

3. Strategic Objective III

Management of long-term risks after wild poliovirus eradication

Milestone 2008 ²⁰	Status
Milestone 1: Long-term immunization policies will be introduced.	Achieved
Milestone 2: Additional tools for the detection and immediate notification of circulating WPV will be finalized (where appropriate).	Achieved
Milestone 3: Assembly of mOPV stockpile will begin.	Not achieved
Milestone 4: Implementation and verification of GAPIII will begin.	Not achieved

Once global WPV transmission has been interrupted, WPV stocks contained and eradication certified worldwide, the greatest risk of polio being re-introduced will derive from the attenuated polioviruses contained in OPV, resulting in vaccine-associated paralytic polio (VAPP) and outbreaks due to VDPVs.

With these risks in mind, the WHA, in its May 2008 resolution, requested the WHO Director-General “to set, if and when appropriate, a date for the eventual cessation of use of OPV” in routine immunization programmes. In response to the WHA's directive, the GPEI intensified its programme of work to develop the most appropriate strategies for managing the post-eradication, long-term risks of polio.

The Polio Research Committee (PRC) was reconstituted in 2008, with experts in the fields of virology, epidemiology, sociology and public health from around

the world. The PRC operates under the auspices of the ACPE and the SAGE. The group held its inaugural meeting in May 2008, and is now providing further guidance to the GPEI on long-term risk management by reviewing polio eradication-related research, identifying knowledge gaps, proposing appropriate studies, determining research priorities and funding levels, reviewing external research proposals and engaging potential new collaborators. This aspect of the GPEI research agenda is focused on three areas:

- Fully characterizing the long-term polio risks, especially VDPVs
- Developing tools to manage the long-term risks
- Contributing to policy frameworks to internationally coordinate the management of the long-term risks of polio.

3.1. Characterization of long-term polio risks

In 2008, significant new knowledge was gained on the post-eradication risks posed by OPV. The risks of VAPP being already well-known²⁰, research activities in 2008 focused on the risks relating to VDPVs.

Experience with circulating VDPV events in the past 10 years suggests that limited population immunity is the main risk for the spread of a cVDPV. In 2008, cVDPVs were reported in the Democratic Republic of the Congo, Ethiopia and Nigeria.

²⁰ Details in Appendix A.

To better detect VDPVs (and further define the extent of this risk), the new state-of-the-art screening method known as rRT-PCR was piloted by the Global Polio Laboratory Network.²¹ Initial data from the Nigeria outbreak shows the test increased cVDPV sensitivity by up to 30%.

A study series continues to measure the prevalence of VDPV excretion among people diagnosed with primary immune (B-cell) deficiency disorders (PIDs), with specific outcomes expected to be: an estimation of the prevalence of

immunodeficiency-associated VDPV (iVDPV) excretion among PIDs in a broad geographical variety of middle- and low-income settings; genetic characterization of iVDPVs; and further insight into the duration of iVDPV excretion. This work is being carried out in Bangladesh, China, Egypt, Iran, the Philippines, the Russian Federation, Senegal and Tunisia. After study protocols were adapted to national contexts, ethical clearances were obtained through national and WHO processes for China, the Russian Federation and Tunisia in 2008, and implementation began in the latter two. The remaining countries are expected to implement their studies in 2009.

3.2. Developing tools to manage long-term risks

To reduce the potential risks associated with OPV cessation and to manage the long-term risks of stored polioviruses, new tools are being developed as called for by the PRC, ACPE and SAGE guidance bodies and mandated by the WHA.

Detection of VDPVs: faster and more sensitive

In addition to more sensitive detection, the advantages of the new rRT-PCR screening method for VDPVs include data output in computerized format and minimal risk of sample contamination. It is planned to fully implement rRT-PCR assays in 13 of the 17 ITD laboratories in EMR and SEAR and to hold a training workshop in AFR by end-2009.

Ensuring outbreak response capacity: monovalent OPV stockpiles

In 2008, more than 1.2 billion doses of type 1 mOPV were administered in 23 countries, and more than 370 million doses of type 3 mOPV administered in eight countries. This experience helps formulate policy on post-eradication immunization strategies. To ensure outbreak response capacity for cVDPVs detected immediately following OPV cessation, an international stockpile of monovalent OPVs must be established, maintained and managed.

By end-2008, six type 1 mOPVs and three type 3 mOPVs had been licensed, as a result of an expedited approach to licensure agreed by WHO and National Regulatory Authorities (NRAs) in monovalent OPV-producing countries. Additionally, one manufacturer licensed a type 2 mOPV and another application for licensure is pending. Before the end of 2009, an initial stockpile tender will be issued by UNICEF for the development and licensing of

all three mOPVs and for the production of initial bulks for the stockpile.

Affordable IPV options

Following OPV cessation, IPV will be the only option with which to maintain population immunity against polio for those countries that need or choose to do so. While the full role of IPV following OPV cessation is still being evaluated, at a minimum IPV will be needed in all countries that continue to store and handle polioviruses. Other countries may perceive that the long-term poliovirus risks warrant continued routine immunization with IPV. Recognizing that the current costs of IPV are substantially higher than OPV, the development of affordable strategies for IPV use (i.e. ideally to achieve immunity at a cost similar to that achieved through OPV) in low-income settings was accelerated in 2008.



A vial of temperature-sensitive monovalent oral polio vaccine in India.

²¹ See section 2.2

To this effect, the GPEI entered into a multi-year collaboration on Sabin-based IPV with the Netherlands Vaccine Institute in 2008. This collaboration encompasses a number of clinical development projects for IPV using Sabin-strain polioviruses to facilitate IPV production in developing country settings, including an assessment of alternative inactivation processes to improve the immunogenicity of these strains. By end-2008, projects already under way included an evaluation of Sabin-virus seed strains, one alternative inactivation process and production of master virus seed-lots.

Other collaborative research on affordable IPV strategies which took place or secured funding through the PRC

in 2008 included four studies on alternate seed-strains of Sabin viruses, four on fractional dosing of IPV and three on the use of adjuvants.

To evaluate the role of IPV before and after OPV cessation and help develop long-term immunization policies, a SAGE working group on IPV was constituted in 2008. In November, the working group presented the SAGE with a framework to assess potential options for immunization in the post-eradication era in low- and middle-income countries. This framework will be completed through a combination of new clinical and operational research.

3.3. Coordinating the management of long-term poliovirus risks



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The Global Polio Eradication Initiative understands the need for agreed processes and policy for the handling of the mOPV stockpile after the final drop is administered.

Of the six major elements of the risk-management strategy for the post-eradication era,²² three require international coordination: synchronization of eventual OPV cessation, use of vaccines from a mOPV stockpile in outbreak response after OPV cessation, and long-term containment of polioviruses.

Synchronization of eventual OPV cessation

Based on a series of expert technical consultations²³, in 2004 the ACPE recommended that use of OPV should cease as soon as possible after the interruption of WPV worldwide in order to minimize the long-term risks. In May 2008, the WHA resolution on polio eradication requested that

22 *Framework for National Policy Makers in OPV-using Countries: Cessation of routine OPV use after global polio eradication*, WHO, 2005.

23 WHO Informal Consultation on Identification and Management of Vaccine-derived Polioviruses, September 2003.

work begin to set a date for the eventual cessation of OPV use in routine immunization programmes, if and when appropriate. In November, the SAGE re-affirmed the ACPE recommendation, and the GPEI will now work on developing, as requested by the WHA, a comprehensive mechanism for managing the risks.

Use of a mOPV stockpile for outbreak response after routine OPV cessation

Given the small but real risk associated with even attenuated polioviruses (i.e. cVDPVs), it is essential that there be internationally-agreed processes governing the use of mOPV for outbreak response after the cessation of trivalent OPV use in routine immunization programmes. Documents such as the *Standard Operating Procedures for a mOPV stockpile* translate such policy advice into actionable guidelines. In 2008, the PRC made a grant to Kids Risk Inc., formerly part of a Harvard University and Massachusetts Institute of Technology collaboration, to continue mathematical modelling of outbreak response scenarios for polioviruses following OPV cessation to further inform policy in this area.

Long-term containment of polioviruses

Based on wide consultation with experts in biosafety and risk management, the *Global Action Plan to minimize poliovirus facility-associated risk in the post-eradication/post-OPV era (GAPIII)* outlines a post-eradication strategy of risk minimization through the destruction of unneeded poliovirus materials in all but a few essential facilities, as well as risk *management* in such facilities by strict adherence to required safeguards. A full list of facilities which will continue to store or handle poliovirus after eradication²⁴ is being compiled to clearly establish the baseline risks they present, which are to be managed by the strategies laid out in *GAPIII*.

Throughout 2008, ongoing consultation and further analysis of the difference in reproductive rates between wild and attenuated polioviruses resulted in refinement of *GAPIII*. After interruption of WPV transmission, facilities retaining WPV will need to meet three safeguards:

- **Primary safeguards:** facilities must retain all virus stocks under international standard containment specifications to minimize the risk of a containment failure
- **Secondary safeguards:** facilities must be located in areas of high IPV immunization coverage to minimize the consequences of any containment failure
- **Tertiary safeguards:** facilities must be located in areas of high standards of personal, domestic and environmental sanitation to minimize the risk of transmission following any containment failure.

Facilities retaining only OPV/Sabin materials will be required to meet only the primary and secondary safeguards, due to the lower potential for transmission of the attenuated strains as compared to WPV. This strategy may permit IPV production in tropical settings using Sabin or more attenuated strains, while at the same time maintaining the high levels of biosafety required. Following verification of VAPP/VDPV elimination, however, safeguards for Sabin IPV may also be enhanced, especially if safer, alternate seed strains for IPV have been developed, characterized and validated by that time.

GAPIII will be released for an extended period of public comment in 2009 before finalization.



A laboratory worker at the US Centers for Disease Control and Prevention (CDC) facilities in Atlanta, USA.

24 See section 2.3