The New Polio Eradication End Game: Rationale and Supporting Evidence

Roland W. Sutter, Lauren Platt, Ondrej Mach, Hamid Jafari, and R. Bruce Aylward
Polio Eradication & Emergency Cluster (PEC), World Health Organization, Geneva, Switzerland

Polio eradication requires the removal of all polioviruses from human populations, whether wild poliovirus or those emanating from the oral poliovirus vaccine (OPV). The Polio Eradication & Endgame Strategic Plan 2013–2018 provides a framework for interruption of wild poliovirus transmission in remaining endemic foci and lays out a plan for the new polio end game, which includes the withdrawal of Sabin strains, starting with type 2, and the introduction of inactivated poliovirus vaccine, for risk mitigation purposes. This report summarizes the rationale and evidence that supports the policy decision to switch from trivalent OPV to bivalent OPV and to introduce 1 dose of inactivated poliovirus vaccine into routine immunization schedules, and it describes the proposed implementation of this policy in countries using trivalent OPV.

Keywords. poliomyelitis; eradication; vaccination.

Poliomyelitis is on the verge of eradication with 223 cases of paralytic disease caused by wild poliovirus (WPV) reported in 2012 [1], and 4 World Health Organization (WHO) Regions have been certified as polio-free. In addition, indigenous WPV type 2 was last detected in Northern India in 1999 [2], and WPV type 3 poliovirus was last reported from Nigeria in November 2012 [1]. Because Sabin-derived polioviruses can replicate for prolonged periods in individuals or in communities and potentially reestablish endemic and epidemic transmission [3, 4], strategies for the elimination of all polioviruses, including the attenuated Sabin vaccine viruses emanating from the oral poliovirus vaccine (OPV), needed to be developed and implemented to achieve polio eradication.

The Strategic Advisory Group of Experts (SAGE) on Immunization is a committee established to advise the WHO on global policies and strategies for vaccines and immunization. In August 2008, SAGE established a working group to advise the Global Polio Eradication Initiative (GPEI), a partnership between WHO, United Nations Children’s Fund (UNICEF), Centers for Disease Control and Prevention, Rotary International, and the Bill & Melinda Gates Foundation, on 2 major programmatic issues: (1) policy recommendations for the use of inactivated poliovirus vaccine (IPV) in low- and middle-income settings and (2) the polio end game strategy to reduce long-term risks associated with OPV [5, 6].

Responding to these imperatives and following technical guidance of SAGE, GPEI has developed a comprehensive and long-term plan entitled the Polio Eradication & Endgame Strategic Plan 2013–2018, which lays out a road map to interrupt the transmission of WPV and achieve the long-term goals of the post-eradication era [7, 8]. The 4 overarching objectives of the plan are (1) to interrupt WPV transmission, (2) to strengthen immunization systems and the withdrawal of OPV, (3) to implement containment of polioviruses and to certify the world as polio-free, and (4) to plan the legacy of polio eradication. This report gives an overview of the rationale and supporting evidence base that led to the key policy changes described in the Polio Eradication & Endgame Strategic Plan 2013–2018: the planned cessation of the type 2 component of OPV (ie, the switch from trivalent OPV [tOPV] to bivalent OPV [bOPV]) and the global introduction of ≥1 dose of IPV into every country’s routine immunization schedule.
SWITCH FROM tOPV to bOPV AND ADDITION OF IPV IN ROUTINE IMMUNIZATION SCHEDULES

There are 3 serotypes of WPVs: types 1, 2, and 3 (WPV1, WPV2, and WPV3). WPV2 was successfully eradicated, with the last case reported in 1999 [2, 9]. However, currently 144 countries continue to use tOPV, containing type 2 live vaccine virus, for routine polio immunizations; 124 of them, including all countries eligible for support from the GAVI Alliance (except Ukraine), use tOPV exclusively, and 20 countries use both tOPV and IPV in sequential immunization schedules. The remaining 50 WHO member states, primarily industrialized countries, use IPV exclusively (Figure 1).

Polioviruses contained in OPV (referred to as Sabin viruses) are live-attenuated polioviruses, which in rare circumstances can revert to neurovirulent forms and cause vaccine-associated paralytic poliomyelitis (VAPP), clinically indistinguishable from paralytic poliomyelitis caused by WPVs [10–13]. It is estimated that each year there are between 250 and 500 cases of VAPP worldwide (WHO, unpublished data).

In addition to causing VAPP, Sabin virus may mutate and subsequently gain the ability to circulate in communities for long periods of time. These polioviruses, referred to as vaccine-derived polioviruses (VDPVs), have also lost their attenuating mutations and therefore reacquired the neurovirulence and transmission characteristics of WPVs. On very rare occasions, VDPVs could potentially reestablish endemic and epidemic transmission, and they are therefore incompatible with polio eradication [3, 4]. Since the eradication of WPV2 in 1999, circulating VDPVs (cVDPVs) caused by type 2 Sabin strains (VDPV2) have been reported from 14 countries, causing 404 reported paralytic cases. It is estimated that 2012 was the first year in history when there were more cases of paralytic poliomyelitis caused by Sabin vaccine polioviruses than caused by WPVs [1]. This burden of disease related to vaccination has become increasingly unacceptable to immunization policy makers and to parents.

OPV is needed to achieve eradication, but it also poses a grave risk to eradication. This paradox needs to be addressed proactively with the strategy of a phased withdrawal of all Sabin strains from OPV, starting with type 2, switching tOPV with bOPV. In addition to the elimination of risk from emergence of VDPV2 outbreaks, another advantage of bOPV is that seroconversion after 1 dose of bOPV was found to be significantly superior when compared with tOPV for types 1 and 3 [14]. In the Indian trial, after 2 doses of OPV, the rate of seroconversion to poliovirus type 1 was 86% (136 of 159) for bOPV, compared with 63% (106 of 168) for tOPV ($P < .001$); the equivalent rates for poliovirus type 3 were 74% (117 of 159) for bOPV and 52% (87 of 168) for tOPV ($P < .001$). Because of higher immunogenicity, it is anticipated that the switch to bOPV will further increase

![Figure 1](image-url)  
**Figure 1.** Map of countries using inactivated poliovirus vaccine (IPV), oral poliovirus vaccine (OPV), or both vaccines (sequential) in their primary immunization schedules (February 2014 data).
population immunity against polioviruses. Introduction of bOPV into campaign use in India is considered one of the main attributes for successful elimination of polio in that country [15].

To eliminate the risks associated with continued use of Sabin type 2–containing vaccines, SAGE recommended the withdrawal of all OPVs containing Sabin type 2 poliovirus, adhering to the following 3 principles: (1) the switch must be universal, (2) the switch must be synchronized, and (3) IPV must be introduced in every country ≥6 months before the switch. The switch must be universal and synchronized because after the switch the population immunity to type 2 polioviruses will decrease (especially the mucosal immunity), and bOPV-vaccinated populations would therefore become vulnerable to VDPV2 importations from areas where tOPV would still be in use. The current “silent” circulation in Israel of WPV type 1 further highlights this risk [16].

This potential risk (silent circulation leading to epidemic transmission) will be highest in the immediate post-OPV2 withdrawal period, when these viruses are still replicating and mutating in the intestinal tract of millions of recently OPV-vaccinated infants. This risk will probably rapidly decline, as illustrated by the detection of OPV virus in environmental samples for up to 3 months after cessation of OPV use [17–20]. During this period, in a population vaccinated with bOPV only, infants will be naïve to type 2 viruses and at increased risk of VDPV2 emergence and outbreak. To mitigate this risk for the immediate post OPV2 cessation era and for the longer term, SAGE recommended the universal, not selective, introduction of an additional dose of IPV to routine immunization schedules in countries using OPV only. Data suggest that 1 dose of IPV will induce an immunity base (ie, seroconversion and priming) that can be rapidly boosted by a second dose of IPV, manifested by high antibody titers that would be expected to mitigate the consequences of a VDPV2 emergence or a threatening outbreak scenario. A priming immune response to poliovirus types 1, 2, and 3, respectively, occurred in 97.6%, 98.3%, and 98.1% of infants who did not seroconvert after receiving a single dose of IPV at 4 months of age in Cuba [21].

In addition to providing protection against VDPV2, IPV boosts mucosal immunity to polioviruses in previously OPV-vaccinated recipients (H. Jafari, unpublished data). IPV also helps close the population humoral immunity gap in children who had not seroconverted after OPV vaccinations [22, 23]. Overall, the bOPV and IPV schedule is expected to provide higher levels of protection against poliomyelitis than the schedule with tOPV alone. Therefore, another benefit for adding IPV into routine immunization schedules is acceleration of polio eradication in WPV-infected areas. It is planned that, once introduced, IPV will remain part of the routine immunization schedule for at least a 10-year period, during which all OPV will be withdrawn.

“TRIGGER” POINT AND OTHER PROGRAMMATIC PRIORITIES FOR SWITCH FROM tOPV to bOPV AND IPV INTRODUCTION

To successfully achieve the planned change in immunization schedules, a “trigger point” must be achieved and several programmatic priorities require further strengthening. The trigger point for the OPV2 withdrawal is that all persistent cVDPV2 outbreaks (documented circulation for >6 months) must be stopped. Currently, 3 persistent outbreaks with cVDPV2 are ongoing: (1) the longstanding cVDPV2 outbreak in Nigeria [24–26]; (2) an outbreak with cases covering Chad, Cameroon, Niger and Nigeria; and (3) an outbreak with cases detected in Afghanistan and Pakistan [1]. In addition, the following programmatic priorities must be established or strengthened: (1) the absence of WPV2 must be validated by the Global Certification Commission; (2) an monovalent OPV2 stockpile must be established and available for outbreak control after a possible postswitch poliovirus type 2 emergence; (3) the laboratory containment standards for type 2 polioviruses must be implemented (phases I and II); (4) sufficient vaccine supplies of bOPV must be available and licensed in all countries for routine immunization use; and (5) sufficient supply of affordable IPV must be available to meet the global demand.

RECENT POLICY DECISIONS REGARDING TIMING OF THE ADDITIONAL IPV DOSE

Age of administration of the third dose of diphtheria-tetanus-pertussis–containing vaccine (DTP3) depends on the individual country’s immunization schedules and is most often between 3.5 and 6 months. In November 2013, SAGE issued a recommendation on the new polio schedule, including the age for the administration of the additional IPV dose with DTP3 at or after age 14 weeks [27].

The decision at what age to administer IPV was influenced by balancing 3 factors: (1) the optimal age for maximizing IPV immunogenicity, (2) the need to protect type 2–naïve infants against VDPV2s and VAPP (due to type 2) at an early age, and (3) the benefit of vaccinating infants at an age when there is maximal coverage and minimal dropout. IPV performance is negatively affected by levels of maternal antibodies against polioviruses, and thus its immunogenicity is limited in early infancy [28, 29]. At the same time, because infants vaccinated with bOPV will have no protection against type 2 until their first IPV dose, IPV needs to be given early. In Nigeria, however, the majority of VDPV2 paralytic cases between 2005 and 2012 were among children 3–12 months of age (273 of 388 cases; 70%) and only a small fraction among infants <3 months of age (8 of 388; 2%; WHO unpublished data set). Finally, coverage with DTP1 is usually higher than coverage with DTP3. Currently, it is considered that the relative gain in

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immunogenicity achieved by administering IPV together with DTP3 vaccination is most beneficial, outweighing the disadvantages of the risk of VDPV2 in the first 3 months of life and potentially lowering vaccination coverage due to dropout between DTP1 and DTP3.

Some countries may want to introduce 2 doses of IPV, for example, in a sequential schedule of IPV followed by OPV or with measles vaccine at ≥9 months of age. These decisions will be guided by analysis of data regarding the incremental benefit of a second dose of IPV in infants who have received previous doses of OPV, including, where available, the immunogenicity of polio vaccines and the epidemiology of VAPP. Studies from Oman, Cote d’Ivoire, India, and The Gambia suggest that 1 dose of IPV after previous OPV doses is sufficient to close the remaining immunity gap (90% of seronegative vaccinees will seroconvert) [22, 23, 29, 30].

**PATH TOWARD IMPLEMENTATION OF THE POLIO END GAME PLAN**

To achieve polio eradication, the GPEI has traditionally focused on polio-infected countries or countries at risk of poliovirus importation. In these areas, the main pillars of the eradication program have been the implementation of high-quality campaigns using OPV, the identification and targeting of at-risk populations, and the highly sensitive system of surveillance for acute flaccid paralysis. The geographic scope of these activities has become more and more focused as fewer and fewer countries are infected with polioviruses. Currently, the majority of polio resources are concentrated in priority countries.

The new polio end game plan calls for changes in immunizations in 125 OPV-only using countries, many of which are countries where GPEI had not been active for long. The introduction of IPV will also be the first time the GPEI will employ an injectable vaccine for routine use in the public sector and not simply in the private sector or for study purposes. New partnerships, including strong collaboration with GAVI and Expanded Programs on Immunization, are being established to successfully implement the Polio Eradication & Endgame Strategic Plan 2013–2018 within the predetermined timeline. The current objective of the GPEI is to achieve universal IPV introduction by the fall of 2015, followed by a synchronized global tOPV to bOPV switch in April 2016. At present, it is planned that the complete withdrawal of OPV (including bOPV) will be implemented 3 years after the last WPV is detected.

While planning for OPV2 cessation and IPV introduction, the GPEI must maintain a holistic approach that considers the challenges of different countries based on their financial resources, technical capacity, and political support. It is recognized that different countries will require different levels of technical and financial assistance. GAVI-eligible and graduating countries will be able to receive technical and financial support for IPV introduction. In addition, some non–GAVI-eligible countries have already initiated the process for IPV introduction and will not require technical assistance but might need alternative forms of support, such as help with advocacy and garnering political support. Finally, some lower- or middle-income countries that are not eligible for GAVI support will need more customized support from the GPEI to implement the end game and will have to negotiate the appropriate financial, technical, and political resources to ensure the timely introduction of IPV and the switch to bOPV. The ability of the GPEI and Expanded Programs on Immunization to balance this large scope of work among highly variable country situations will be key to the success of the end game. However, successful implementation of the new polio end game offers the best opportunity to achieve polio eradication and secure it forever.

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