PERSPECTIVE

Polio Eradication and Endgame Plan – Victory within Grasp

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Since the launch of the Global Polio Eradication Initiative (GPEI) by the World Health Assembly (WHA) in 1988, the number of polio-endemic countries has decreased from 125 to 2 (Afghanistan and Pakistan). To secure the gains and to address the remaining challenges, the GPEI developed the *Polio Eradication and Endgame Strategic Plan, 2013-2018* (the Plan), endorsed by all Member States at the WHA in May 2013. One of the major elements that distinguishes this Plan from previous GPEI strategies is the approach to ending all polioviruses, both wild and vaccine-derived. Overall, the Plan outlines four main objectives: (1) to stop all wild poliovirus (WPV) transmission; (2) to introduce inactivated polio vaccine (IPV), withdraw all oral polio vaccines (OPV), and strengthen immunization systems in countries with weak immunization systems and strong polio infrastructure; (3) to certify all regions as polio-free and safely contain all poliovirus stocks; (4) and to mainstream the investment in polio eradication to benefit other priority public health initiatives for years to come. Implementing the Plan and meeting the milestones in a timely manner will help to ensure that that the world remains permanently polio-free.

Keywords: *Endgame, IPV, OPV, oral polio vaccine, Poliovirus*.

India's last polio case was reported on January 13, 2011. Three years later, in March 2014, the Global Certification Commission officially certified the World Health Organization's (WHO) South-East Asia Region, where India is located, polio-free [1]. India was once considered by experts as the most challenging country for interrupting transmission of polio, and in noting its immense success, enthusiasm was renewed among partners, donors, and countries that indeed polio can be eradicated globally. The road to polio eradication began nearly a century ago with defining the disease burden, isolating and culturing the virus, identifying the immunological mechanisms of protection, and developing safe and effective vaccines to prevent disease. These early milestones paved the path for polio eradication but the journey has not been smooth, requiring creative and steady modifications in the vaccines, policy, and implementation strategies [2-10]. Since the World Health Assembly (WHA) announced a goal to eradicate polio in 1988 and created the Global Polio Eradication Initiative (GPEI), polio cases have declined dramatically from over 350,000 cases annually to only 359 cases reported in 2014 [11]. To capitalize on the building momentum and the latest tools and technologies, the WHA in May 2013 endorsed GPEI's *Polio Eradication and Endgame Strategic Plan, 2013-2018* (the Plan), which provides a detailed approach and concrete timeline for complete eradication of polio [12].This renewed focus has already shown progress. In September 2015, WHO declared the eradication of the wild type 2 poliovirus strain, one of the three strains responsible for paralyzing children and adults since ancient times. In the same month, Nigeria was removed from the list of polio endemic countries, leaving only Afghanistan and Pakistan to interrupt wild poliovirus transmission.

The current Plan is different from previous strategies because it provides direction and approaches for both the eradication and containment of polio caused not only by wild viruses, but also for paralytic cases that derive from oral polio vaccines (OPV) [12,13]. The Plan also incorporates a strategy to use the backbone of the polio effort for strengthening routine immunization (RI) systems and delivering other health services to the world's most vulnerable children. The Plan outlines four objectives (***Table* I**) that comprehensively address eradication of polio, the endgame strategy, containment, and the polio legacy process.

Objective one of the Plan was to complete the eradication of polio once and for all, with interruption of WPV worldwide by end of 2015. This objective focuses on Pakistan, Afghanistan, and Nigeria, the three countries that were polio endemic when the Plan was established. Since then, GPEI has made substantial progress towards eradication. In 2015, only 74 cases of wild polio virus (WPV) were reported (from Pakistan (73%) and Afghanistan (27%), compared to 359 in 2014 [11]. Importantly, no cases of WPV have been detected in Nigeria since its last case on 24 July 2014, bringing the

TABLE I OVERVIEW OF THE POLIO ERADICATION AND ENDGAME STRATEGIC PLAN, 2013-2018

Objective	*Description*	*Key Activities and Milestones, 2013-2019*
Objective 1	Poliovirus detection and interruption	• Interruption by end 2016 (revised from end 2015) • Eradication by end 2019 (revised from end 2018) • Enhancing poliovirus surveillance • Improving OPV campaign quality • Revising outbreak response protocol & ensuring rapid outbreak response
Objective 2	IPV introduction, OPV withdrawal, and strengthening immunization systems	• Access to IPV to all countries • Switch from tOPV to bOPV in all 155 OPV using countries and territories in April 2016 • Ensure both bOPV and IPV in routine immunization until polio eradication • Develop framework for using GPEI assets to improve routine immunization and monitor their contributions in 10 countries with substantial polio resources
Objective 3	Containment and certification	• Implement appropriate containment of WPV type 2 in essential laboratory and vaccine production facilities by end 2015 • Containment of type 2 OPV within 3 months of tOPV-bOPV switch
Objective 4	Legacy planning	• Consultation, development of plan (end 2015), implementation (beginning 2015- 2016) • Core components of planning: • Maintaining and mainstreaming polio functions • Sharing lessons learned to improve child health • Transition polio functions to improve child health

**OPV denotes oral polio vaccine; tOPV denotes trivalent OPV; bOPV denotes bivalent OPV; IPV denotes inactivated polio vaccine; GPEI denotes Global Polio Eradication Initiative*

Africa region closer than ever to being certified polio-free. Despite this progress in Nigeria, immunity gaps still exist in both Pakistan and Afghanistan, where polio cases continue to occur, continuing to threaten children everywhere. That said, Pakistan has made substantial strides in the past year, driven by an Emergency Operations Centre, improving access to children in inaccessible areas, and working towards the Plan's goal of interrupting polio transmission in 2016, and achieving official certification of eradication by 2019 [1]. Meanwhile, Afghanistan had more cases in 2015 than in 2014. An Independent Monitoring Board (IMB) has evaluated the GPEI Polio Oversight Board's conclusion that interruption of transmission is most likely to occur in 2016, leading to eradication in 2019 [14]. IMB opined that this goal is possible but would require Nigeria to adapt and maintain focus, Pakistan to continue momentum, and Afghanistan to make immediate improvements in operational structure of its program.

The second objective of the Plan addresses the Endgame component to address the challenges of vaccine derived polioviruses [15]. Oral polio vaccines (OPV) have been indispensable for successful control of paralytic polio globally. However, use of OPV is very rarely associated with cases of vaccine-related polio. First, the live attenuated vaccine can also very rarely cause paralytic polio in vaccinated individuals or close contacts (vaccine-associated paralytic polio [VAPP]). In addition, individuals can shed slightly modified polio vaccine viruses into the environment. Accumulation of mutations can occur through circulation of these modified polio vaccine viruses in the community, particularly in communities with lower population immunity to polio. With sufficient mutations, these vaccine viruses may achieve the same transmissibility and neurovirulence as WPV (circulating vaccine-derived polioviruses [cVDPV]) [16]. Since the detection of the last naturally occurring case of type 2 polio in October 1999 (in Aligarh, India), the type 2 component of OPV has caused an estimated 1600-3200 cases of VAPP and over 600 cases of cVDPV2 [9]. Today, over 95% of all

cVPDV cases are related to type 2 OPV. To address this limitation associated with OPV use, the Plan calls for a phased withdrawal of OPV globally. This phased withdrawal will begin with removal of the type 2 component of OPV through a switch globally from trivalent OPV (tOPV, containing antigens 1, 2, and 3) to bivalent OPV (bOPV, containing only antigens 1 and 3) in 2016. Withdrawal of OPV may lead to gaps in immunity that could risk the emergence of cVDPV or the re-introduction of WPV. To manage these risks associated with OPV withdrawal, beginning with removal of the type 2 component of OPV, WHO's Strategic Advisory Group of Experts (SAGE) has recommended that all countries introduce at least one dose of the inactivated polio vaccine (IPV) to routine immunization programs prior to the switch from tOPV to bOPV. The need to introduce IPV into all OPV using countries globally in a relatively short time represents a major and unprecedented challenge. However, it is also a timely opportunity to improve collaborations between global immunization partners and make efficient use of GPEI resources to strengthen routine immunization services, particularly in countries with the highest risk target populations and weak immunization systems.Thus, the launch of Mission Indradhanush by the Government of India with support from partners is an appropriate innovation to improve routine immunization coverage and strengthen routine immunization systems. Mission Indradhanush aims to immunize all children against seven vaccine preventable diseases (diphtheria, pertussis, tetanus, polio, tuberculosis, measles, and hepatitis B) by 2020.

Introduction of IPV alone is insufficient to reduce the risks of cVDPV2 emergence after the tOPV-bOPV switch, and may not prevent cVDPV2 emergence during the highest risk period of 6-12 months after the switch [8]. Thus, all current cVDPV2 outbreaks must be controlled in advance of the switch, which is on target with no detections of cVDPV2 at the time of the switch in April 2016. Programs with lower routine coverage have conducted tOPV campaigns to boost type 2 immunity before the switch, which further reduces risk. SAGE has recommended a multipronged strategy that includes controlling and aggressively responding to any VDPV outbreaks after the switch, implementing appropriate containment of polioviruses, creating a global stockpile of monovalent type 2 OPV (mOPV), and finalizing a protocol for responding to type 2 outbreaks. The race between the disappearance of the vaccine derived viruses and accumulation of susceptibles in the population would determine the low but real risk of potential outbreaks of type 2 vaccine derived viruses in the first 6-12 months after the switch. In the longer term, type 2 virus would be contained only in a few essential facilities with adequate safeguards to prevent release of virus into the community. However, breaches in containment or potential bioterrorism events are possible and could lead to re-introduction of virus. There are a very limited number of immunodeficient individuals, who are chronic excretors of polioviruses, who may also pose an additional low risk of re-introduction but models suggest this risk to be very low.

Research to develop and test candidate antiviral drugs is ongoing. While indications for use have not yet been determined, these drugs could possibly be useful in the Endgame for reducing or stopping shedding of polioviruses by immunodeficient people who are chronically shedding poliovirus, persons exposed to poliovirus through breaches in containment, or perhaps even in communities exposed to cVDPV outbreaks in the post-eradication era [17-21].The Plan also recognizes that achieving gains towards eradicate and sustaining them relies on a strong routine immunization system for delivery of childhood vaccines. Thus, the Plan calls for GPEI to commit at least 50% of its resources in 10 countries to strengthen routine immunization. The 10 selected countries that were deemed to have the highest polio risk and greatest GPEI assets are: Afghanistan, Angola, Chad, the Democratic Republic of the Congo, Ethiopia, India, Nigeria, Pakistan, Somalia, and South Sudan.

Objective three of the Plan calls for all 194 WHO Member States to certify polio eradication and to ensure that all polioviruses are safely contained by 2018. As a first step, all member states have committed to implementing appropriate containment of wild poliovirus type 2 in essential laboratory and vaccine production facilities by end of 2015, and of type 2 OPV within 3 months of the tOPV-bOPV switch [22]. Following guidance provided in third *Global Action Plan to minimize poliovirus facility-associated risk* (GAPIII), all national authorities will need to certify that all essential facilities they host meet the containment requirements. SAGE has advised GPEI to develop a targeted advocacy and community plan to engage key countries and stakeholders to ensure completion of containment activities as outlined by GAPIII. As use of OPV is stopped after polio eradication, containment of all polioviruses will ensure that viruses are not inadvertently or intentionally released into a polio-free world.

The fourth and final objective of The Plan is focused on ensuring that the lessons learned and infrastructure of GPEI are appropriately transferred to other priority global health initiatives [23]. Legacy planning will help to guarantee that polio immunity is sustained through the

use of IPV for as long as it is deemed necessary. The polio infrastructure and workforce contribute substantially to immunization services beyond polio, and thus an important component of legacy planning will be to avoid a vacuum in immunization programs after polio eradication, and to adequately and responsibly transition these resources into other public health priorities.

Inability to meet timelines of interrupting transmission of polio according to The Plan can have immense risks to the program primarily in terms of donor, partner, government, provider, and parental fatigue with regard to sustaining this intensive eradication effort against polio. Recently, the Polio Oversight Board estimated that the delay in eradication to 2019 requires an additional $1.5 billion and each additional year would cost another $1 billion to the program. Beyond the financial cost, the credibility and the resolve of donors, partners, and governments to maintain momentum may also be at jeopardy with each additional year of delay in eradication of polio.

A fundamental reason for the global withdrawal of the type 2 component of OPV is that the world has eradicated type 2 poliovirus – a truly monumental success for partners and countries worldwide. Switching from tOPV to bOPV will prevent several hundred unnecessary cases of vaccine-derived polioviruses per year. However, to avoid jeopardizing the behemoth gains that the countries have made will require interrupting transmission of WPV in Pakistan and Afghanistan,introduction of at least one dose of IPV in all routine immunization programs globally, implementing the synchronized tOPV-bOPV switch in all 155 OPV using countries and territories in April 2016, and coordinated planning for the polio legacy. Interrupting polio transmission in India for over four years has provided many tools, technologies, and the necessary grist and enthusiasm for donors, partners, and countries to remain motivated and complete eradication of polio once and for all. The *Polio Eradication and Endgame Strategic Plan, 2013-2018* provides the world with the vision and the framework for capitalizing on these gains in India, and ending one of humanity's devastating diseases.

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