polio pipeline

News from the world of polio eradication research and development

POLIO GLOBAL ERADICATION INITIATIVE

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TWO YEARS INTO NEW POLIO ENDGAME PLAN, WORLD PREPARES FOR TRIVALENT OPV TO BIVALENT OPV SWITCH

Two years into the life of the *Polio Eradication and Endgame Strategic Plan 2013-2018* (Endgame Plan), the world is gearing up for the global, synchronized switch from trivalent oral poliovirus vaccine (OPV) to bivalent OPV in routine immunization programmes.

The phased cessation of OPV is a cornerstone strategy in the drive to secure a lasting polio-free world. While OPV is extremely safe and needed to interrupt transmission of wild polioviruses, the live attenuated polioviruses within OPV can, on extremely rare occasions, cause cases due to vaccine-associated paralytic poliomyelitis (VAPP) or circulating vaccine-derived polioviruses (cVDPVs). With wild poliovirus type 2 (WPV2) having been eradicated in 1999, the Global Polio Eradication Initiative (GPEI) is intensifying its work to remove all poliovirus type 2 containing OPV from routine immunization programmes, by switching from trivalent OPV to bivalent OPV as early as 2016.

Such a switch would be associated with significant humanitarian benefits. Over the past five years, 97% of all cVDPV cases were due to type 2. Of the estimated 250-500 annual VAPP cases, almost half are due to type 2. These cases would no longer occur. The switch would subsequently be followed by the cessation of all OPVs, once the remaining strains of wild poliovirus types 1 and 3 have been successfully eradicated.

However, the switch must be carefully prepared and implemented. Five criteria must be fully met ahead of the switch, as recommended by the Strategic Advisory Group of Experts on immunization (SAGE):

1. Introduction of at least one dose of inactivated poliovirus vaccine (IPV);
2. Access to a bivalent OPV that is licensed for routine immunization;
3. Implementation of surveillance and response protocols for type 2 polioviruses (including constitution of a stockpile of monovalent OPV type 2);
4. Completion of phase I poliovirus containment activities, with appropriate handling of residual type 2 materials; and,
5. Verification of global eradication of WPV2.

The trigger for setting a definitive date for the withdrawal of the type 2 component of OPV globally will be the absence of all persistent cVDPV type 2 for at least six months. The current target date for this withdrawal is April 2016. At its October 2014 meeting, SAGE reviewed the readiness criteria for type 2 OPV withdrawal and concluded that preparations were on track for the switch in early 2016. It urged all countries to accelerate preparations and facilitate international coordination.

This issue of *Polio Pipeline* examines in depth the ongoing work towards each of the five criteria.

In this issue:

- Preparing the trivalent to bivalent OPV switch
- Overview of the five switch 'criteria'
- What will be the 'trigger' for the switch?

Special polio supplement published in Journal of Infectious Diseases

The Final Phase of Polio Eradication and Endgame Strategies for the Post-Eradication Era has been published as a supplement to the Journal of Infectious Diseases.

The supplement, the first published on polio in nearly 18 years, features more than 60 scientific articles by global polio experts, focusing on topics ranging from the acceleration of eradication, to regional and country experiences, to overviews of novel surveillance mechanisms, through to the polio 'endgame', including ensuring the legacy of polio eradication can be secured.

Individual articles or the full supplement can be ordered at http://jid.oxfordjournals.org/content/210/suppl_1.toc

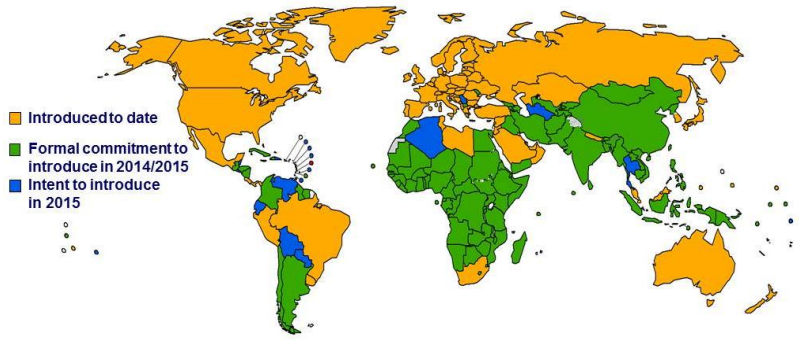
Criteria 1: Introduction of at least one dose of inactivated poliovirus vaccine

The Endgame Plan calls for the introduction of inactivated poliovirus vaccine (IPV) into routine immunization programmes globally by the end of 2015, in preparation for the phased removal of oral polio vaccines (OPV).

Of the 126 OPV-only countries, many are working with WHO, UNICEF, Gavi – the Vaccine Alliance and other GPEI partners to finalize IPV introduction plans before the end of 2014. By December 2014, all but three countries in the world had either already introduced IPV or had established a plan to do so by end-2015. Discussions are underway with the three countries which had yet to establish a plan for IPV introduction, however these comprise less than 0.05% of the global birth cohort, and are not among those considered at highest risk of cVDPV2 emergence following the withdrawal of the type 2 component of OPV. Of 73 countries eligible for Gavi support for IPV introduction, 66 have already successfully applied for such support, and the remainder are expected in January 2015. In September, Nepal became the first GAVI-eligible country to introduce IPV into its routine immunization programme.

The introduction of IPV is a critical step in managing any risks associated with the phased removal of OPV. Adding IPV to routine immunization programmes will maintain immunity against type 2 poliovirus while removing OPV type 2 globally. It will help reduce risks related to OPV type 2 withdrawal. Adding IPV to OPV will also help close any remaining immunity gaps to type 1 and 3 polioviruses, thereby helping to hasten eradication of remaining wild polio serotypes in the world.

Countries using IPV vaccine to date and formal decision/intent to introduce



In November 2013, the Strategic Advisory Group of Experts on immunization (SAGE) recommended that all countries introduce at least one dose of IPV into their routine immunization schedule. The latest WHO recommendations are summarised in the polio Position Paper published in February 2014.

In February 2014, UNICEF announced a procurement price of approximately US$1 per dose of IPV in 10-dose vials for GAVI-eligible countries, and a price of approximately US$2-US$3.28 per dose for middle-income countries. Work continues to develop and license new products and approaches for IPV, which may contribute to further reductions in the cost of IPV for the medium-term.

Beyond polio eradication, IPV introduction offers a golden opportunity to strengthen immunization systems and build capacity in some of the countries with the lowest routine immunization coverage levels. A set of focus countries are targeted for support specifically tailored to strengthening routine programmes as part of the Endgame Plan, helping to ensure that GPEI assets contribute to raising immunization coverage.

Criteria 2: Access to a bivalent OPV that is licensed for routine immunization

In December 2009, a new vaccine was used for the first time in Afghanistan – the bivalent oral polio vaccine (bivalent OPV). In a clinical field trial held in June that year, bivalent OPV was found to be at least 30% more effective against both remaining strains of wild poliovirus (WPV type 1 and WPV type 3) than trivalent OPV, and almost as effective as the monovalent OPVs, yet in a package that could deliver both at once.

In addition to providing greater protection against WPV1 and WPV3, bivalent OPV does not carry the type 2 attenuated virus. Since the risk of paralytic disease due to OPV type 2 now outweighs its benefits, trivalent OPV (which protects against all three strains) will be replaced with bivalent OPV.

However, not every OPV-using Member State has licensed bivalent OPV for use within its national borders. WHO is working with Member States to speed up the licensure process to enable them to make the switch from trivalent OPV to bivalent OPV.

Today several bivalent OPV products are licensed and

prequalified by WHO (see: http://www.who.int/immunization_standards/vaccine_quality/PQ_vaccine_list_en/en/), and more than 4.5 billion doses have been used in 43 countries, using the licensed indication:

In the context of the Polio Endgame and the declaration of polio as a public health emergency of international concern (PHEIC), and considering the timelines for OPV2 withdrawal, WHO and National Regulatory Authorities (NRAs) have been working to identify alternative options to the standard vaccine licensure process and facilitate the timely bivalent OPV introduction while ensuring safety.

As a consequence, WHO proposes as a way forward in the unique context of polio as a public health emergency, that all countries should accept bivalent OPV for use in their routine immunization programme on the basis of the prequalification granted by WHO.

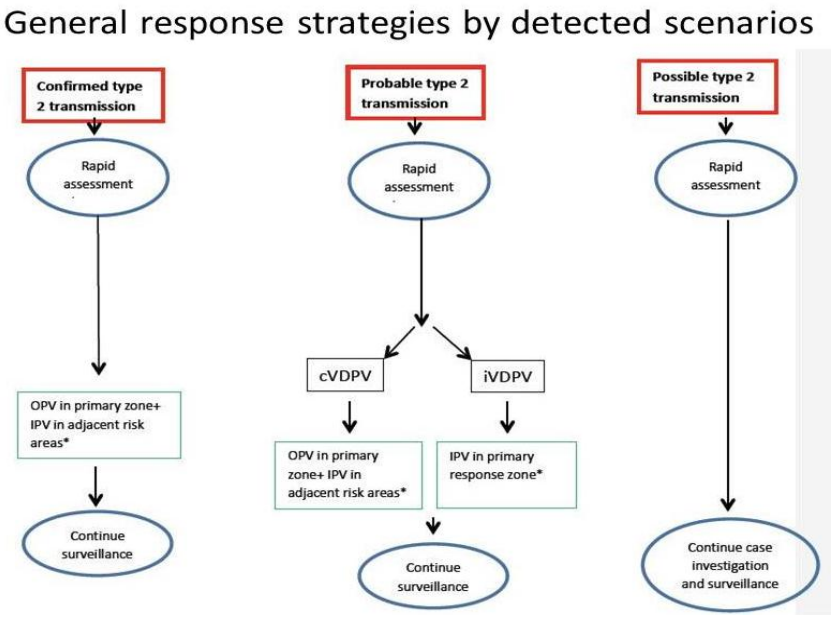
Countries for which a formal licensing process is legally required should initiate this process in parallel to the "acceptance for use" option in order to not jeopardize the Polio Endgame strategy and its timelines.

Criteria 3: Implementation of surveillance and response protocols for type 2 polioviruses (including constitution of a stockpile of monovalent OPV type 2)

Following the switch from trivalent OPV to bivalent OPV, outbreak response capacity against type 2 poliovirus will have to be maintained and assured. This includes securing the supply and management of stockpiles of appropriate type 2-containing vaccines to facilitate an appropriate outbreak response should it be necessary. Outbreak response protocol was endorsed by SAGE in October 2014.

Sensitive surveillance will be vital to enable the rapid detection of any circulating poliovirus and initiate an immediate response. Environmental surveillance will be further scaled up as a complement to acute flaccid paralysis (AFP) surveillance. Notification of the confirmed detection of any type 2 poliovirus will be an urgent notifiable event under the International Health Regulations (IHR 2005), triggering an immediate response. 'Probable' or 'possible' detected transmission will also trigger specific responses.

The type and extent of response will be determined by a number of factors, including: time since OPV2 withdrawal and last detection of poliovirus type 2; nature of the virus (eg wild vs Sabin virus); geographic location and proximity to high-risk communities with immunity gaps; and, population characteristics (eg underserved, mobile, conflict-affected, history of virus importation).



Outbreak response should utilize both monovalent OPV type 2 and IPV to rapidly boost and establish population immunity around the outbreak response zone to prevent the emergence of cVDPVs. The use of monovalent OPV type 2 is needed to induce the intestinal immunity among those who have not been vaccinated against type-2 previously.

Given this need, the GPEI and its partners are working to establish a 500 million dose stockpile of monovalent OPV type 2 to be available specifically for outbreak response after OPV2 withdrawal.

Criteria 4: Completion of phase I poliovirus containment activities, with appropriate handling of residual type 2 materials

The *Polio Eradication & Endgame Strategic Plan* 2013-2018 recommends the implementation of poliovirus safe handling and containment measures to minimize the risks of facility-associated reintroduction of virus into the polio-free community. Laboratory and vaccine manufacturing facilities around the world are the only remaining source of WPV2. After the planned trivalent OPV to bivalent OPV (tOPV-bOPV) switch, they will soon be the only remaining source of OPV2/Sabin2 polioviruses, as well. In order to continue essential diagnostic, research and vaccine production functions, it will be necessary for a small number of these facilities to continue to retain stocks of WPV2 and/or OPV2/Sabin2 materials. At the same time, each 'essential' poliovirus facility will represent a potential risk for the reintroduction of poliovirus type 2 into communities.

Countries will be responsible to ensure essential poliovirus facilities within their national borders meet containment requirements.

Currently, the world is in Phase I of containment: inventories of facilities storing and handling WPV and potentially infectious materials in the American, European, South-East Asian and Western Pacific Regions of WHO are available. Such inventories are currently being completed in the African and Eastern Mediterranean Regions.

Following WHO guidance (GAPIII), the destruction or transfer of WPV2 materials to certified essential facilities for their containment is expected to be completed by end-2015. The destruction of unneeded OPV2/Sabin type 2 materials, or their transfer to certified essential facilities is expected to be completed shortly after.

The global strategy for minimizing risks associated with poliovirus facilities and described in the *WHO global action plan to minimize poliovirus facility-associated risk after type-specific eradication of wild polioviruses and sequential cessation of routine OPV use* (GAPIII) consists of:

- risk elimination through the destruction of unnecessary poliovirus materials in all but certified essential facilities, and;
- risk management of certified essential facilities by strict implementation of required:
  - a) **primary** safeguards of containment, intended to minimize the likelihood of poliovirus release from essential facilities;
  - b) **secondary** safeguards of population immunity in countries where essential facilities are located, in order to minimize the consequences of poliovirus release; and
  - c) **tertiary** safeguards of facility locations in areas with low transmission potential (R_0) for wild polioviruses, in order to also minimize the consequences of poliovirus release.

From end-2015 onwards, storage and handling of WPV2 materials will only be permitted under certified containment conditions.

Within three months of the global tOPV-bOPV switch, Sabin-inactivated poliovirus vaccine (IPV) production will only be allowed under approved containment conditions in certified facilities.

The Strategic Advisory Group of Experts on immunization (SAGE) endorsed the proposed poliovirus containment strategy at its October 2014 meeting.

Criteria 5: Verification of global eradication of WPV2

Before all type 2 containing OPV can be withdrawn, the Global Commission for Certification of the Eradication of Poliomyelitis (GCC) must formally confirm that wild poliovirus type 2 (WPV2) has been eradicated globally. The last case of polio due to WPV2 was reported from India in Aligarh district, western Uttar Pradesh, in October 1999.

While it is widely understood that the transmission of WPV2 has been interrupted globally, it is important that this is independently verified. Under the proposed process, WHO Regional Offices, in coordination with Regional Certification Commissions (RCCs) and the GCC, will formally request all Member States to confirm when WPV2 was last isolated in the country, or to confirm that WPV2 has never been detected previously.

RCCs in four WHO Regions (the Americas, Europe, South-East Asia and the Western Pacific) have already certified the regional interruption of transmission of all indigenous wild polioviruses, including WPV2. Interruption of WPV2 in the two remaining uncertified Regions (Africa and the Eastern Mediterranean) can be assumed, since certification-quality surveillance has failed to detect WPV2 for more than ten years in those Regions, while being sensitive enough to detect wild poliovirus type 1 in the few remaining infected areas.

The GCC will review the responses received from Member States at their next meeting, expected to be held during the first half of 2015, and decide whether to proceed with a formal declaration on the global eradication of WPV2.

Trigger for setting a definitive date for the withdrawal of the type 2 component of OPV globally

Following the implementation of the five criteria for the withdrawal of type 2 OPV, the trigger for setting a definitive date for the trivalent OPV to bivalent OPV switch will be the absence of all persistent cVDPV type 2 for at least six months. The current operating target date for the switch is April 2016, meaning the remaining persistent cVDPV2 outbreaks in Pakistan and Nigeria must be stopped by March 2015 (as it requires a further six months to verify the outbreaks to be fully stopped and another six months for countries and vaccine suppliers to prepare for the switch).

In both Pakistan and Nigeria, outbreak response is being implemented, optimising the vaccine mix (trivalent OPV, bivalent OPV and IPV) to target both wild poliovirus type 1 (WPV1) and cVDPV2 transmission simultaneously. A delay in interrupting these cVDPV2 outbreaks could result in a delay in the target date for the trivalent to bivalent OPV switch. The GPEI and its partners are putting in place contingency plans for this eventuality, including with regard to global vaccine supply.