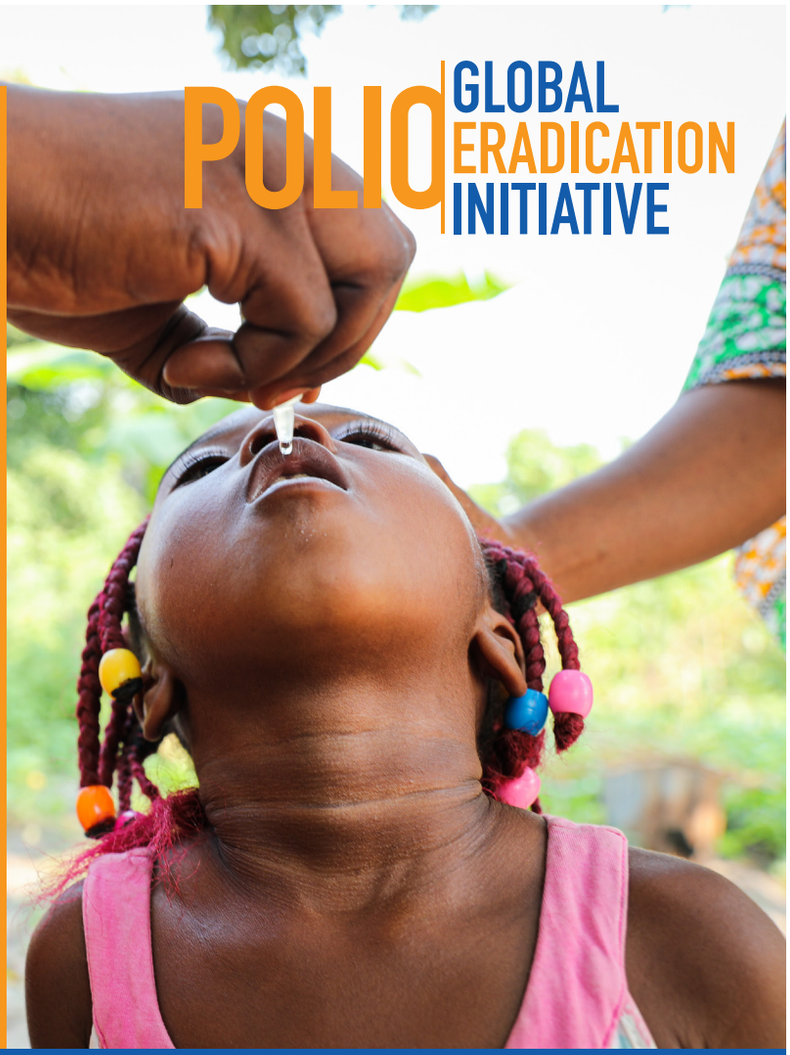
Towards Polio Eradication Using nOPV2: A Story of Innovation and Global Collaboration

POLIO GLOBAL ERADICATION INITIATIVE



The development of the novel oral polio vaccine type 2 (nOPV2) began in 2011. Ten years later, n March 2021, it was rolled out for fieldуse under an emergency use listing (EUL) as an innovative tool to more sustainably stop the spread of type 2 circulating vaccine-derived poliovirus (cVDPV2) outbreaks. Since the rollout of the vaccine began, more than 1 billion doses of nOPV2 had been administered in 35 countries by February 2024. In December 2023, nOPV2 was granted WHO prequalification, making it the first vaccine to move through the EUL pathway, paving the way for other drug innovations to use the EUL.

As the nOPV2 rollout continues, it is important to celebrate the decade of dedicated work that went into the vaccine and to take stock of the lessons learned along the way The main lessons learned from nOPV2's development and rollout fall into three main categories: **technology/development, global health, and organization & governance**

Key Lessons Learned

Technology Development

- Foresighting needed technology, based on modelling
- Putting public health value at the centre of clinical development
- Building confidence in product safety and efficacy at all levels
- Fast-tracking vaccine delivery through early investment models in manufacturing
- Understanding the need for supply security through multiple manufacturers

Global Health

- Pursuing EUL as a viable regulatory pathway for vaccines and other products
- Building on existing systems for supply chain and data management, and monitoring
- Developing local capacity and resources for rapid deployment and greater self-sufficiency

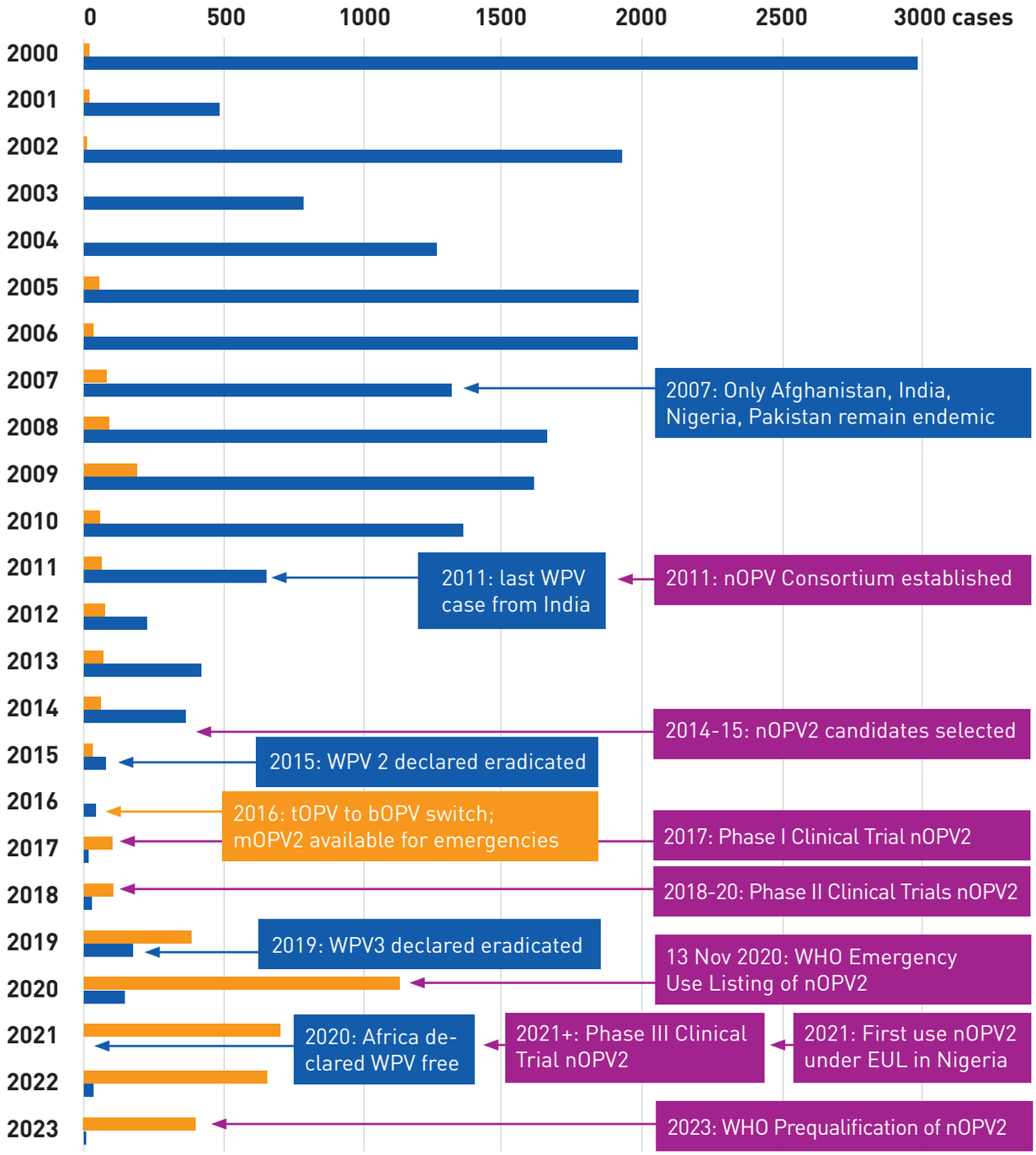
Organization & Governance

- Working towards a common vision
- Securing funding upfront for product development & rollout for a global public good
- Creating a new structure for product development and building on existing governance structures for the rollout
- Fostering trust, collaboration and leveraging each partners' strengths.

Cross-Cutting Learnings: A combination of technology and organisation and governance factors were often crucial to recognising, adapting to and overcoming challenges while seeing how the new vaccine development fits into the broader global health landscape. This shows the intertwined, multi-faceted, and complex nature of a new vaccine's development and rollout, which requires a holistic consideration of the three categories at once.

Foresight and context as key lessons from nOPV2 development

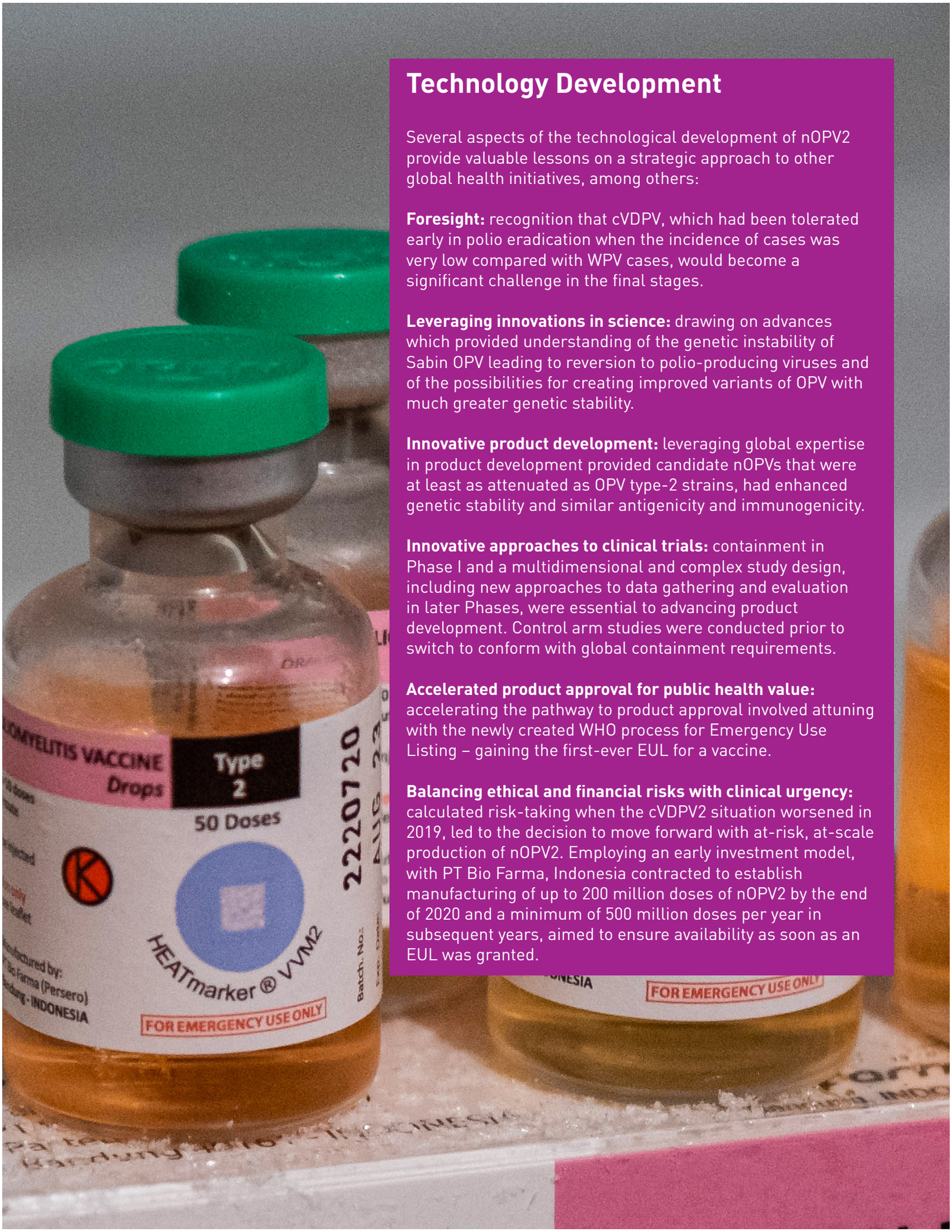
WPV eradication, cVDPV and nOPV2 development



Worldwide annual cases of polio fell more than 99% from 350'000 in 1988 to 3'000 in 2000. However, further progress was slow and erratic. Of the three WPV strains, type 2 was declared eradicated in 2015 and type 3 in 2019.

Sabin oral polio vaccine (OPV) strains can, in rare instances, revert to virulent forms leading to vaccine-associated paralytic polio in recipients or their immediate contacts and, in regions with persistently under-immunized populations, to circulating vaccine-derived poliovirus (cVDPV) strains causing outbreaks. cVDPV became a significant concern after 2000. A switch began in 2016 from using trivalent OPV to bivalent OPV lacking attenuated WPV2, which seems particularly prone to reverting to virulent forms. Monovalent mOPV2 was used for emergency response to outbreaks of cVDPV2.

In 2011, a consortium funded by the BMGF began to develop novel (nOPV) products with a very low probability of cVDPV generation. With cVDPV2 emerging as the main source of polio cases globally, clinical trials to develop nOPV2 began in 2017 and manufacturing in 2019. nOPV2 received WHO Emergency Use Listing (EUL) in 2020 and was first used in 2021.



Technology Development

Several aspects of the technological development of nOPV2 provide valuable lessons on a strategic approach to other global health initiatives, among others:

Foresight: recognition that cVDPV, which had been tolerated early in polio eradication when the incidence of cases was very low compared with WPV cases, would become a significant challenge in the final stages.

Leveraging innovations in science: drawing on advances which provided understanding of the genetic instability of Sabin OPV leading to reversion to polio-producing viruses and of the possibilities for creating improved variants of OPV with much greater genetic stability.

Innovative product development: leveraging global expertise in product development provided candidate nOPVs that were at least as attenuated as OPV type-2 strains, had enhanced genetic stability and similar antigenicity and immunogenicity.

Innovative approaches to clinical trials: containment in Phase I and a multidimensional and complex study design, including new approaches to data gathering and evaluation in later Phases, were essential to advancing product development. Control arm studies were conducted prior to switch to conform with global containment requirements.

Accelerated product approval for public health value: accelerating the pathway to product approval involved attuning with the newly created WHO process for Emergency Use Listing – gaining the first-ever EUL for a vaccine.

Balancing ethical and financial risks with clinical urgency: calculated risk-taking when the cVDPV2 situation worsened in 2019, led to the decision to move forward with at-risk, at-scale production of nOPV2. Employing an early investment model, with PT Bio Farma, Indonesia contracted to establish manufacturing of up to 200 million doses of nOPV2 by the end of 2020 and a minimum of 500 million doses per year in subsequent years, aimed to ensure availability as soon as an EUL was granted.

GLOBAL HEALTH

Some key features in the rollout of nOPV2 offer important lessons for the wider global health agenda, including:

Adapting to the disruptive global context: managing the effects of the COVID-19 crisis through ensuring alternative vaccine supplies and enhancing communication was important in limiting the rise of cVDPV and leveraging COVID-19 experiences for the nOPV2 rollout.

Building on a well-established platform for polio eradication and bringing in new partners: providing an ideal opportunity to ensure all relevant stakeholders collaborated around a common goal and high priority issue.

Extensive consultative processes with country stakeholders: acknowledging the different contexts and levels of risk, adapting the global recommendations and approach to local campaigns – with transparent sharing of evidence, targeted communications, and strong advocacy.

Proactive and effective communication: planning for product acceptance and uptake, countering misinformation, and using digital social mobilisation means to raise awareness and confidence in the vaccine was key at several stages of development and rollout.

Forecasting supply needs: requiring multi-channel communication with countries, flexible procurement models, and adaptive manufacturing processes, amidst the contextual challenges of COVID-19.

Prioritized informed decision-making at country level: ensuring the availability of materials in multiple languages to facilitate decision-making, build support and enable a better verification process.

ORGANIZATION & GOVERNANCE

Insights gained on the organization and governance of nOPV2 can also serve other global health initiatives, for example:

High-Level political commitment: commitment by Ministers of Health was critical at all stages and the continuous support by WHO Member States through decisions and resolutions at the Executive Board and the World Health Assembly provided a necessary backing.

Centralised and collective decision-making: centralising decisions within the governance bodies while taking the decision collectively allowed coherent messaging, fast-paced decisions, and strong ownership; linking the process to the advice of the WHO scientific advisory bodies, such as SAGE and GACVS, ensured legitimacy and acceptance of decisions.

Funding and investment model: having guaranteed funding committed from the outset through a sole funder created highly favourable conditions for collective decision-making, facilitated a focus on quality and pace, ensured efficiency and effectiveness.

Adaptive and innovative models of collaboration according to needs: governance structures evolved from a consortium of researchers into integration of the broader GPEI partnership and creation of the nOPV2 Working Group. Sub-groups and membership were adjusted along the process, even if it meant taking difficult decisions.

Manifold roles of BMGF: serving as funder and providing an institutional framework, contributing to managing complex processes, especially with regulators, and engaging with countries.