World Health Organization

Scaling Life-Saving Interventions Faster
Case Studies Series

Novel Oral Polio Vaccine Type 2 (nOPV2)

Vaccine-derived polio type 2 outbreaks are increasing in under-immunized populations around the world. A new vaccine, nOPV2, has been developed to prevent the spread of these outbreaks and save children from paralysis, and even death, from the poliovirus. nOPV2 was granted the world's first Emergency Use Listing (EUL) for a vaccine by the World Health Organization in November 2020.

November 1, 2021

Dzidzai Muyengwa, Duke Global Health Innovation Center
Ananda S. Bandyopadhyay, Bill & Melinda Gates Foundation
Simona Zipursky, World Health Organization
Sarah Wanyoike, World Health Organization
Diana Silimperi, Duke Global Health Innovation Center

This case study is part of a series that explores pathways and important factors that contribute to the development and uptake of global health interventions—from proof of concept to scale-up.

LAUNCH & SCALE SPEEDOMETER

Duke | GLOBAL HEALTH Innovation Center

LAUNCH & SCALE SPEEDOMETER

Novel Oral Polio Vaccine Type 2 (nOPV2)

Photo from UNICEF, Liberia 2021

nOPV2 is a more genetically stable, next generation version of the monovalent oral polio vaccine type 2 (mOPV2) and was granted the world's first Emergency Use Listing (EUL) for a vaccine by the World Health Organization in November 2020.

GLOBAL BURDEN OF DISEASE: 1,069 CASES OF CIRCULATING VACCINE-DERIVED POLIOVIRUS TYPE 2 (cVDPV2) OCCURRED GLOBALLY IN 2020 COMPARED TO 366 CASES IN 2019.[1,2]

WHY AND WHERE OUTBREAKS ARE OCCURRING: cVDPV2 OUTBREAKS SPREAD AMONG PERSISTENTLY UNDER-IMMUNIZED POPULATIONS WHEN THE WEAKENED POLIOVIRUS STRAIN CONTAINED IN ORAL TYPE 2 VACCINES REVERTS TO A FORM THAT CAN CAUSE PARALYSIS.

COUNTRIES WITH cVDPV2 OUTBREAKS: THE VIRUS IS TRANSMITTED VIA THE FECAL-ORAL ROUTE IN SETTINGS OF POOR SANITATION (E.G., IN PARTS OF AFRICA AND ASIA) AND CAN SPREAD RAPIDLY TO NEW AREAS AND COUNTRIES VIA POPULATION MOVEMENT (FROM 17 COUNTRIES IN 2019 TO 24 IN 2020).[3,4]

TIMELINE FROM nOPV2 IDEATION TO 1ST COUNTRY LAUNCH: 10 YEARS

10 YEARS

2011
IDEATION
New OPV Consortium "tasked with the development of [more genetically stable] OPV strains based on innovative strategies."[5,6]

2017
FIRST IN HUMAN STUDY
Phase I clinical study in adults to establish the safety and immunogenicity of nOPV2.[7]

2020
PROOF OF CONCEPT
Phase II clinical studies show nOPV2 is more genetically stable than mOPV2 and effective in providing immunity against polio in relevant age groups.[8]

2020
WHO EMERGENCY USE LISTING
nOPV2 becomes first-ever vaccine to be issued an Emergency Use Listing (EUL) by WHO.[9]

2021
1ST COUNTRY LAUNCH
Rollout of nOPV2 begins under EUL to tackle cVDPV2 outbreaks.[10]

BACKGROUND AND TIMELINE

In 1988, approximately 350,000 children around the world were paralyzed every year by poliomyelitis (polio), a highly infectious disease caused by the poliovirus.[11] Today that number has been reduced by over 99%, and five out of the six World Health Organization (WHO) regions—including the African region in 2020—are certified wild polio-free.[11,12]

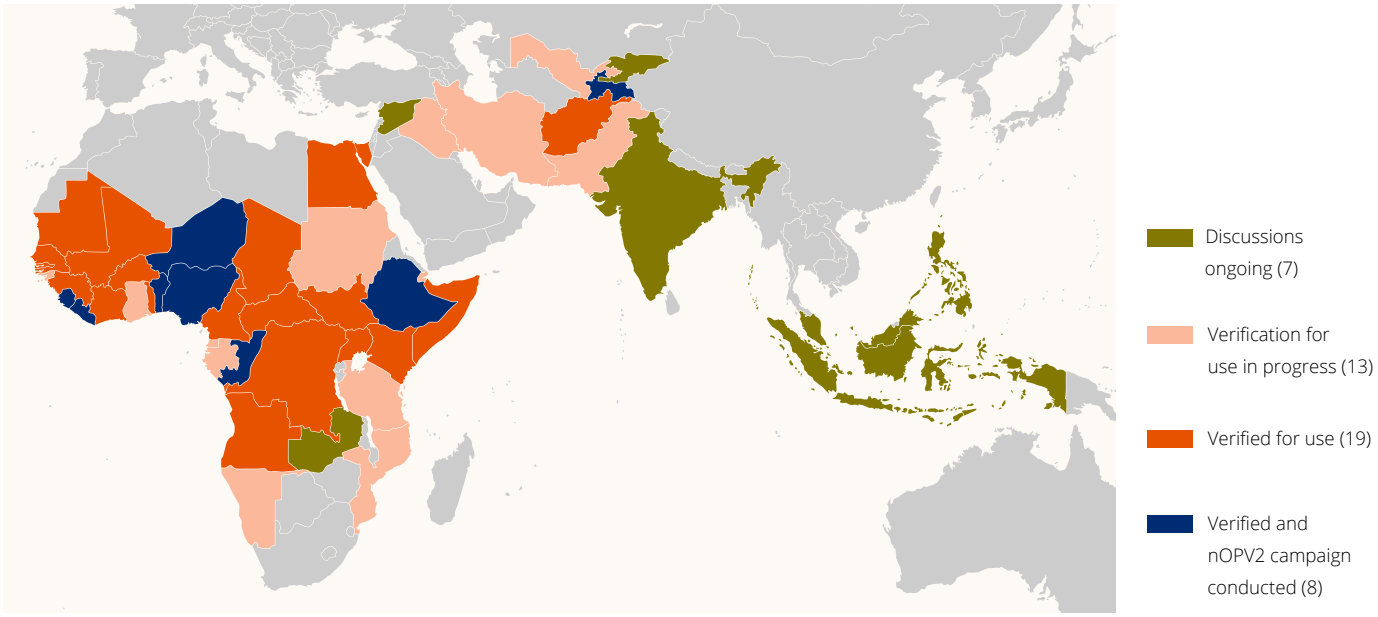
Unlike previous generations, many children today have been protected from the devastating consequences of polio infection, such as permanent paralysis, and in extreme cases, death. Much of this success can be attributed to effective administration of oral polio vaccines (OPVs) through campaigns that helped eradicate two out of the three strains of wild poliovirus (wild poliovirus type 2 and 3 (WPV2 & 3)).[11,13]

While there has been a significant reduction in the incidence of polio, the continued spread of poliovirus remains a Public Health Emergency of International Concern (PHEIC) and wild polio is still endemic in Pakistan and Afghanistan.[11,14] Moreover, outbreaks of circulating vaccine-derived poliovirus (cVDPV) are continuing to spread across countries, primarily in Africa and Asia.

cVDPV infections occur when the live attenuated poliovirus in OPV circulates in the environment for a sustained period due to persistently low immunization coverage, and reverts to virulence.[13] The majority of cVDPV cases (>90%) are from type 2 (cVDPV2).[15] Cases of cVDPV2 have risen since the 2016 "global switch from the trivalent oral polio vaccine (tOPV) to bivalent (types 1, 3) oral polio vaccine (bOPV)" for routine immunization.[15] While modelling suggested there would be a small upsurge in cVDPV2 cases in the immediate aftermath of the switch, reported cases increased from fewer than 100 in 2014 to over 1,000 in 2020.[5,13,15] The nearly three-fold increase in cases from 2019 to 2020 could be partially attributable to COVID-19-related disruptions in polio campaigns.

A more genetically stable type 2 oral polio vaccine to address cVDPV2s has been under development since 2011. Development of nOPV2, a next generation version of the existing monovalent OPV type 2 (mOPV2), was initially led by the New OPV Consortium (nOPV Consortium), with additional partners joining for clinical development and rollout in subsequent years. The decision to develop nOPV2 was driven by epidemiological evidence and modeling forecasts indicating that, even after the global switch, cVDPV2 would likely present an ongoing challenge to the eradication of all forms of poliovirus.[5,10,16]

Image 1. **Scale-up of nOPV2 as of end of October 2021.** Source: Adapted from WHO 2021.



Currently, the global partnership to support development and rollout of nOPV2 includes GPEI partner agencies (the Bill & Melinda Gates Foundation (BMGF), US Centers for Disease Control (CDC), Rotary International, Gavi, the Vaccine Alliance, UNICEF and the World Health Organization (WHO)), along with Fighting Infectious Diseases in Emerging Countries (FIDEC), Cevaxin, US FDA, Intravacc, University of California San Francisco (UCSF), University of Antwerp, the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), the National Institute for Biological Standards and Control (NIBSC), PATH and Bio Farma (an Indonesian, state-owned commercial vaccine manufacturer). Within this partnership: the Gates Foundation serves as a funder; NIBSC, UCSF and CDC led the development of nOPV2 candidate strains, with CDC also leading the laboratory assessment; PATH is the coordinating partner on research and development; Bio Farma—the world's largest manufacturer of OPVs—handles the manufacturing and regulatory processes; the University of Antwerp, FIDEC, icddr,b sponsored phase I and II clinical trials, and the GPEI, through a dedicated "nOPV2 Working Group" that includes partners such as WHO and UNICEF, leads implementation and rollout of the vaccine for outbreak response.[5,16,17]

The global partnership for novel OPV championed the development of nOPV2 by sponsoring continuous and ongoing fora for discussion among vaccine and public health experts, delineating future country needs and delivery challenges, and promoting accelerated nOPV2 development to respond to the PHEIC that polio outbreaks constitute.[5,10] In 2019, the first results of a phase I clinical trial led by the University of Antwerp were published and showed that nOPV2 was safe and elicited a similar immune response as mOPV2 against poliovirus in humans.[7,18] Following this research, two additional, larger clinical trials took place in Belgium and Panama (phase II clinical trials) led by the University of Antwerp and FIDEC respectively. In December 2020, the clinical trial results were published, demonstrating that nOPV2 was more genetically stable than mOPV2, safe, and effective in providing immunity against polio across different age groups.[7,8]

To urgently address the spread of cVDPV2 infections, and considering polio's status as a PHEIC as well as the promising clinical data, Bio Farma, with support from the global partnership, was able to put forward nOPV2 for consideration for WHO Emergency Use Listing (EUL). The EUL procedure is a rigorous assessment of pre-clinical, clinical, and manufacturing information to allow pre-licensure use of a vaccine, during a PHEIC, based on a favorable benefit-risk assessment.[9]

During nOPV2's research and development phase, regular discussions were held between the WHO Polio Eradication and Prequalification teams, Bio Farma, PATH, and others, to provide updates, share technical input, and incorporate country feedback.[19,20] Concurrently, Bio Farma began to address how to rapidly scale up manufacturing to enable a sufficient supply of nOPV2 for priority countries where the new vaccine was urgently needed.[10] These coordinated efforts and the fulfillment of WHO EUL requirements/criteria led to nOPV2 becoming the first vaccine to receive an EUL recommendation in November, 2020.[9,20] This recommendation paved the way for nOPV2 to be used in cVDPV2 outbreak-affected countries, as long as these countries met the requirements for use as outlined by the EUL.[9]

WORLD HEALTH ORGANIZATION EMERGENCY USE LISTING CRITERIA[20]

- The disease for which the product is intended is serious or immediately life threatening, has the potential of causing an outbreak, epidemic or pandemic and it is reasonable to consider the product for an EUL assessment, e.g., there are no licensed products for the indication or for a critical subpopulation (e.g., children).
- Existing products have not been successful in eradicating the disease or preventing outbreaks (in the case of vaccines and medicines).
- The product is manufactured in compliance with current Good Manufacturing Practices (GMP) in the case of medicines and vaccines and under a functional Quality Management System (QMS) in the case of IVDs.
- The applicant undertakes to complete the development of the product (validation and verification of the product in the case of IVDs) and apply for WHO prequalification once the product is licensed.

In less than four months, in March 2021, after demonstrating readiness to meet key EUL requirements (e.g. functional safety surveillance system, obtaining national regulatory approval, having a suitable logistical plan for distribution of the vaccine, preparing communications and advocacy plans etc.) nOPV2 was rolled out in Nigeria, with Liberia following soon after.[10,21] As of the end of October 2021, over 130 million doses of nOPV2 have been administered in eight countries, and almost 40 countries that are experiencing or are at-risk of cVDPV2 outbreaks are preparing to meet or have already met the EUL requirements for nOPV2 use.[10,22]

LAUNCH AND SCALE ENABLERS, CHALLENGES AND LESSONS LEARNED

Throughout the nOPV2 journey, various factors affected the speed and processes from research and development to launch. One key challenge in the development of nOPV2 was finding the right manufacturing partner. Typically, companies developing high-quality medical therapeutics have historically focused on creating products for high-income settings due to low profit margins and limited financial incentives to develop products for low-income regions.[10,23] The Bill & Melinda Gates Foundation awarded a grant to Bio Farma to support their development and manufacturing costs related to nOPV2. This grant funding enabled at-scale production of the vaccine before EUL approval so that it was ready to be rolled out shortly after the EUL was issued.[10]

Bio Farma, the world's largest manufacturer of polio vaccines, was on-board but had to overcome a few challenges to assume its role in the process. One such challenge, which took time, involved repurposing a measles vaccine factory for nOPV2 manufacturing.[10] In addition, Bio Farma's expertise was primarily in manufacturing and not clinical research, a key component for nOPV2 development. Accordingly, global and regional agencies, along with several global subject matter experts collaborated with Bio Farma for nOPV2 clinical studies in Belgium and Panama, thereby supplementing Bio Farma's manufacturing expertise.[10,17]

Several key factors enabled nOPV2's accelerated implementation and scale. The existence of Sabin mOPV2 meant that the research for nOPV2 could focus more specifically on demonstrating genetic stability and a lower likelihood of reversion to virulence when compared to the existing Sabin vaccine. The significant and sustained coordination and communication across scientists, university researchers, global vaccine advocates, policymakers, vaccine manufacturers and their respective organizations also facilitated nOPV2's path to rollout.[10]

In addition, diverse factors were identified that could limit rapid uptake of nOPV2 among countries at risk for cVDPV2 including: a lack of understanding regarding the need for a new vaccine given the availability of an existing polio vaccine; limited promotion in the face of competing priorities like the COVID-19 pandemic; rigorous surveillance requirements; and, the uniqueness of nOPV2 as the first vaccine to be released via EUL approval.[10] Recognizing these in advance and developing advance plans to address them were instrumental for a rapid nOPV2 rollout. At the end of 2019, GPEI established a global level nOPV2 Working Group that was tasked with bridging the upstream development and downstream rollout components, by ensuring that data generated from studies was shared in clear and accurate ways with regional and country counterparts. A suite of materials, from technical fact sheets to guidance for developing communication plans for nOPV2 rollout, to vaccine handling guidance, was developed and released alongside the EUL recommendation, to ensure country preparations would not be delayed. Moreover, a strong monitoring plan (including safety monitoring, genetic stability monitoring and environmental surveillance) was developed to ensure that the field performance of nOPV2 aligned with expectations.[10]

Furthermore, strong early country adopters of nOPV2, such as Nigeria, helped increase confidence and buy-in from other countries. Technical assistance, country-level Ministry of Health leadership, and engagement from WHO regional teams all facilitated the uptake of this pivotal intervention in early adopter countries. To help streamline and facilitate the regulatory process, the WHO Executive Board issued a decision in February 2020 encouraging WHO Member States to authorize the expedited importation of nOPV2 on the basis of its EUL recommendation.[24] Coordinated, transparent sharing of experiences and data amongst early adopter countries and with others globally was critical for raising confidence in the new vaccine. National and local advocates generated awareness in key stakeholders about cVDPV2 risks, obtained buy-in from ministries of health, and put nOPV2 on agendas

for key meetings.[10] As a result, nOPV2 launched successfully and relatively quickly and has been rolled out in eight countries by the end of October 2021.[10]

CONCLUSION

The nOPV2 research, development, and EUL approval process offers lessons and key insights for future interventions. The engagement and partnership of key strategic stakeholders, ongoing communication across stakeholders, and early country engagement were particularly important drivers of uptake.

The global partnership for nOPV2 development utilized the expertise of academic partners, not-for-profit organizations, governmental agencies, manufacturers, the public and private sectors, as well as global organizations that positively influenced the process towards broader inclusion, division of labor, and a built-in body of influential supporters directed towards a common cause for global good. To pre-empt and rapidly address challenges, the strategic inclusion of key global and national decision makers, as well as recognized local leaders, ensured a strong group of advocates. Clear and frequent public communication around the unique need for a new vaccine was critical for success. In terms of acceleration, a key insight from the nOPV2 story was the value of non-linear, concurrent, and at-risk activities and the need to be strategically proactive: working on steps at the same time or working on endpoints before completing earlier stages to accelerate the process. A great example of this is how nOPV2 developers and implementers started addressing delivery challenges even before EUL approval.

Ultimately, the nOPV2 story offers a tangible pathway for other vaccines to follow. The timeline for nOPV2 was accelerated with the goal of averting paralytic outbreaks because collaborators were engaged in their areas of comparative advantage quickly and worked together in a coordinated, proactive manner on planning, funding, and implementation, as well as sharing risks. The nOPV2 story is a successful and unique example of what is possible when a dedicated network of key collaborators come together (with or without a formal mandate) driven by the need to protect children from getting paralyzed. nOPV2's unique trajectory of being the first vaccine to receive WHO EUL approval charts a new course in the launch and scale of interventions aimed at improving global health. While strong surveillance and high levels of vaccination coverage will be needed to stop outbreaks, the vaccine could be a significant step towards a world without polio that blazes a trail for other innovations to follow.

KEY INSIGHTS TO LAUNCH AND SCALE

The importance of aligned strategic champions focused on a common goal cannot be overstated. nOPV2 had financial support from the Bill & Melinda Gates Foundation and technical support of various partners in the global health sector including various ministries of health, Bio Farma, GPEI implementing partners including UNICEF and WHO global, regional, and country leaders. These collaborators saw this vaccine through research and development, EUL process approval, and implementation, working closely with country and regional partners who provided leadership for implementation of clinical studies and data generation efforts. The driving factor in this partnership was for a global public health need to control a PHEIC.

Epidemiology was used to catalyze and direct action. The epidemiology of cVDPV2 drove the knowledge and emphasis on the development of nOPV2. Epidemiologists and modelers were able to show that continued use of mOPV2 could contribute to seeding of cVDPV2s in certain settings with low immunity to type 2 poliovirus, which would make eradication difficult. Additionally, epidemiological assessments of the possible impact of cVDPV2 allowed for risk-benefit assessments of a yet-to-be-licensed vaccine compared to the risk of ongoing outbreaks and paralysis in children.

Engagement with the right partners at the right time is key. It is important to "socialize understandings and bring the right partners on board" by involving an array of strategic partners—regulatory bodies, public health teams, and governments—to discuss the pros and cons early in the development process, and continually along the launch and scale continuum.[10] In addition, these partners were empowered to use their respective capabilities along the path to their common goal. Early engagement helped align research focus and allowed for relevant recommendations during the development phase and in the collection of relevant data. Strategic engagement with the right stakeholders, periodically and iteratively, was thus critical in accelerating the launch and scale of this intervention.

The WHO EUL process can facilitate a safe and rapid response to a public health emergency. The WHO EUL process can serve a regulatory function in emergencies and in situations when stringent regulatory agencies like the USFDA or European authorities do not have a compelling justification to conduct assessments. The WHO EUL process (specifically for, but not limited to vaccines) provides a new avenue for expediting the delivery of clinically demonstrated life-saving interventions to low- and middle-income countries, and the people who need them the most. Lessons from this first experience can inform WHO Prequalification about standardization of the criteria and an expedited process for EULs for vaccines.

GLOSSARY OF TERMS

bOPV: bivalent oral polio vaccine

cVDPV2: circulating vaccine-derived poliovirus type 2

EUL: Emergency Use Listing

FIDEC: Fighting Infectious Diseases in Emerging Countries

GMP: Good Manufacturing Practices

GPEI: Global Polio Eradication Initiative

icddr,b: International Centre for Diarrhoeal Disease Research, Bangladesh

NIBSC: National Institute for Biological Standards and Control

mOPV2: monovalent oral polio vaccine type 2

nOPV2: novel oral polio vaccine type 2

PHEIC: Public Health Emergency of International Concern

QMS: Quality Management System

tOPV: trivalent oral polio vaccine

COVID IMPACT

- The attention, focus and resources of governments have turned to COVID-19 during the pandemic. However, there are opportunities for synergy between COVID-19 and polio vaccine programs, particularly around surveillance and tracking strategies.
- The process to get nOPV2 to countries where it has been approved for use has been impacted by issues related to the on-going pandemic. For example, after a country has been approved, the nOPV2 vaccines must be shipped from Bio Farma to that country, but there are fewer cargo planes currently available because COVID-19 has impacted international travel. Additionally, travel and quarantine restrictions limited the ability to organize in-country support teams and move implementation plans forward. Furthermore, all trainings, including lab, had to be conducted remotely due to the pandemic, which impacted preparations and country nOPV2 rollout planning workshops.
- Bio Farma had to adjust nOPV2 vaccine production capacity based on COVID-19 control measures and pivots to COVID vaccines, which impacted the global stockpile of the nOPV2 vaccine.
- On a positive note, while nOPV2 may have been the first vaccine to get an EUL and thus paved the way for COVID vaccine EUL approvals, it is also true that COVID vaccines were instrumental in helping with the use and acceptance of EUL vaccines globally.

SUGGESTED CITATION FOR THIS PUBLICATION

Muyengwa, D, Bandyopadhyay, A, Zipursky, S, Wanyoike, S, & Silimperi, D. (2021). Scaling Life-Saving Interventions Faster: Novel Oral Polio Vaccine Type 2. Duke Global Health Innovation Center.

RESEARCH METHODS AND ACKNOWLEDGMENTS

Our research included a review of websites, reports, academic literature, gray literature, news articles as well as virtual interviews. We would like to thank our interviewees from WHO, Bio Farma, Bill & Melinda Gates Foundation, and PATH for sharing additional insights with our research team into the launch and scale of this intervention.

ABOUT US

The Launch and Scale Speedometer, led by the Duke Global Health Innovation Center, seeks to understand key factors for successful and fast launch and scale of global health interventions to help save lives.

CONTACT US

Duke Global Health Innovation Center
https://dukeghic.org/

Launch and Scale Speedometer
info@launchandscalefaster.org
https://launchandscalefaster.org/

REFERENCES

1. GPEI. Vaccine-Derived polioviruses. Retrieved March 23, 2021, from https://polioeradication.org/polio-today/polio-prevention/the-virus/vaccine-derived-polio-viruses/

2. World Health Organization. (2021, August 31). Global Circulating vaccine-derived poliovirus (cVDPV). World Health Organization. From https://polioeradication.org/wp-content/uploads/2021/08/weekly-polio-analyses-cVDPV-20210803.pdf.

3. GPEI. (2021). GPEI strategy for the response to cVDPV 2020-21. World Health Organization. From https://polioeradication.org/wp-content/uploads/2021/03/GPEI-cVDPV2-nOPV2-Factsheet-20210312-EN.pdf

4. Macklin, G. R., O'Reilly, K. M., Grassly, N. C., Edmunds, W. J., Mach, O., Santhana Gopala Krishnan, R., Voorman, A., Vertefeuille, J. F., Abdelwahab, J., Gumede, N., Goel, A., Sosler, S., Sever, J., Bandyopadhyay, A. S., Pallansch, M. A., Nandy, R., Mkanda, P., Diop, O. M., & Sutter, R. W. (2020). Evolving epidemiology of poliovirus serotype 2 following withdrawal of the serotype 2 oral poliovirus vaccine. *Science* (New York, N.Y.), 368(6489), 401–405. https://doi.org/10.1126/science.aba1238

5. Konopka-Anstadt, J. L., Campagnoli, R., Vincent, A., Shaw, J., Wei, L., Wynn, N. T., . . . Burns, C. C. (2020). Development of a new oral poliovirus vaccine for the eradication end game using codon deoptimization. Npj Vaccines, 5(1). doi:10.1038/s41541-020-0176-7

6. Te Yeh, M., Bujaki, E., Dolan, P.T., Smith, M., Wahid, R., Konz, J., Weiner, A.J., Bandyopadhyay, A.S., Van Damme, P., De Coster, I. and Revets, H., 2020. Engineering the live-attenuated polio vaccine to prevent reversion to virulence. *Cell host & microbe*, 27(5), pp.736-751.

7. Van Damme, P., De Coster, I., Bandyopadhyay, A. S., Revets, H., Withanage, K., De Smedt, P., . . . Gast, C. (2019). The safety and immunogenicity of two Novel live ATTENUATED monovalent (SEROTYPE 2) oral poliovirus vaccines in healthy adults: A double-blind, SINGLE-CENTRE Phase 1 study. *The Lancet*, 394(10193), 148-158. doi:10.1016/s0140-6736(19)31279-6

8. Sáez-Llorens, X., Bandyopadhyay, A. S., Gast, C., Leon, T. D., Deantonio, R., Jimeno, J., . . . Rüttimann, R. (2020). Safety and immunogenicity of two novel type 2 oral poliovirus vaccine candidates compared with a monovalent type 2 oral poliovirus vaccine in children and infants: Two clinical trials. The Lancet, 397(10268), 27-38. doi:10.1016/s0140-6736(20)32540-x

9. WHO. (2020, November 13). First ever vaccine listed under WHO emergency use. Retrieved January 15, 2021, from https://www.who.int/news/item/13-11-2020-first-ever-vaccine-listed-under-who-emergency-use

10. Duke Global Health Innovation Center. nOPV2 Intervention Research Interviews (2021). Launch and Scale Speedometer. Duke University

11. WHO. Poliomyelitis (polio). Retrieved March 24, 2021, from https://www.who.int/health-topics/poliomyelitis#tab=tab_1

12. WHO. (2020, August 25). Global polio eradication INITIATIVE applauds WHO African region for WILD polio-free certification. Retrieved February 05, 2021, from https://www.who.int/news/item/25-08-2020-global-polio-eradication-initiative-applauds-who-african-region-for-wild-polio-free-certification

13. GPEI. (2018). Fact Sheet: Vaccine-Derived Poliovirus. Retrieved from https://polioeradication.org/wp-content/uploads/2018/07/GPEI-cVDPV-Fact-Sheet-20191115.pdf

14. GPEI. (2021). *Public health emergency status*. GPEI. https://polioeradication.org/polio-today/polio-now/public-health-emergency-status/

15. GPEI. (2020, December). GPEI Strategy for Control of cVDPV2 2020-2021. Retrieved from https://polioeradication.org/wp-content/uploads/2020/12/cVDPV2-strategy-nOPV-rollout-fact-sheet-20201211.pdf

16. Van Damme, P., Coster, I. D., Bandyopadhyay, A. S., Suykens, L., Rudelsheim, P., Neels, P., Oberste, M. S., Weldon, W. C., Clemens, R., & Revets, H. (2019). Poliopolis: Pushing boundaries of scientific innovations for disease eradication. *Future Microbiology*, 14(15), 1321–1330. https://doi.org/10.2217/fmb-2019-0196

17. PATH. (2021, January). Center for Vaccine Innovation and Access: Advancing novel oral polio vaccines: planning for long-term protection against polio resurgence. Retrieved from https://path.azureedge.net/media/documents/nOPV-Fact-Jan2021.pdf

18. GPEI. (2020, December). nOPV2 Frequently Asked Questions (FAQ). Retrieved from https://polioeradication.org/wp-content/uploads/2020/12/nOPV2-FAQ-20201218.pdf

19. WHO. (2020). Recommendation for an Emergency Use Listing (EUL) of Novel Oral Polio Vaccine Type 2 (nOPV2) Submitted by PT BIOFARMA (PERSERO). Retrieved from https://extranet.who.int/pqweb/sites/default/files/documents/nOPV2_EUL_recommendation.pdf

20. WHO. (2020). Regulation and Prequalification: Emergency Use Listing. Retrieved April 12, 2021, from https://www.who.int/teams/regulation-prequalification/eul

21. GPEI. (2020). Implementation of novel oral polio vaccine type 2 (nOPV2) for circulating vaccine-derived poliovirus type 2 (cVDPV2) outbreak response: Technical Guidance for Countries. https://apps.who.int/iris/bitstream/handle/10665/333520/9789240008588-eng.pdf

22. WHO. (2021, March 26). Circulating vaccine-derived poliovirus type 2 – Global update. Retrieved August 11, 2021 from https://www.who.int/emergencies/disease-outbreak-news/item/circulating-vaccine-derived-poliovirus-type-2-global-update

23. Access to Medicine Foundation. (2019, May 16). Are pharmaceutical companies making progress when it comes to global health? Retrieved March 28, 2021, from https://accesstomedicinefoundation.org/media/uploads/downloads/5d93329e141cb_Access-to-Medicine-Index-10-Year-Analysis.pdf

24. WHO. (2020, February 7). WHO Executive Board Meeting - Polio eradication. From: https://apps.who.int/gb/ebwha/pdf_files/EB146/B146(11)-en.pdf