Uganda National Immunization Technical Advisory Group (UNITAG)

Recommendation on Introduction of novel Oral Polio Vaccine type 2 (nOPV2) in Uganda

July, 2021

Executive Summary

On 5th May 2014, the Director-General of World Health Organization (WHO) declared the international spread of poliovirus a Public Health Emergency of International Concern (PHEIC) under the International Health Regulations.

The eradication of indigenous WPV2 in 1999, coupled with the continuing emergence of neuro-virulent circulating type 2 vaccine---derived polioviruses (cVDPV2s) as well as vaccine- associated paralytic poliomyelitis (VAPP), led to the recommendation that there should be coordinated global cessation of use of the type 2 component of OPV and a switch from tOPV to bOPV. While cVDPVs are rare, they have been increasing in recent years due to low immunization rates within communities. cVDPV type 2 (cVDPV2) are the most prevalent, with 959 cases occurring globally in 2020.

The Global Polio Eradication Initiative is working to deploy an improved outbreak response tool: the novel oral polio vaccine type 2, or nOPV2. This vaccine is similar to mOPV2 (the monovalent oral polio vaccine type 2), the current outbreak response vaccine that is used when cVDPV type 2 outbreaks occur. However, it contains improvements that help make the vaccine virus less likely to mutate and cause disease in communities with low immunization rates – meaning that it can help reduce the risk of cVDPV2 outbreaks. The novel oral polio virus is a modified version of mOPV2 which is more genetically stable and less likely to return to virulence. The novel vaccine received emergency Use Listing from WHO, and countries at risk of cVDPV2 are encouraged to use it as the vaccine of choice for outbreak response.

The most recent cases of poliomyelitis in Uganda were VDPV2 in three districts, Kween, Kamuli and Kisoro in 2014, In the region, in 2021, cVDPVv2 has been detected in South Sudan (10 cases) DRC (2 cases) and Kenya (3 cases). Uganda is thus at risk of cVDPV2 and is considering the use of nOPV2. The Uganda National Immunisation Technical Advisory Group considered the evidence regarding the use of nOPV2 and found the following:

Efficacy and Safety: the nOPV2 has a comparable efficacy and safety profile as the currently used mOPV2. In clinical trials, solicited events among infants and children receiving any nOPV2 vaccination included predominantly mild or moderate abnormal crying, drowsiness, fever, irritability, loss of appetite, and vomiting, with similar rates among mOPV2 control vaccinees. However, nOPV2 is more genetically stable and is less likely to revert to virulence and cause paralysis. Regarding co-administration with other infant vaccines, although no data are available for nOPV2, it is assumed that, as for mOPV2 or tOPV, no interference would occur with other routinely administered vaccines, as far as it will be of relevance in the emergency setting. The vaccine is contraindicated in those with primary immune deficiency disease or suppressed immune response from medication, leukemia, lymphoma or generalized malignancy.

Economic and Programmatic considerations: the cost of nOPV2 is expected to be comparable to that of mOPV2. The production of nOPV2 is expected to be similar to production of the existing type 2 oral polio vaccine, which is US$ 0.15 per dose. The Bill and Melinda Gates Foundation have made available funds for the production of 200 million doses of nOPV2. The nOPV2 vaccine is stored and transported at 2-8^{O}C for up to 3 months, and is administered orally using droppers similarly as mOPV2. No major logistical changes are required to switch between the use of mOPV2 and nOPV2.

Policy and ethical considerations: nOPV2 received Emergency Use Listing from WHO in November 2020, for use in a three-months Initial Use Period, under careful monitoring and surveillance for vaccine effectiveness and safety. A set of essential criteria that a country must fulfil before roll out of nOPV2 were clearly set out, including: The detection of vaccine-derived poliovirus type 2 (VDPV2) (as per GPEI standard operating procedures), the capacity to acquire/distribute vaccine in a timely, manner (e.g. suitable country vaccine approval/importation processes), the capacity to respond to unanticipated findings, the capacity to conduct post-deployment surveillance (acute flaccid paralysis (AFP) surveillance, environmental surveillance (ES), adverse event following immunization (AEFI) surveillance), and a waiting period of 12 weeks after the last mOPV2 use in the area. Additional criteria for consideration include: a waiting period of six weeks after bOPV outbreak response campaigns (to minimize the risk of recombination between nOPV2 and mOPV1/mOPV3), Access or security issues, Vaccine acceptance. Uganda has met all the requirements of these criteria, and has put in plans for communication, including crisis communication.

Having carefully considered the different aspects of evidence relevant to nOPV2 introduction for outbreak response in Uganda, UNITAG came to the following **conclusions**:

1. Uganda is at risk of outbreak of CVDPV2 following reports of outbreaks in neighboring countries, and considering the in-country risk factors, such as low coverage of polio vaccines in several districts and gaps in the surveillance systems.
2. There is sufficient evidence to show that nOPV2 is comparable to mOPV2 in terms of efficacy and safety. There is clear scientific theory and some limited data to show that nOPV2 is more genetically stable than mOPV2 and is less likely to revert to virulence causing paralysis. However, there is no data from large scale studies to show this conclusively.
3. Uganda through the Ministry of Health has made sufficient preparations required for the introduction of nOPV2. However, with the increased use of vaccines under WHO Emergency Use Listing, the country needs a clear national framework, for use of such vaccines.

From the above conclusions, UNITAG came to the following **recommendations**:

1. Uganda should switch to use of nOPV2 as the vaccine of choice for cVDPV2 outbreak response following the WHO Emergency Use Listing guidelines.
2. The roll out of nOPV2 should be guided by the WHO initial use framework and criteria, Additionally, for Uganda, **when a case of cVDPV2 is confirmed in a neighbouring country**, the nOPV2 vaccine should be rolled out in targeted Supplementary Immunisation Activities **(SIAs) only in high-risk districts** as identified by the most UpToDate polio risk analysis mapping. This recommendation should be guided by advice from the WHO Regional Director. When **a case of cVDPV2 is confirmed in country, a full country vaccine roll-out should be implemented**.
3. In View of of the risk of paralysis associated with cVDPV2, the outbreak response should go ahead even in the COVID-19 pandemic, while strictly following the Standard Operating Procedures.
4. Considering of the difficulties previously experienced in obtaining consent for childhood vaccinations, which resulted in poor coverage, the nOPV2 roll out should not require parental consent.
5. The Ministry of Health should develop a framework for use of Emergency Use vaccines.

1. Introduction

Context of the question

Ministry of Health requested the Uganda National Immunization Technical Advisory Group (UNITAG) to review contextually relevant evidence in light of global guidance and recommendations provided by World Health Organization and advise on the application of nOPV2 vaccine in Uganda as an additional tool for responding to circulating vaccine derived polio virus outbreaks.

(MoH Letter attached as Annex 1).

General Information on Polio Vaccination

Poliomyelitis is a communicable disease in humans that mainly affects unimmunised children under five years of age. Wild poliovirus (WPV), which has three strains (serotype 1, 2 and 3) causes paralysis. The paralysis is also caused, albeit rarely, by the oral polio vaccine (OPV), which involves the same three serotypes. WPV spreads primarily by faecal-to-oral transmission in poor sanitary conditions. It can also spread through pharyngea-to-oral secretions. The virus enters the body through the oral and nasal cavities, replicates in the gastrointestinal tract, and is then shed, through faeces, into the environment. Initial symptoms of polio infection include fever, fatigue, headache, vomiting, stiffness in the neck, and pain in the limbs. One in 200 infections leads to irreversible paralysis. Five to 10 per cent of those paralysed die when their breathing muscles become immobilised (WHO 2015b).

In the pre-vaccination era, most cases of paralysis were caused by serotype 1. Worldwide, sustained use of polio vaccines since 1988 has led to a precipitous drop in the global incidence of poliomyelitis by >99% and the number of countries with endemic polio from 125 to just 2 in 2015 (Afghanistan and Pakistan).

While there is no cure for polio, polio vaccines can protect a child for life (WHO 2015). Two types of poliovirus vaccines are available, inactivated poliovirus vaccine (IPV) introduced in 1955 and the live attenuated oral poliovirus vaccine (OPV) introduced in the early 1960s.

Since the introduction of OPV, five of the six regions of the World Health Organization (WHO) have been certified free of Wild Pilo Virus (WPV): the Americas in 1994; Western Pacific in 2000; Europe in 2002; South East Asia in 2014 and Africa in 2020. (CDC 2015), (WHO AFRO 2020- https://www.afro.who.int/news/africa-eradicates-wild-poliovirus). However, continued use of OPV has been linked to vaccine-associated paralytic poliomyelitis (VAPP) and vaccine derived polioviruses (VDPVs) (Platt 2014). VAPP is defined as an event of paralysis that occurs in a vaccinee between seven and 60 days after receiving a dose of OPV, with the neurological deficit remaining 60 days after onset. Platt 2014 calculated the risk of VAPP in OPV using countries as 3.8 cases per million births (range = 2.9 to 4.7 cases) (Platt 2014).

Unlike serotypes 1 and 3, serotype 2 caused a number of cases of circulating Vaccine Derived Polio Virus cVDPV (cVDPV-2; 65 cases in 2013, 56 in 2014, 30 in 2015 and 5 in 2016). Between 2000 and 2016, 798 cases of cVDPV were reported in 25 countries around the world. None of these cases occurred with the inactivated polio vaccine (IPV), and only two cases occurred with IPV-OPV. The remaining cases (99.7%) occurred with OPV or OPV-IPV, representing a combined annual incidence of 14 cVDPV/million (95% confidence interval (CI) 13 to 15), ranging annually from 3 to 26 cVDPV/million.

There is no evidence that cVDPV tends to disappear and it is virtually only associated with exclusive use of OPV (Ciapponi 2017).

The eradication of indigenous WPV2 in 1999, coupled with the continuing emergence of neuro-virulent circulating type 2 vaccine---derived polioviruses (cVDPV2s) as well as vaccine- associated paralytic poliomyelitis (VAPP), led to the recommendation that there should be coordinated global cessation of use of the type 2 component of OPV and a switch from tOPV to bOPV.

While cVDPVs are rare, they have been increasing in recent years due to low immunization rates within communities. cVDPV type 2 (cVDPV2) are the most prevalent, with 959 cases occurring globally in 2020. The oral polio vaccine (OPV) that has brought the wild poliovirus to the brink of eradication has many benefits: the live attenuated (weakened) vaccine virus provides better immunity in the gut, which is where polio replicates. The vaccine virus is also excreted in the stool, and in communities with low-quality sanitation, this means that it can be spread from person to person and actually help protect the community. In communities with low vaccination rates, as the virus is spread from one unvaccinated child to another over a long period of time (12-18 months), it can mutate and take on a form that can cause paralysis just like the wild poliovirus. This mutated poliovirus can then spread in communities, leading to cVDPVs.

The Global Polio Eradication Initiative (GEPI) is implementing an **Endgame Strategy (2019-2023)** that includes tactics to address cVDPVs, focusing on preventing cases in high-risk communities with populations that may be under immunised due to conflict, insecurity or weakened health infrastructure. Given the cause of cVDPVs being low immunization rates, the ideal way to prevent them and stop them when there is an outbreak is to vaccinate children. The polio vaccine protects children whether the kind of polio is wild poliovirus or vaccine-derived poliovirus. Outbreaks (whether WPV or cVDPV) are usually rapidly stopped with 2–3 rounds of high-quality supplementary immunization activities.

Additionally, GPEI is working to deploy an improved outbreak response tool: the novel oral polio vaccine type 2, or nOPV2. This vaccine is similar to mOPV2 (the monovalent oral polio vaccine type 2), the current outbreak response vaccine that is used when cVDPV type 2 outbreaks occur. However, it contains improvements that help make the vaccine virus less likely to mutate and cause disease in communities with low immunization rates – meaning that it can help reduce the risk of cVDPV2 outbreaks. The novel oral polio virus is a modified version of mOPV2 which is more genetically stable and less likely to return to virulence. The modification that was made to mOPV2 to achieve nOPV2 include;

a) Stabilizing the Sabin-2 attenuation phenotype by modifying the nucleotides in the 5'UTR. The Sabin-2 attenuation phenotype was modified by making mutations in the 5' UTR.
b) Ensuring the maintenance of the modified 5'UTR or increasing attenuation by relocation of a genetic element(*cre*), which is required for replication, to the 5'UTR of the viral genome. The cre genetic element was relocated to the 5'UTR of the viral genome.
c) Reducing the rate of mutation in the viral genome through the selection of mutations that increase the fidelity/accuracy of RNA-dependent RNA polymerase. They reduced the rate of mutations in the genome of oPV2 by carrying out point mutations in genes

d) Attenuating the virus by modifying the nucleotide sequence of the viral capsid by codon deoptimization where capsid amino acid sequence is unchanged (encoding triplets altered to no-preferred, synonymous codons).

The modified vaccine, nOPV2 has a favorable general safety and reactogenicity profile. nOPV2 is said to be immunogenic compared with mOPV2.

In November 2020, SAGE endorsed the initial use framework of nOPV2 under Emergency Use Listing. More recently in October 2020, the Strategic Group of Experts on Immunization (SAGE) re-affirmed its April 2020 recommendation on the use of nOPV2 initial use criteria under Emergency Use Listing (EUL). SAGE endorsed in principle nOPV2 becoming the vaccine of choice for response to cVDPV2 outbreaks after the interim recommendation of the EUL is issued and after the review of the initial use period is completed and all requirements are met. The initial use period is expected to last around three months after the first use of nOPV2 under the EUL.

2. Methodology

i. Establishment of an nOPV2 working group

In line with the UNITAG Internal Procedures Manual, the UNITAG Chair in consultation with the Secretariat commissioned a working group to develop a Recommendation Framework on the introduction of novel oral polio vaccine as additional tool to respond to circulating vaccine derived polio virus, conduct a systematic search, appraisal and synthesis of relevant evidence based on which, recommendations would be proposed.

The Working Group Composition: The working group was chaired by a core member, who is a Microbiologist, and comprised of the following UNITAG members: Vaccinologist, Epidemiologist, Paediatrician and supported by liaison members from UNEPI, WHO and UNICEF. A microbiologist/geneticist expert was also co-opted to the group. All members signed a declaration form stating that they had no known conflict of interest on the topic.

Work Process: The working group met twice to understand the context of the nOPV2 advice request from Ministry of Health, develop critical sub topics for the recommendation framework, review evidence and develop conclusions and recommendations. The work process report is attached as Annex 2.

ii. Recommendation Framework

The working group developed a recommendation framework, outlining the issues and specific data needed to inform a recommendation on novel oral polio vaccine type 2. The recommendation framework considered 4 categories of issues: 1) Disease burden (Burden Polio disease and Epidemiology of Polio Viruses in the African region and in Uganda) 2) Vaccine characteristics and immunization (efficacy and safety of nOPV2) 3) Programmatic and Economic Considerations of switching from mOPV2 to nOPV2 and 4) Policy issues. A detailed Recommendation Framework is attached as Annex 3

iii. Evidence Search and Assessment

- Step 1: Framing questions for the literature search

For each issue in the recommendation framework, the WG went further in specifying the specific data that were needed. For each data, queries were specified in the form of clear, unambiguous and structured questions before beginning the search work. Queries were categorised as those that required a systematic search in databases and those for which information could be found in reference documents (WHO papers, text books, vaccine manufacturers' websites). These documents were used as source of background information. For systematic search of data, the queries were formulated to specify the specific outcomes of interest from the use of the intervention in the population considered as per UNITAG method of working for issuing evidence-based recommendation (using the PICO approach to search for evidence on the efficacy, effectiveness and safety of an intervention). Queries requiring systematic literature search proceeded to step 2. Grey literature (Ministry of Health Reports, Immunisation partner surveys, websites and unpublished local reports) and reference documents were looked for to answer background data queries.

- Step 2: Identifying relevant peer reviewed articles

Search strategies were developed to ensure that search terms covered all known terms relevant to the question. Considering that WHO had conducted a review of relevant articles up to 2016, the search process sought to find updated literature for the last 5 years to update the WHO table. PubMed was searched with English language restriction to generate relevant title-abstracts. Inclusion and exclusion criteria were set for each query, to flow directly from the review question and was specified a priori. Articles obtained were screened (titles and abstracts) for relevance to the question. The search strategy and result were recorded; the report is available at the secretariat.

- Step 3: Assessing the quality of articles

Selected title abstracts were extracted in full text and subjected to review and, if still relevant to the question, to a more refined quality assessment by use of a design-based quality checklist (CASP) according to the study design. These detailed quality assessments were used for exploring for bias or flaws of the study by evaluating its methodological quality, certainty of results, and relevance to the question, hence ensuring quality of the evidence sustaining the recommendation. List of articles retrieved and assessed is also indicated in the search strategy and evidence results report.

- Step 4: Summarizing the evidence

Selected full text articles were read and relevant findings under each query were summarised in a standard UNITAG working group outline report.

- Step 5: Interpreting the findings

The Working Group conducted a meeting for review of the evidence presented on each issue of the recommendation framework and, from sense-making of the overall body of evidence, propose recommendations to submit to the entire UNITAG for decisions. During the meeting the group worked on the write-up of the discussion section, analysing the findings with the view of joining the pieces together that will lead to the proposed recommendations.

3. Presentation of Evidence

a) Vaccine and Immunization characteristics

Presentation, formulation and administration of nOPV2 vaccine

	nOPV2
Presentation	Novel Oral Poliomyelitis Vaccine Type 2 (nOPV2) 50 doses is a clear sterile suspension of live attenuated Poliomyelitis virus type 2 of modified Sabin strain prepared in Vero cells derived from African green monkey kidney. The nOPV2 strain S2/cre5/S15domV/rec1/hifi3 is an attenuated serotype 2 poliovirus derived from a modified Sabin-2 infectious cDNA clone. Increased genetic stability and decreased recombination rate are achieved with five modifications in the parental genome affecting domain V, cre element and RNA dependent RNA polymerase.
Formulation	The live type 2 novel oral poliomyelitis is a live monovalent vaccine containing suspensions of type 2 attenuated poliomyelitis virus (modified Sabin strains) prepared in Vero cells. Each dose (2 drops=0.1ml contains not less than $10^{5.0}$ $CCID_{50}$ infective units of type 2. Sucrose is used as a stabilizer.
Administration	A dose of nOPV2 consists of two drops of the vaccine delivered orally directly into the mouth from the multi-dose vial by dropper or dispenser. Care should be taken not to contaminate a multi dose dropper of the vaccine with saliva.

Administration schedule and possibility of combination with other vaccines

Initially, use of nOPV2 in countries affected by cVDPV2 will be limited to immunization with nOPV2 only for to outbreak response. Before using nOPV2, there is a required waiting period of 12 weeks after the last mOPV2 use in an area to help correctly attribute any safety signals or environmental detections to nOPV2 and gather data on nOPV2's effectiveness in stopping outbreaks and preventing cases. Following an initial use period of approximately three months, nOPV2 may be administered alongside IPV and OPV in suitable country contexts. IPV and bOPV will continue to be used in routine immunization programmes.

Vaccine Indirect effects

Possible impact of use of mOPV2

mOPV2 will continue to be used in some countries even though nOPV2 is now available. The use of mOPV2 is dependent on several factors, including the ability of individual countries to authorize the use and import of nOPV2 in a timely manner, evolving poliovirus epidemiology, and the ability of countries to meet the post-deployment requirements under the EUL. The polio programme would likely stop using mOPV2 in outbreak response prior to nOPV2 prequalification and if nOPV2 proves successful in outbreak response, in carrying the lower risk of cVDPV2 emergence and if there is a sufficient stockpile of the vaccine (GPEI nOPV2 Technical Guidance).

Vaccine intervention and outcome specific data

Safety

Safety of nOPV2 compared to mOPV2

Article: Llorens. et al. Lancet, 2020; Volume 397.Issue 10268: Pages 27-38. https://doi.org/10.1016/S0140-6736(20)32540-X

Method: Two single-center, multi-site, partly-masked, randomized trials in healthy cohorts of children (aged 1-4 years) and infants (aged 18-22 weeks) in Panama: a control phase 4 study with monovalent Sabin OPV2 before global cessation of monovalent OPV use, and a phase 2 study with low and high doses of two novel OPV2 candidates.

Findings: Study found that both novel OPV2 candidates were safe, well tolerated in children and infants. Vaccinations are safe and well tolerated with no casually associated serious adverse events or important medical events in any group. Solicited and unsolicited adverse events were overwhelmingly mild or moderate irrespective of vaccine or dose.

Article: Coster. et al. Lancet. 2020; Volume 397, Issue 10268: pages 39-50. https://doi.org/10.1016/S0140-6736(20)32541-1

Method: Two randomized studies at two centers in Belgium. The first was a phase 4 historical control study of monovalent OPV2 in Antwerp, done before global withdrawal of OPV2 and the second was a phase 2 study in Antwerp and Ghent with novel OPV2-c1 and novel OPV2-c2. Eligible participants were health adults aged 18-50 years with documented history of at least three polio vaccinations, including OPV or inactivated poliovirus vaccine (IPV) in the novel OPV2 phase 2 study, with no dose within 12 months of study start. In the historical control trial, participants were randomly assigned to either one or two doses of monovalent OPV2. In the novel OPV2 trial, participants with previous OPV vaccinations were randomly assigned to either one or two doses of novel OPV2-c1 or to one or two doses of novel OPV-c1, novel OPV2-c2 or placebo.

Findings: Results showed that novel OPV2 candidates were safe and well tolerated as mOPV2 in previously OPV-vaccinated and IPV vaccinated adults.

Article: Damme. et.al, 2019. Lancet. Volume 394. Issue 10193: pages 148-158. https://doi.org/10.1016/S0140-6736(19)31279-6

Method: In this double-blind, single-centre phase 1 trial, participants were isolated in a purpose-built containment facility at the University of Antwerp Hospital (Antwerp, Belgium), to minimise the risk of environmental release of the novel OPV2 candidates. Participants, who were recruited by local advertising, were adults (aged 18–50 years) in good health who had previously been vaccinated with IPV, and who would not have any contact with immunosuppressed or unvaccinated people for the duration of faecal shedding at the end of the study. The first participant randomly chose an envelope containing the name of a vaccine candidate, and this determined their allocation; the next 14 participants to be enrolled in the study were sequentially allocated to this group and received the same vaccine. The subsequent 15 participants enrolled after this group were allocated to receive the other vaccine. Participants and the study staff were masked to vaccine groups until the end of the study period.

Findings: Study found that nOPV2 candidates had acceptable tolerability, and no serious adverse events occurred during the study. However, severe events were reported in six (40%) participants receiving candidate 1 (eight events) and nine (60%) participants receiving candidate 2 (12 events); most of these events were increased blood creatinine phosphokinase but were not accompanied by clinical signs or symptoms.

Article: Llorens.et al. 2016. (6):321-30 https://doi.org/10.1016/s1473-3099(15)00488-0

Method: Observer-blind, comparative, randomised controlled trial was done in a single centre in Panama. Healthy infants who had not received any previous vaccination against poliovirus were enrolled. Infants were randomly assigned (1:1) by computer-generated randomisation sequence to receive a single dose of either mIPV2HD or standard trivalent IPV given concurrently with a third dose of bOPV at 14 weeks of age. At 18 weeks, all infants were challenged with one dose of monovalent type 2 OPV (mOPV2).

Findings: Serious adverse events were reported for six (5%) of 117 infants in the mIPV2HD group and seven (6%) of 116 infants in the IPV group during the 8-week period after vaccination; none were related to vaccination. No important medical events were reported.

Efficacy and Effectiveness of nOPV2 Vs mOPV2

Article: Llorens. et al. Lancet, 2020; Volume 397.Issue 10268: Pages 27-38. https://doi.org/10.1016/S0140-6736(20)32540-X

Method: Two single-center, multi-site, partly-masked, randomized trials in healthy cohorts of children (aged 1-4 years) and infants (aged 18-22 weeks) in Panama: a control phase 4 study with monovalent Sabin OPV2 before global cessation of monovalent OPV use, and a phase 2 study with low and high doses of two novel OPV2 candidates.

Findings: Study results show that novel oral polio vaccine type 2 candidates are immunogenic. Non inferiority was shown for low dose and high dose novel OPV2-c1 and high OPV-c2 despite monovalent OPV2 recipients having higher baseline immunity. Nearly all children were seroprotected at baseline, indicating high baseline immunity. In children, the seroprotection rate 28 days after one dose was 100% for monovalent OPV2 and both novel OPV2 candidates. In infants at day 28,91(94% (95% CI 87-98) of 97 were seroprotected after receiving monovalent OPV2, 134(94% (88-97) of 143 after high dose novel OPV2-c1, 138(95% (90-98) of 146 after high dose novel OPV2-c2 and 115(91% (84-95) of 127 after low dose novel OPV2-c2.

Article: Coster. et al. Lancet. 2020; Volume 397, Issue 10268: pages 39-50. https://doi.org/10.1016/S0140-6736(20)32541-1

Method: Two randomized studies at two centers in Belgium. The first was a phase 4 historical control study of monovalent OPV2 in Antwerp, done before global withdrawal of OPV2 and the second was a phase 2 study in Antwerp and Ghent with novel OPV2-c1 and novel OPV2-c2. Eligible participants were health adults aged 18-50 years with documented history of at least three polio vaccinations, including

OPV or inactivated poliovirus vaccine (IPV) in the novel OPV2 phase 2 study, with no dose within 12 months of study start. In the historical control trial, participants were randomly assigned to either one or two doses of monovalent OPV2. In the novel OPV2 trial, participants with previous OPV vaccinations were randomly assigned to either one or two doses of novel OPV2-c1 or to one or two doses of novel OPV-c1, novel OPV2-c2 or placebo.

Findings: Study found that novel oral polio vaccine candidates were immunogenic as monovalent OPV2 in previously IPV vaccinated and OPV-vaccinated participants, 286 (97%) of 296 were seropositive at baseline; after one dose, 100% of novel OPV2 vaccinees and 97 (97%) of monovalent OPV2 vaccinees were seropositive.

Article: Damme. et.al, 2019. Lancet. Volume 394. Issue 10193: pages 148-158. https://doi.org/10.1016/S0140-6736(19)31279-6

Method: In this double-blind, single-centre phase 1 trial, participants were isolated in a purpose-built containment facility at the University of Antwerp Hospital (Antwerp, Belgium), to minimise the risk of environmental release of the novel OPV2 candidates. Participants, who were recruited by local advertising, were adults (aged 18–50 years) in good health who had previously been vaccinated with IPV, and who would not have any contact with immunosuppressed or unvaccinated people for the duration of faecal shedding at the end of the study. The first participant randomly chose an envelope containing the name of a vaccine candidate, and this determined their allocation; the next 14 participants to be enrolled in the study were sequentially allocated to this group and received the same vaccine. The subsequent 15 participants enrolled after this group were allocated to receive the other vaccine. Participants and the study staff were masked to vaccine groups until the end of the study period.

Findings: Both novel OPV2 candidates were immunogenic and increased the median blood titre of serum neutralising antibodies; all participants were seroprotected after vaccination. Reversion to neurovirulence, assessed as paralysis of transgenic mice, was low in isolates from those vaccinated with both candidates, and sequencing of shed virus indicated that there was no loss of attenuation in domain V of the 5'-untranslated region, the primary site of reversion in Sabin OPV.

Duration of protection

Clinical trials have shown that nOPV2 provides comparable protection to mOPV2 against type 2 poliovirus while being more genetically stable and therefore less likely to revert to a form that can cause paralysis in under-immunized communities (GPEI nOPV2 Technical Brief).

The disease

i. Burden of disease

The most recent cases of poliomyelitis in Uganda were VDPV2 in three districts, Kween, Kamuli and Kisoro in 2014(Nanteza et. al,2018). In the region, in 2021, cVDPVv2 has been detected in South Sudan (10 cases) DRC (2 cases) and Kenya (3 cases).
In 2018, cVDPV type 2 cases were detected in five countries (Democratic Republic of Congo, Kenya, Mozambique, Niger and Nigeria) and in 2019 in 14 countries (Democratic Republic of Congo (DRC),

Kenya, Mozambique, Niger and Nigeria). Additionally, 12 cVDPV cases type 2 and 3) were reported in 2018(including one coinfection with types 2 and 3 and three cVDPV cases were reported in 2019(Lickness et. al,2020).

ii. Population at risk of acquiring cVDPV2

If a population is seriously under-immunized, there are enough susceptible children for the excreted vaccine-derived polioviruses to begin circulating in the community. If the vaccine-virus is able to circulate for a prolonged period of time uninterrupted, it can mutate and, over the course of 12-18 months, reacquire neurovirulence. Uganda's immunisation coverage for Polio is sub-optimal. According to DHIS 2015, OPV3 coverage for Uganda is 60%. The last tOPV campaign in Uganda was conducted in April 2016, in 112 districts with a coverage of 92%.

Uganda also has a high number of refugees from South Sudan and DRC. The refugee population in Uganda is estimated to reach 1,484,356 by the end of 2021. While Uganda's borders are officially closed due to COVID-19, it is expected that new refugee arrivals will continue to cross into Uganda through unofficial crossing points, fleeing political instability, violence and declining economies in neighbouring countries, including the Democratic Republic of the Congo, South Sudan and Burundi.

With regards to surveillance, the NPAFP rate is 0.41/100,000 children 0 - 14 years, and the adequate samples collection rate is 93.55%, however, most of the border districts were reported as silent districts in week 4 Jan 2021.

Regionally, a survey of 19 countries in the ESA region observed an overall increase in the sensitivity of the AFP surveillance performance for the ESA sub-region countries from 2012 to 2019 using the national performance indicators. The COVID-19 pandemic paused an operational challenge for AFP surveillance performances from 2020.

b) Economic considerations

Vaccine related costs and resource use

According to GPEI, the production of nOPV2 is expected to be similar to production of the existing type 2 oral polio vaccine, which costs US $0.15 per dose. This means that over the long-term, prices for nOPV2 could approach those for nOPV2 once investments in research, facilities and testing have been recouped.

Vaccine Affordability

The cost of nOPV2 is expected to be comparable to that of mOPV2, which is currently used for outbreak response to cVDPV2. The production of nOPV2 is expected to be similar to production of the existing type 2 oral polio vaccine, which is US$ 0.15 per dose.

Health policy and programmatic issues

Feasibility

The Bill and Melinda Gates Foundation have made available funds for the production of 200 million doses of nOPV2. The nOPV2 vaccine is stored and transported at 2-8^{O}C for up to 3 months, and is administered orally using droppers similarly as mOPV2. No major logistical changes are required to switch between the use of mOPV2 and nOPV2

Wastage

Wastage should be assessed during the initial use period and the current 50-dose vial size could potentially be changed in the future.

Communication

One of the requirements for country readiness for deployment of nOPV2 is the ability of communication plans including crisis communication plans to support nOPV2 implementation.

These have both been developed by the Ministry of Health.

Ability to evaluate

Ministry of Health of Uganda currently meets the country requirements for nOPV2 vaccine deployment of having at least one functional environmental surveillance site if nOPV2 is to be used. The AFP and environmental surveillance are functional.

Additionally, Uganda adopted the Integrated Disease Surveillance and Response (IDSR) Strategy in 2000 serve as a comprehensive strategy to improve disease surveillance and to improve laboratory and response capacities of WHO member states in Africa. There is a functional department of Integrated epidemiology, surveillance public health emergencies that deals with surveillance.

Regional and International Considerations

In November 2020, nOPV2 received a recommendation for use under WHO's Emergency Use Listing (EUL) procedure. WHO's Strategic Advisory Group of Experts on Immunization (SAGE) endorsed accelerated clinical development of nOPV2 and its assessment under EUL in October 2019.

Equity

In areas with under-immunized populations like for the case of some parts of Uganda, the live weakened virus contained in OPV can mutate and spread causing the circulating vaccine derived polio virus and therefore nOPV2 will be more useful and beneficial in these areas.

iii. Discussion

Analysis of the available body of evidence leads to the following conclusions;

Disease burden

i. Uganda is at risk of circulating vaccine derived polio virus type 2 due to the current ongoing cVDPV2 outbreak in close neighboring countries of South Sudan, Kenya and Democratic Republic of Congo.
ii. The low vaccine coverage in some areas of Uganda poses a serious risk of circulating vaccine derived polio virus given the cause of cVDPVs is a low immunized population with enough susceptible children for the vaccine derived polio viruses to begin circulating.
iii. The current available vaccine mOPV2 presents a further risk of cVDPV2 due to its likelihood to return to virulence.

Vaccine characteristics

i. **Safety**: In clinical trials, solicited events among infants and children receiving any nOPV2 vaccination included predominantly mild or moderate abnormal crying, drowsiness, fever, irritability, loss of appetite, and vomiting, with similar rates among mOPV2 control vaccinees. However, nOPV2 is more genetically stable and is less likely to revert to virulence and cause paralysis. Regarding co-administration with other infant vaccines, although no

data are available for nOPV2, it is assumed that, as for mOPV2 or tOPV, no interference would occur with other routinely administered vaccines, as far as it will be of relevance in the emergency setting. The vaccine is contraindicated in those with primary immune deficiency disease or suppressed immune response from medication, leukemia, lymphoma or generalized malignancy.

Although no data are available specific to the use of nOPV2 in individuals infected with human immunodeficiency virus (HIV), both asymptomatic and symptomatic, given the derivation of this vaccine from the Sabin type 2 strain, health authorities may consider adopting an approach for nOPV2 similar to that accepted for Sabin 2 in this population.

ii. **Efficacy considerations:** nOPV2 is expected to be as effective in preventing paralytic disease as the current vaccine because the immunogenicity of nOPV2 was found to be non-inferior to mOPV2 in infants. Most importantly, it was established that nOPV2 is significantly more genetically stable and thus less likely to revert to neurovirulence compared to nOPV2. Non-inferiority for sero protection was established for both low dose and high dose potencies of nOPV2 and there was no significant difference in seroconversion rates between nOPV2 and mOPV2). Across all studies, nOPV2 demonstrated robust immune responses with high seroconversion rates that were comparable with mOPV2.

iii. **Contraindications:**

The vaccine is contraindicated in those with primary immune deficiency disease or suppressed immune response from medication, leukemia, lymphoma or generalized malignancy.

iv. Economic considerations

Administering of nOPV2 is affordable in Uganda because the global stock pile of 200 million doses is being funded by Bill and Melinda Gates Foundation for production and deployment in affected areas. The cost of nOPV2 is comparable to the cost of mOPV2 that is currently used for cVDPV2 outbreak response in Uganda

v. Health policy and programmatic aspects

i. Changing from use of mOPV2 to nOPV2 as the vaccine to deal with cVDPV2 outbreaks does not call for any additional cold chain requirements as nOPV2 fits in the existing cold chain requirements

ii. Global recommendations for use of nOPV2 under Emergency Use Listing are available.

UNITAG Conclusions and Recommendations

The UNITAG, based on the available evidence made the following conclusions and recommendations;

Conclusions

Risk of cVDPV2

1. Uganda is at risk of cVDPV2 due to the ongoing outbreak in the close neighboring countries in South Sudan, Democratic Republic of Congo and Kenya, the low vaccination rates in some

parts of Uganda, the high influx of refugees in Uganda and the current outbreak response vaccine mOPV2 likelihood to return to virulence.

nOPV2 Vs mOPV2

2. There is sufficient evidence to show that nOPV2 is comparable to mOPV2 in terms of efficacy and safety. There is clear scientific theory and some limited data to show that nOPV2 is more genetically stable than mOPV2 and is less likely to revert to virulence causing paralysis. However, there is no data from large scale studies to show this conclusively.

Country Readiness for nOPV2 according to the essential criteria for use

3. Uganda has a surveillance system in place so there is ability to do AFP surveillance and monitoring of any effects due to vaccination
4. The communication strategy has been developed according to the initial use required criteria. The Ministry of Health could benefit from the UNICEF pool of consultants which is available to help build capacity on how to implement the communication strategy.
5. The National Drug Authority has licensed nOPV2 for use in Uganda.
6. However, with the increased use of vaccines under WHO Emergency Use Listing, the country needs a clear national framework, for use of such vaccines.

From the above conclusions, UNITAG came to the following **recommendations**:

1. Uganda should switch to use of nOPV2 as the vaccine of choice for cVDPV2 outbreak response following the WHO Emergency Use Listing guidelines.
2. The roll out of nOPV2 should be guided by the WHO initial use framework and criteria, Additionally, for Uganda, **when a case of cVDPV2 is confirmed in a neighbouring country**, the nOPV2 vaccine should be rolled out in targeted Supplementary Immunisation Activities **(SIAs) only in high-risk districts** as identified by the most UpToDate polio risk analysis mapping. This recommendation should be guided by advice from the WHO Regional Director. When **a case of cVDPV2 is confirmed in country, a full country vaccine roll-out should be implemented**.
3. In View of of the risk of paralysis associated with cVDPV2, the outbreak response should go ahead even in the COVID-19 pandemic, while strictly following the Standard Operating Procedures.
4. Considering of the difficulties previously experienced in obtaining consent for childhood vaccinations, which resulted in poor coverage, the nOPV2 roll out should not require parental consent.
5. The Ministry of Health should develop a framework for use of Emergency Use vaccines.

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Lickness JS, Gardner T, Diop OM, et al. Surveillance to Track Progress Toward Polio Eradication — Worldwide, 2018–2019. MMWR Morb Mortal Wkly Rep 2020;69:623–629 https://www.cdc.gov/mmwr/volumes/69/wr/mm6920a3.htm

Annexes

1. Official letter from Ministry of Health

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UGANDA

IN ANY CORRESPONDENCE ON
THIS SUBJECT PLEASE QUOTE NO. **ADM:168/216/01**

9 April 2021

Dr. Nelson Sewankambo,
Chairperson for NITAG, Uganda.

USE OF THE NOVEL ORAL POLIO VACCINE TYPE 2 AS AN ADDITIONAL TOOL FOR RESPONDING TO CIRCULATING VACCINE-DERIVED POLIO VIRUS TYPE 2 OUTBREAKS

After the decision of the 146th Session of the WHO Executive Board in February 2020 to use the novel oral polio vaccine (nOPV2) under emergency use listing, with further endorsement by the independent WHO Strategic Advisory Group of Experts on Immunization, and rigorous review of data on safety and efficacy by WHO headquarters; the WHO issued the emergency use listing recommendation for the nOPV2.

The ongoing cVDPV2 outbreaks in the DRC, Kenya and Republic of South Sudan put Uganda at risk. Hence, there is need to prepare for an outbreak response with nOPV2 in case Uganda registers a confirmed polio outbreak. The Minister of Health has endorsed implementation of the preparatory activities.

The purpose of this letter is to request the UNITAG to review contextually relevant evidence in light of global guidance and recommendations provided by WHO to advise the Ministry of Health on the application of the nOPV2 vaccine in Uganda.

Your advice within the next two weeks will be highly appreciated.

Yours sincerely,

Dr. Henry G. Mwebesa
DIRECTOR GENERAL HEALTH SERVICES

Cc: The Hon. Minister of Health
Cc: The Hon. Minister of Health for Primary Health care
Cc: The Hon. Minister of Health for General Duties
Cc: The Permanent Secretary, Ministry of Health
Cc: The Director Health Services, Clinical and Community
Cc: Commissioner Health Services, National Disease Control
Cc: The Program Manager, UNEPI

Evidence to Recommendation Framework

Element	Discussion topic	Specific discussion items	Evidence summary
DISEASE	**Burden of Disease**	***Prevalence of Disease*** The most recent cases of poliomyelitis in Uganda were VDPV2 in three districts, Kween, Kamuli and Kisoro in 2014(Nanteza et. al,2018). In the region, in 2021, cVDPVv2 has been detected in South Sudan (10 cases), DRC (2 cases) and Kenya (3 cases).	https://virologyj.biomedcentral.com/articles/10.1186/s12985-018-0990-y https://polioeradication.org/wp-content/uploads/2021/05/weekly-polio-analyses-cVDPV2-20210504.pdf
		Disease Occurrence over time In 2018, cVDPV type 2 cases were detected in five countries (Democratic Republic of Congo, Kenya, Mozambique, Niger and Nigeria) and in 2019 in 14 countries (Democratic Republic of Congo (DRC), Kenya, Mozambique, Niger and Nigeria). Additionally, 12 cVDPV cases type 2 and 3) were reported in 2018(including one coinfection with types 2 and 3 and three cVDPV cases were reported in 2019(Lickness et. al,2020).	17th meeting of the SAGE polio working group conclusions and recommendations note for the record, https://www.cdc.gov/mmwr/volumes/69/wr/mm6920a3.htm https://polioeradication.org/wp-content/uploads/2021/05/weekly-polio-analyses-cVDPV2-20210504.pdf

	Epidemic potential	***population at risk of acquiring cVDPV2*** If a population is seriously under-immunized, there are enough susceptible children for the excreted vaccine-derived polioviruses to begin circulating in the community. If the vaccine-virus is able to circulate for a prolonged period of time uninterrupted, it can mutate and, over the course of 12-18 months, reacquire neurovirulence. Uganda's immunisation coverage for Polio is sub-optimal. According to DHIS 2015, **OPV3 coverage for Uganda is 60%**. The last tOPV campaign conducted in Uganda was in April 2016, in 112 districts with a coverage of 92%. Uganda also has a high number of refugees from South Sudan and DRC. The **refugee population in Uganda is estimated to reach 1,484,356 by the end of 2021**. While Uganda's borders are officially closed due to COVID-19, it is expected that new refugee arrivals will continue to **cross into Uganda through unofficial crossing points**, fleeing political instability, violence and declining economies in neighbouring countries, including the Democratic Republic of the Congo, South Sudan and Burundi. . With regards to **surveillance**, the NPAFP rate is 0.41/100,000 children 0 - 14 years, and the adequate samples collection rate is 93.55%, however, most of the border districts were reported as silent districts in week 4 Jan 2021.	https://apps.who.int/immunization_monitoring/globalsummary/countries?countrycriteria%5Bcountry%5D%5B%5D=UGA https://reporting.unhcr.org/uganda http://library.health.go.ug/sites/default/files/resources/Weekly%20epidemiological%20Bulletin%20Week%204%2021.pdf Manyanga et al 2020.

		Regionally, a survey of 19 countries in the ESA region observed an overall increase in the sensitivity of the AFP surveillance performance for the ESA sub-region countries from 2012 to 2019 using the national performance indicators. The COVID-19 pandemic paused an operational challenge for AFP surveillance performances from 2020.	doi: 10.11604/pamj.2020.36.71.23173
		Short- and long-term consequences of infection and frequency Most poliovirus infections cause asymptomatic viral replication that is limited to the alimentary tract. However, following an incubation period of approximately 7-10 days (range, 4-35 days), about 24% of those infected develop clinical signs such as fever, headache and sore throat (considered a minor illness). Paralytic poliomyelitis, experienced in less than 1% of poliovirus infections, occurs when the virus enters the central nervous system and replicates in anterior horn cells (motor neurons) of the spinal cord. When it multiplies in the nervous system, the virus can destroy nerve cells (motor neurons) which activate skeletal muscles. The affected muscles lose their function due to a lack of nervous enervation, a condition known as acute flaccid paralysis. In the most severe cases (bulbar polio), poliovirus attacks the motor neurons of the brain stem, reducing breathing capacity and causing difficulty in swallowing and speaking. Without respiratory support, bulbar polio can result in death.	https://www.who.int/biologicals/areas/vaccines/poliomyelitis/en/
Vaccine and immunization characteristics	Vaccine presentation and use	***Vaccine presentation, storage volume and cold chain requirement*** nOPV2 looks similar to mOPV2. The liquid is similar in colour and the same type of dropper dispensers are used. Differences include the packaging and vaccine vial labelling as well as the size of the vaccine vial: nOPV2 comes in a larger 50-dose vial as opposed to the typical 20-dose vial. The	https://polioeradication.org/wp-content/uploads/2021/03/nOPV2-FAQ-20210312EN.pdf

		different labelling and packaging design are important to differentiate the two vaccines, although they will not be used together in the field during the initial use period. nOPV2 vials also feature the same type of vaccine vial monitor (VVM) as mOPV2nOPV2 should be kept in the cold chain at all times. It should be kept in a freezer at -20c for as long as possible, until it is being used. Once opened, multi dose vials should be kept between $+2^0$ C and $+8^0$ C	https://extranet.who.int/pqweb/sites/default/files/documents/20201003_EUL_nOPV2_50dose_BioFarma_PI.pdf
		Dosage and Route of Administration A dose of nOPV2 consists of two drops of the vaccine delivered orally directly into the mouth from the multi-dose vial by dropper or dispenser. Care should be taken not to contaminate a multi dose dropper of the vaccine with saliva.	http://polioeradication.org/wp-content/uploads/2021/03/nOPV2-FAQ-20210312EN.pdf https://extranet.who.int/pqweb/vaccines/polio-vaccine-novel-oral-nopv-monovalent-type-2 https://extranet.who.int/pqweb/sites/default/files/documents/20201003_EUL_nOPV2_50dose_BioFarma_PI.pdf
		Administration schedule and possibility of combination with other vaccines Initially, use of nOPV2 in countries affected by cVDPV2 will be **limited to immunization with nOPV2 only for to outbreak response**. Before using nOPV2, there is a **required waiting period of 12 weeks after the last mOPV2 use** in an area to help correctly attribute any 3 safety signals or environmental detections to nOPV2 and gather data on nOPV2's effectiveness in stopping outbreaks and preventing cases Following an initial use period of approximately	http://polioeradication.org/wp-content/uploads/2021/03/nOPV2-FAQ-20210312EN.pdf https://polioeradication.org/wp-content/uploads/2020/12/Introduction-of-nOPV2-for-Polio-Outbreak-Response-Supervisory-Manual-20201208.pdf

		three months, nOPV2 may be administered alongside IPV and OPV in suitable country contexts. IPV and bOPV will continue to be used in routine immunization programmes.	
Vaccine intervention outcomes specific data	Safety	Safety data from all the clinical studies indicate that nOPV2 is well-tolerated in adults, young children, and infants. No safety concerns were identified from the available data. No serious adverse events have been identified that are considered to be related to vaccination with nOPV2. In clinical trials, solicited events among infants and children receiving any Nopv2 vaccination included predominantly mild or moderate abnormal crying (15%), drowsiness (7%), fever (11%), irritability (15%), loss of appetite (11%), and vomiting (13%), with similar rates among Mopv2 control vaccines. Among adults, most subjects reported mild or moderate solicited events composed predominantly of abdominal pain, diarrhea, fatigue and headache, with severe events of headache (2.2%) and myalgia (0.8%). ***Contraindications*** The vaccine is contraindicated in those with primary immune deficiency disease or suppressed immune response from medication, leukemia, lymphoma or generalized malignancy. Although no data are available specific to the use of nOPV2 in individuals infected with human immunodeficiency virus (HIV), both asymptomatic and symptomatic, given the derivation of this vaccine from the Sabin type 2 strain, health authorities may consider adopting an approach for nOPV2 similar to that accepted for Sabin 2 in this population.	https://polioeradication.org/wp-content/uploads/2021/02/nOPV2-Clinical-Development-Summary-1.29-EN.pdf https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)31279-6/fulltext https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32541-1/fulltext https://extranet.who.int/pqweb/sites/default/files/documents/20201003_EUL_nOPV2_50dose_BioFarma_PI.pdf

	Efficacy and effectiveness nOPV2 vs mOPV2	nOPV2 is expected to be as effective in preventing paralytic disease as the current vaccine because the immunogenicity of nOPV2 was found to be non-inferior to mOPV2 in infants. Most importantly, it was established that nOPV2 is significantly more genetically stable and thus less likely to revert to neurovirulence compared to nOPV2. Non-inferiority for sero protection was established for both low dose and high dose potencies of nOPV2 and there was no significant difference in seroconversion rates between nOPV2 and mOPV2). Across all studies, nOPV2 demonstrated robust immune responses with high seroconversion rates that were comparable with mOPV2.	https://polioeradication.org/wp-content/uploads/2021/02/nOPV2-Clinical-Development-Summary-1.29-EN.pdf https://polioeradication.org/wp-content/uploads/2021/02/nOPV2-technical-brief-20201231-EN.pdf https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)31279-6/fulltext https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32541-1/fulltext
	Duration of protection	Clinical trials have shown that nOPV2 provides comparable protection against type 2 poliovirus while being more genetically stable and therefore less likely to revert to a form that can cause paralysis in under-immunized communities.	https://polioeradication.org/wp-content/uploads/2021/02/nOPV2-technical-brief-20201231-EN.pdf
Economic Considerations	Vaccine related costs and resource use	The production of nOPV2 is expected to be similar to production of the existing type 2 oral polio vaccine, which costs US $0.15 per dose. This means that over the long-term, prices for Nopv2 could approach those for nOPV2 once investments in research, facilities and testing have been recouped.	https://polioeradication.org/wp-content/uploads/2021/03/nOPV2-FAQ-20210312EN.pdf

	Vaccine affordability	There is currently global funding for production of 200 million doses of nOPV2 to ensure it will be ready and can be deployed quickly in affected countries. This is being funded by the Bill and Melinda Gates Foundation.	https://polioeradication.org/wp-content/uploads/2021/03/nOPV2-FAQ-20210312EN.pdf
Health Policy and Programmatic Issues	Supply	***Availability of the vaccine and long-term supply***	No data
	Wastage	Wastage should be assessed during the initial use period and the current 50-dose vial size could potentially be changed in the future.	https://polioeradication.org/wp-content/uploads/2021/02/nOPV2-technical-brief-20201231-EN.pdf
	Communication	Communication strategy in place, including crisis communication. This was developed by the department of strategic health communication division Ministry of Health of Uganda that include setting up communications plans, including crisis communication plans to support nOPV2 implementation.	https://polioeradication.org/wp-content/uploads/2020/12/nOPV2-Technical-Guidance-20201210.pdf Ref Dr Immaculate presentation slide 33
	Ability to evaluate	Ministry of Health of Uganda currently meets the country requirements for nOPV2 vaccine deployment of having at least one functional environmental surveillance if nOPV2 is to be used. Currently AFP and environmental surveillance are functional. Uganda adopted the Integrated Disease Surveillance and Response (IDSR) strategy in 2000 serve as a comprehensive strategy to improve disease	https://polioeradication.org/wp-content/uploads/2020/12/nOPV2-Technical-Guidance-20201210.pdf

		surveillance and to improve laboratory and response capacities of WHO Member States in Africa. There is also department of integrated epidemiology, surveillance public health emergencies that deals with surveillance.	
	Regional and international considerations	In November 2020, nOPV2 received a recommendation for use under WHO's Emergency Use Listing (EUL) procedure. WHO's Strategic Advisory Group of Experts on Immunization (SAGE) endorsed accelerated clinical development of nOPV2 and its assessment under EUL in October 2019.	https://polioeradication.org/wp-content/uploads/2021/03/nOPV2-FAQ-20210312EN.pdf
Acceptability and Equity	Equity	Areas with under-immunized populations, the live weakened virus contained in mOPV2 can mutate and spread, causing cVDPV2. nOPV2 will be more useful in these areas.	http://polioeradication.org/wp-content/uploads/2018/07/GPEI-cVDPV-Fact-Sheet-20191115.pdf)