a microneedle device: A randomized controlled trial


ORIGINAL ARTICLE

Priming after a Fractional Dose of Inactivated Poliovirus Vaccine

Author	Year published	Country	Schedule	One full-dose IPV	*Two fractional doses given intradermally*
Resik S	2013 Shown above	Cuba	IPV	63% (4 mos)	**98%** (4+8 mos)
Anand A	2015 Shown above	Bangladesh	IPV	39% (6 wks)	**81%** (6+14 wks)
Anand A	2016 In publication	Bangladesh	IPV	73% (14 wks)	

→ ***Two fractional doses are more immunogenic***

WHO Position Paper on Polio Vaccines

25 March 2016 (in press)

… *"As an alternative to the intramuscular injection of a full dose of IPV, countries may consider using fractional doses (1/5 of the full IPV dose) via the intradermal route, but the programmatic cost and logistic implications of this option should be considered.* ***In the context of an IPV shortage, countries could consider instituting a 2-dose fractional dose option which could ensure that all eligible infants receive IPV, is dose-sparing, and results in better immunogenicity than a single full dose of IPV.*** *This option may be particularly appropriate for outbreak response if supplies are limited."* …

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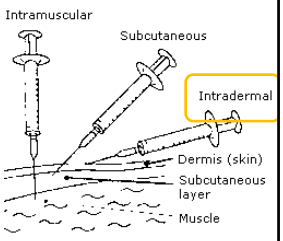
Fractional dose of IPV
Programmatic considerations

- Syringes and devices:
  - 0.1ml syringe is recommended (0.05ml for BCG)
- Timing in the schedule:
  - Starting at or after 6 weeks, with a minimum interval of 4 weeks, e.g. at 6 and 14 weeks
- Administration:
  - Added health worker training may be required
- Data recording:
  - Will involve adjustments to registers and records
- Communications:
  - Advance planning and careful messaging needed



Operational guidance to come!

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For materials to support the implementation of IPV and the OPV switch:

http://www.who.int/immunization/diseases/poliomyelitis/endgame_objective2/en/

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