Report of the Polio WG Meeting
(held on 21-22 August 2019)

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Polio WG Discussions: Objectives

- To review the GPEI programme update, including the WPV and VDPV epidemiology.
- To take note of the specific challenges of eradicating WPV1 in Afghanistan and Pakistan and discuss potential solutions for acceleration of eradication.
- To review scenarios for cVDPV2 outbreak response including OPV2 vaccine restart in routine immunization.
- To review results from one-drop mOPV2 study and, if positive, consider endorsing its use.
- To review clinical data from nOPV trials and consider recommending accelerated assessment of nOPV2 under Emergency Use Listing (EUL).
- To review options for IPV only vaccination schedules in polio free regions.

Progress towards eradication

The WG expressed serious concerns with the status of the eradication program and the inadequacy of currently available tools:

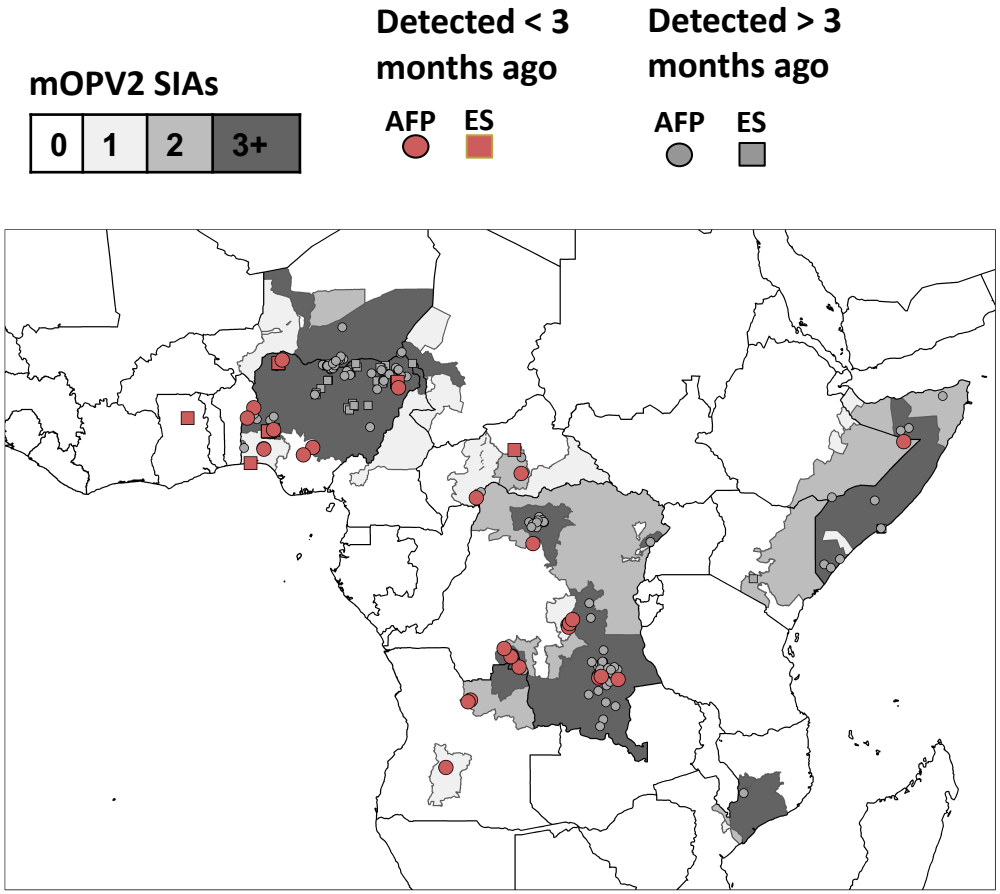
- Increased circulation of WPV1 in Pakistan and Afghanistan, with bans on vaccinations and increasing community resistance.
- Expanding outbreaks of cVDPV2 in Africa in the context of decreasing population immunity.
  - Sustained transmission (>6 months) in Nigeria, Niger, Democratic Republic of Congo and Somalia.
- Limited supply of mOPV2 vaccine to control these outbreaks.
- Repeated seedings of VDPV2s following low-quality campaigns with mOPV2.

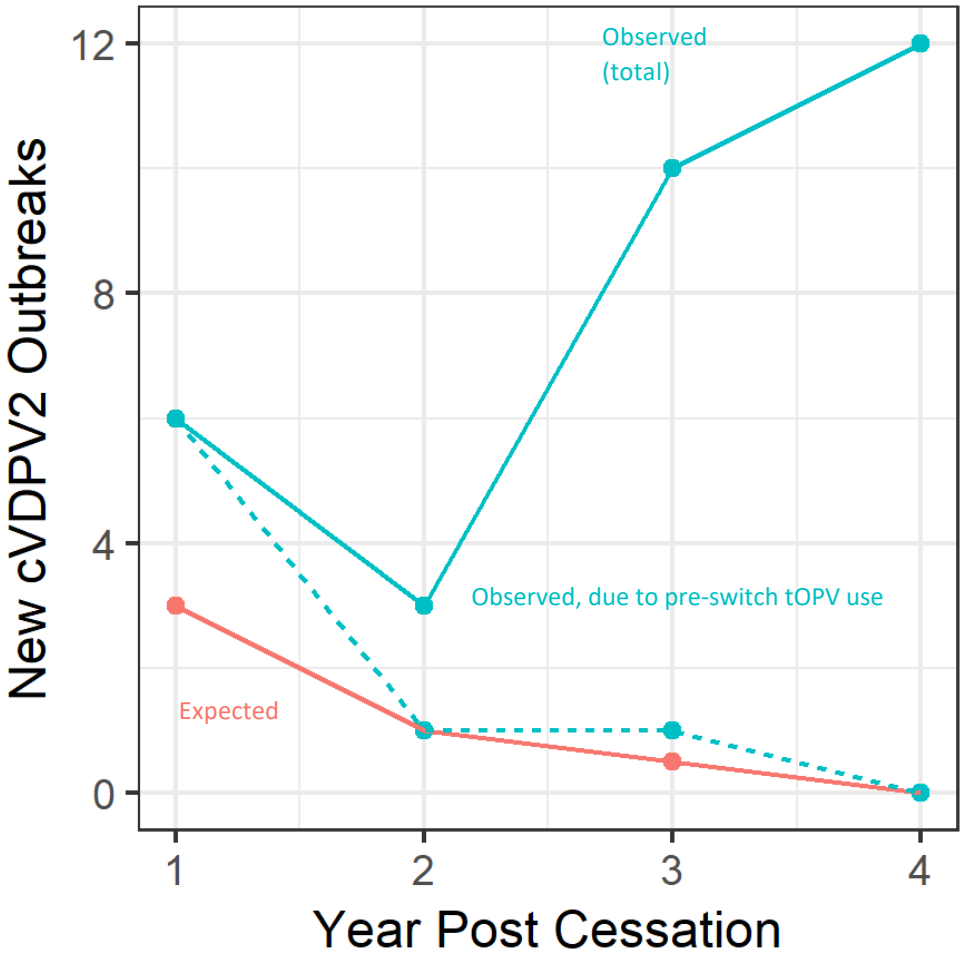
Progress towards eradication

The WG acknowledged the positive developments in polio eradication:

- No WPV3 detected globally since November 2012 (to be certified by GCC)
- No WPV of any serotype detected in the African continent since September 2016
  - Increased surveillance sensitivity in Nigeria

Challenges in cVDPV2 Outbreak Response (1/2)





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Challenges in cVDPV2 Outbreak Response (2/2)

- The WG reviewed the epidemiology of cVDPV2 and conclusions from the Cessation Risk Task Team meeting.
- The WG was extremely concerned over the cVDPV2 outbreaks in sub-Saharan Africa.
- An effective response to cVDPV2 outbreaks is essential. The quality and timing of the response by countries in Africa must improve.

The WG agreed with the Cessation Risk Task Team on the necessity of changes to the Standard Operating Procedures (SOPs), which will be revised on scope, quality and timeliness of the mOPV2 response.

The WG also agreed that acceleration of clinical development and assessment of novel OPV2 (nOPV2) is of paramount importance.

mOPV2 Supply Update

- The WG concluded that it is essential to ensure an un-interrupted supply of mOPV2, for:
  a) Short-term use to control outbreaks
  b) Contingency planning

- The WG recommended:
  – Urgently identify sites capable of Fill and Finish of existing mOPV2 bulk for utilisation.
  – Consider restart bulk production of mOPV2, given the 15-18-month lead time required by manufacturers.

Development of nOPV2

The safety and immunogenicity of two novel live attenuated monovalent (serotype 2) oral poliovirus vaccines in healthy adults: a double-blind, single-centre phase 1 study

Pierre Van Damme, Ilse De Coster*, Ananda S Bandyopadhyay, Hilde Revets, Kanchanamala Withanage, Philippe De Smedt, Leen Suykens, M Steven Oberste, William C Weldon, Sue Ann Costa-Clemens, Ralf Clemens, John Modlin, Amy J Weiner, Andrew J Macadam, Raul Andino, Olen M Kew, Jennifer L Konopka-Anstadt, Cara C Burns, John Konz, Rahnuma Wahid, Christopher Gast*

- The WG were presented preliminary data from adult, toddler and infant trials of both nOPV2 candidate vaccines.
- The WG supported the clinical development of nOPV2 and recommended the accelerated assessment of nOPV2 under EUL.
- The WG acknowledged that there are risks associated with nOPV2 development, and contingency plans that include mOPV2 production must be put in place.

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One vs Two mOPV2 Drop Immunogenicity Study
Objective and Methods

- **Objective:** To compare humoral immunogenicity for poliovirus 2 after one dose with either 1-drop or 2-drop administration of mOPV2 in mostly poliovirus type 2 naive children

- **Methods:**
  - RCT: 2 study arms (1 drop vs 2 drops); Sample size: 180 children in each arm
  - Inclusion criteria: 9-22 months children residing in Mocuba, Mozambique
  - Enrolled children not exposed to live vaccine containing PV2

- Study design:
  - **Visit 1**: bleed, mOPV2 either 1 or 2 drops (mOPV2 administered as part of cVDPV2 outbreak response in Mozambique)
  - **Visit 2**: (~1 month later) bleed

One vs Two mOPV2 Drop Immunogenicity Study

Immunogenicity

Results	1-drop			2-drops			Difference (95% CI)
	%	95%CI	n/N	%	95%CI	n/N	
Seroconversion	**64.8**	50.6 – 77.3	35/54	**67.6**	55.7 – 78.0	50/74	**-2.8** (-19.4, 13.8)
Boosting	**45.1**	33.2 – 57.3	32/71	**51.6**	38.6 – 64.5	32/62	**-6.5** (-23.5, 10.5)
Immune response	**53.6**	44.5 – 62.6	67/125	**60.3**	56.1 – 73.4	82/136	**-6.7** (-18.7, 5.3)

One vs Two mOPV2 Drop Immunogenicity Study

Projected immunogenicity after multiple rounds

	Immune Response			Seroconversion only		
mOPV2 rounds	1-drop immune response	2-drops immune response	Difference (%)	1-drop seroconversion	2-drops seroconversion	Difference (%)
	%	%		%	%	
Round 1	**53.6**	**60.3**	**-6.7**	**64.8**	**67.6**	**-2.8**
Round 2	**78.5**	**84.2**	**-5.7**	**87.6**	**89.5**	**-1.9**
Round 3	**90.0**	**93.7**	**-3.7**	**95.6**	**96.6**	**-1.0**

Projected immunity loss after 3 rounds between 1.0% to 3.7%

One vs Two mOPV2 Drop Immunogenicity Study
Limitations

- Study conducted under emergency conditions because mOPV2 use is allowed only in context of VDPV2 response (including for clinical trials)
- Power of the study was reduced:
  - Drop-out higher than expected due to rumors about witchcraft
- Cannot completely rule out secondary transmission of PV2 as the first round of mOPV2 vaccination campaign started March 16 still during visit 1

One vs Two mOPV2 Drop Immunogenicity Study
SAGE WG on Polio Recommendation

*The WG recommended that the **preference is to use two-drops** (the standard dose) of mOPV2 vaccine.*

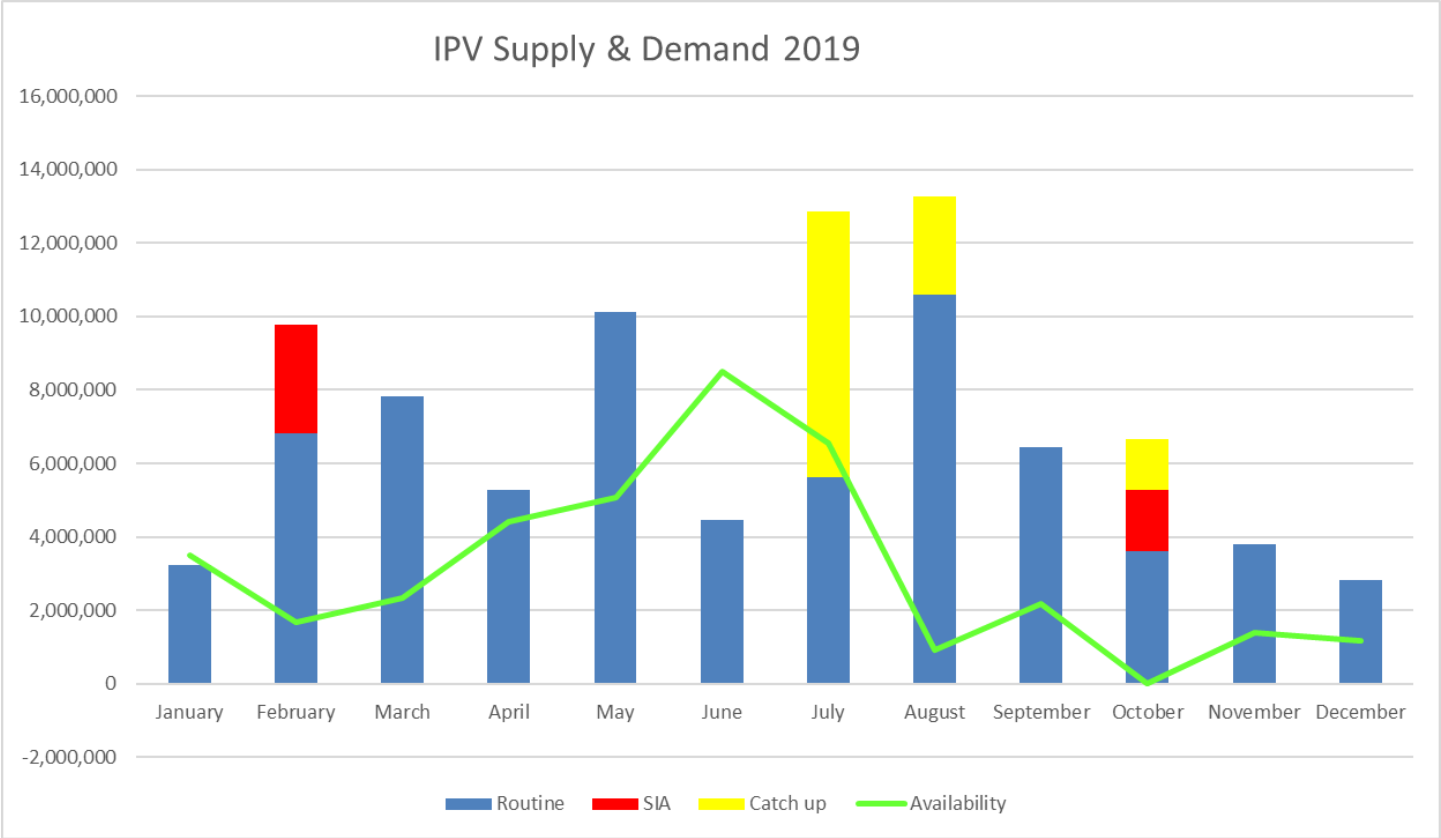
*However, in the event that mOPV2 supply deteriorates to levels inadequate to cover the required population, the off-label use of **one drop mOPV2 should be considered**.*

"One drop is unquestionably better than no drops." -Roland Sutter

Reducing Outbreak Risks Associated with OPV Withdrawal

- A reduction in preventative SIAs due to budget cuts could lead to a risk in cVDPV1 and cVDPV3 outbreaks and WPV1 vulnerability.
- A proposed pathway to reduce outbreak risks was presented, through focusing on the worlds highest risk geographies.
- The WG approved the approach and to combine preventative SIAs with other vaccines or health interventions.
- The WG recommended that those countries affected by cVDPV2 and conducting mOPV2 campaigns do not overlook bOPV SIAs.

IPV Supply Update (1/2)



In 2019, IPV supply met requirements for routine immunization with one IPV dose, SIAs in endemic countries, and for catch up campaigns in 5 priority countries.

IPV Supply Update (2/2)

The WG **recommend that** the prioritization order for IPV allocation be updated as follows* :

1. Ensure routine immunization needs in all countries are met.

2. Allocate to the populations that are IPV-unvaccinated since the switch, due to IPV supply shortages, based on risk assessment.

3. Ensure requirements for the acceleration of the interruption of wild poliovirus transmission are fully met (requests from endemic countries for SIAs to interrupt WPV).

**Switched order of (2) and (3)*

Summary of Main Recommendations

1. The WG was extremely concerned over program deterioration in Afghanistan and Pakistan.
   - Polio eradication must be prioritized in these countries.
   - High-level advocacy and immediate action to ensure government and community commitment is required.

2. The WG was extremely concerned over the cVDPV2 outbreaks.
   - The response to cVDPV2 outbreaks must improve.
   - The WG agreed that the Standard Operating Procedures (SOPs) will be revised, on scope, quality and timeliness of the mOPV2 response.

3. The WG recommended ensuring an un-interrupted supply of mOPV2, for short-term use to control outbreaks and contingency plans.
   - Urgently identify sites to Fill and Finish existing mOPV2 bulk.
   - Consider restart bulk production of mOPV2, given the 15-18-month lead time.

Summary of Main Recommendations

4. The WG support the accelerated clinical development of nOPV2 and endorsed the accelerated assessment of nOPV2 under Emergency Use Listing (EUL).

5. The WG recommended that the preference is to use two-drops (the standard dose) of mOPV2 vaccine.
   - However, in the event that mOPV2 supply deteriorates to levels inadequate to cover the required population, the off-label use of one drop mOPV2 should be considered.

6. The WG is concerned bOPV SIAs are being cut due to budget limitations.
   - The WG recommend countries experiencing cVDPV2 outbreaks do not forget about the importance of SIAs with bOPV to prevent poliovirus type 1 and 3.
   - To improve type 1 and type 3 immunity, combined administration of bOPV and mOPV2 during campaigns should be considered.

7. The WG recommended an updated prioritization order for IPV allocation.

Discussion of SAGE WG Chairs with WHO's DG

At the conclusion of 18th SAGE WG meeting, WG expressed the need to discuss grave concerns about the polio program with the WHO's DG and request his immediate actions.

The call between DG and WG chairs took place on Sept 4 and discussed:

- Overall concern with the polio program and steps to ensure that polio eradication in Afghanistan and Pakistan and in cVDPV2 outbreak countries in Africa is prioritized
- Adequate mOPV2 supply
- Emergency Use Licensure (EUL) of nOPV2

The DG committed to:

- Maintaining high-level discussions with the governments of polio affected countries to ensure high level governmental commitment to the polio program
- Continuing high-level talks with national authorities of countries with fill and finish capacity to explain the importance of mOPV2 filling and to request that they allow it
- Prioritizing the review of the EUL submission by the WHO PQ (nOPV2)

Polio
Main asks from SAGE

- Main points for deliberations (from SAGE WG on polio):
  - Endorse accelerating clinical development and prioritize assessment under WHO's Emergency Use Listing (EUL) procedure for nOPV2
  - Endorse securing uninterrupted supply of mOPV2 through identification of fill and finish capacity and new bulk production
  - Endorse using one-drop mOPV2 strategy ONLY IF mOPV2 supply reaches critically low levels and is not sufficient for cVDPV2 outbreak control