Note for the Record

Consultation between the Global Polio Eradication Initiative and Poliovirus Vaccine Manufacturers, National Authorities for Containment and National Regulatory Authorities

Virtual meeting, 12-13 October 2021

POLIO GLOBAL ERADICATION INITIATIVE

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Foreword

Vaccine supply is essential to delivering on the promise of a polio-free world. As a result, the annual *Consultation between the Global Polio Eradication Initiative and poliovirus vaccine manufacturers, National Authorities for Containment and National Regulatory Authorities* presents a key opportunity to interface with you – our fellow stakeholders – on the road to polio eradication.

There are many important elements that contribute to polio eradication – developing a diversified base of vaccine manufacturers, working to ensure a viable market for manufacturers, researching and developing new technologies, implementing certification and containment requirements, amongst many others – and your engagement on these topics is vital for the GPEI to deliver on its promise.

Recent times have posed fresh challenges for all of us. The onset of the pandemic has been disruptive, rendering unique challenges. There have been limitations placed on manufacturers' ability to produce vaccines, on the GPEI's ability to conduct immunization campaigns, for staff to physically attend their workplaces, all of which has required resilience, and rapid and deft adaptation. We have observed as you've adapted impressively to new context of operating in a pandemic. In this context, we were delighted that over 170 unique accounts from 29 countries logged in during each session, representing 41 manufacturers, the NACs of 20 countries and the NRAs of seven countries.

Despite these disruptions and challenges, there has been some immense progress, such as the rollout of the Novel Oral Polio Vaccine Type-2, and the development of vaccines that provide protection against the Coronavirus. With this in mind, and as we turn our attention to the future, I wish to emphasise that your commitment to the cause of polio eradication is essential to its success, and we – all of the GPEI partners – very much look forward to working with you as we continue to drive towards our shared goal of a polio-free world.

Aidan O'Leary

Director of Polio Eradication, WHO; Chair, GPEI Strategy Committee

Acronyms and Abbreviations

AQAS	Auditor Qualification and Audit Support Plan 2021–2023
bOPV	bivalent oral poliovirus vaccine
CAG	Containment Advisory Group
CC	certificate of containment
CCS	Containment Certification Scheme to support the WHO Global Action Plan for Poliovirus Containment (GAPIII)
COVID-19	coronavirus disease 2019
CP	certification of participation
cVDPV	circulating vaccine-derived poliovirus
dPEF	designated poliovirus-essential facility
EUL	emergency use listing
GACVS	Global Advisory Committee on Vaccine Safety
Gavi	Gavi, the Vaccine Alliance
GAPIII	WHO Global Action Plan to minimize poliovirus facility-associated risk after type-specific eradication of wild polioviruses and sequential cessation of oral polio vaccine use
GCC	Global Commission for the Certification of the Eradication of Poliomyelitis
CWGGCC	Containment Working Group
GMP	Good Manufacturing Practices
GPEI	Global Polio Eradication Initiative
ICC	interim certificate of containment
IPV	inactivated poliovirus vaccine
mOPV	Sabin monovalent oral poliomyelitis vaccine
NAC	national authority for containment
nOPV	novel oral myelitis vaccine
PQ	Prequalification team
SAGE	Strategic Advisory Group of Experts on immunization
SIA	supplementary immunization activity
tOPV	trivalent oral poliovirus vaccine
VLP	virus-like particle
wP	whole-cell pertussis
WPV	wild poliovirus

Executive Summary

The overarching goal of the Consultation is to enable the polio vaccine manufacturers to optimally plan their production over the span of the eradication strategy. Accordingly, three objectives that underpin this goal.

Objective I: Updating on the new 2022-26 polio eradication strategy, and changes to the GPEI

The first objective was primarily addressed by Aidan O'Leary, the Director of Polio Eradication. Mr. O'Leary detailed the timelines of the new strategy, such as interrupting WPV1 transmission and stopping outbreak by the end of 2023, and certifying WPV1 eradication by the end of 2026. Mr. O'Leary also emphasised the need to operate with an emergency tempo, and to re-establish polio eradication as a public health emergency of the highest priority. From GPEI's perspective, there will also be a rebalancing of capacity and decision-making between WHO headquarters and regional and country teams.

Objective II: Developing a shared understanding of the current epidemiology, the status of the programme towards eradication and stopping outbreaks, and the projected demand for polio vaccines over the span of the strategy

In terms of the second objective, Mr. O'Leary detailed the increasingly positive poliovirus epidemiology. Specifically, cases of WPV type 1 (WPV1) and cVDPV are currently decreasing in comparison to the previous 12 months. Mr. O'Leary noted the positive rollout and efficacy of nOPV2, and the ongoing work on preparedness for the use of the vaccine in more outbreak zones.

In terms of the projected demand for polio vaccines over the span of the strategy, Ann Ottosen and Ian Lewis presented on bOPV and emphasised that securing the right vaccines to achieve global eradication requires close collaboration with manufacturers and regulators. Ms. Ottosen noted that SIA calendar for 2023 and beyond has been approved in principle. The assumptions are that funding is available to implement the GPEI SIA calendar; China, India and other countries that use domestic or bilateral funds continue to do so, while 85 countries continue to source OPV for routine programmes through UNICEF. To achieve eradication, GPEI's preliminary demand forecast through to cessation is for 600-700 million doses annually to ensure an uninterrupted supply for preventive SIAs, routine immunization and buffer stock to meet short-term surges in vaccine demand.

In terms of the Global Stockpile of OPV2-containing vaccines, Vachagan Harutyunyan outlined that the stockpile is a mechanism for equitable supply of OPV2-containing vaccines to respond to poliovirus outbreaks and events and is an essential component of the strategy to sustain a polio-free world after global certification. Dr. Harutyunyan detailed that, between 2016 and 2020, over one billion doses of OPV2-containing vaccines were released to countries, and that the demand scenario for OPV2 in 2021-2026 includes the base demand, a 50% buffer and a rolling stockpile, with a supply of Sabin vaccine in case of nOPV2 failure. It is assumed that nOPV2 will continue to be successful and will receive WHO prequalification in 2023, with maintenance of a supply of Sabin OPV2 in the interim; and that nOPV1 and nOPV3 will potentially be available by 2025-2026. Mr. O'Leary emphasised that the current global stockpile of OPV2-containing vaccines is adequate for outbreak response, despite significant challenges to securing an adequate supply of finished nOPV2.

In terms of IPV, Yann Folly detailed Gavi's support for the provision of first and second doses of IPV in the 73 Gavi-eligible countries, with exceptions due to co-financing and eligibility policy. Alejandro Ramirez Gonzalez outlined that the supply and demand for IPV in 2021 was dramatically different from previous years; noting also that the current tender is for the period 2019-2022 with an option for a 12-month extension if the offers contribute to achieving the tender objectives. Ian Lewis outlined that the assumptions for the maximum demand scenario of IPV are that all countries have introduced a second dose of IPV, none will change to a hexavalent product or fractional-dose IPV, and there will

be no change to the Gavi funding policy. UNICEF will request offers to meet the maximum forecasted demand, although it may not award the full quantities. As awards have already been made for 80 million doses for 2023, the unawarded demand is projected to be 30-40 million doses.

Objective III: Provide updates on new vaccine technologies, the regulatory pathways for the licensing of poliovirus vaccines, and the Containment updates and requirements (including the revision of GAPIII and its implementation)

On new vaccine technologies, Simona Zipursky detailed nOPV2, noting how the genome carries five modifications of the Sabin 2 genome, each of which contributes to genetic stability and attenuation and the combination of which prevents detectable reversion to neurovirulence by reducing the capacity of the virus to acquire mutations that increase replication fitness in neuronal tissues. Ms. Zipursky also outlined how clinical trials have shown that nOPV2 provides comparable immunity against PV2 but is more genetically stable and therefore less likely to revert to a form that can cause paralysis in under-immunized communities. nOPV2 can therefore help stop the spread of cVDPV2 outbreaks. She noted that nOPV2 is being rolled out under a WHO emergency use listing (EUL) recommendation, which requires countries to meet readiness requirements prior to deployment of the vaccine. The data collected from use of nOPV2 in the field as well as in ongoing studies has been reviewed by the Global Advisory Committee on Vaccine Safety (GACVS) as well as SAGE. Both groups continue to endorse the use of nOPV2 under EUL. As of end October, over 100 million doses of nOPV2 have been used in seven countries for outbreak response.

In terms of research and product development, Martin Eisenhawer outlined that the priorities for research are vaccine development, laboratory assays, antiviral therapies and clinical trials of different vaccine schedules. Dr. Eisenhawer emphasised that cVDPV2s threaten polio eradication, and nOPV2 must be fully licensed and prequalified; and that the use of S19 strains should be accelerated, and cessation of bOPV after eradication should be planned. On Novel oral poliovirus vaccines, nOPV1 and 3 and IPVs should continue their development, as they will be required in the long term, with an adequate supply and an accessible price. Dr. Eisenhawer also noted that a possible future is that of polio vaccines based on non-infectious processes such as VLP.

On regulatory pathways for poliovirus vaccines, Mathias Janssen outlined that nOPV2 is available in a 50-dose presentation, with a 12-month shelf life at –20 °C – the first vaccine approved under EUL, in November 2020. Mr. Janssen described the steps leading up to EUL, from final clinical and non-clinical studies and quality control with post-listing commitments, inspections for compliance with good manufacturing practice, discussions with WHO on lot release and a protocol review and testing. Since EUL, post-listing commitments include additional clinical data for confirmation of safety and immunogenicity, a report on genetic stability and responses to pending questions on quality, with no major impact on the overall quality of the vaccine.

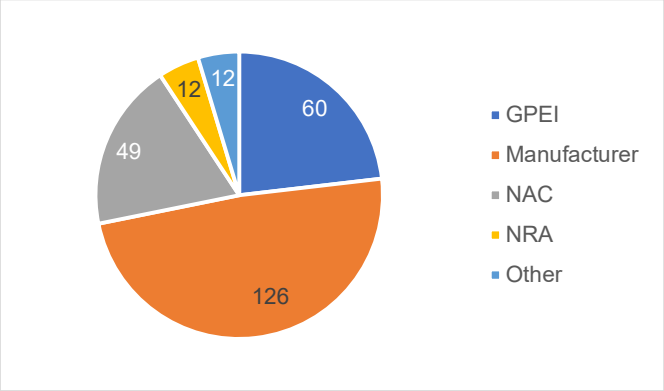
On Containment, Arlene King emphasised that, since 2018, the number of dPEFs has decreased from 89 to 68 (~24%), while 49 of 60 certificates of participation (CPs) have been awarded. In October 2021, 25 countries were retaining poliovirus type-2 material, 20 of 25 countries have nominated NACs, and 19 of the 25 NACs have submitted CP applications for their dPEFs. The challenges to containment are: the five countries that have not managed to initiate containment certification; continued use of mOPV2 for outbreak response, which creates a continuous cycle of surveys and inventories, as will reintroduction of tOPV; lack of priority for poliovirus containment during the COVID-19 pandemic; and the variable readiness of countries to move to the next steps in certification. Dr. King noted that investigations of vaccine “contamination” and reported facility breaches underscore the importance of vigilance in containment.

On GAPIII revision, Harpal Singh outlined that the main changes made are in harmonization and language to reduce redundancy, improve clarity and flow, distinguish requirements from guidance and a change to a risk-based approach taken for polio-prescriptive requirements. Stakeholders’ roles,

activities involved in inventory and destruction and in containment, novel poliovirus strains and criteria for determining containment requirements have been added. Safeguards have been categorized as “laboratory” and “community”, where community safeguards allow a risk-based approach, in addition to vaccination requirements recommended by SAGE. On implementation, the new approach to implementation separates inventory and destruction from containment and assigns the GCC to set the global containment status of strains, in addition to a trigger-based approach.

Attendance

Around 170-180 unique accounts logged in during each session at the Consultation representing the total of 259 participants from 29 countries having registered for the event. Moreover, 41 different manufacturers (126 people registered) attended, as well as 20 countries’ NACs (49 representatives), and seven countries’ NRAs (12 representatives).



Pie chart: The number of registrations per type of organization.

Conclusion

The *Polio Eradication Strategy 2022–2026* offers a comprehensive set of actions that will position the GPEI to deliver on a promise that brought the world together in a collective commitment to eradicate polio. These actions will strengthen and empower the GPEI – in close collaboration with the manufacturers, NACs and NRAs – to achieve and sustain a polio-free world.

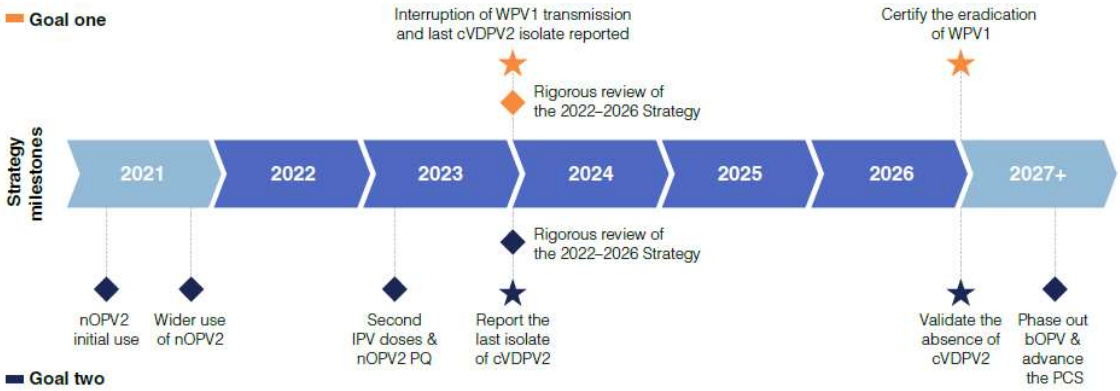
1. Update on strategy and epidemiology

Update on the new strategy, epidemiology, progress towards eradication and stopping outbreaks – Aidan O'Leary (WHO)

The meeting was opened by Aidan O'Leary, Director, Polio Eradication, WHO, and Chair, Global Polio Eradication Initiative's (GPEI) Strategy Committee, who welcomed the many participants from around the world. Mr. O'Leary noted that the main goal of the consultation was to enable the polio vaccine manufacturers to plan optimally their production over the duration of the eradication strategy, from 2022 and 2026. He noted that, despite the limitations imposed by the COVID-19 pandemic on both vaccine manufacturers and polio programme staff, governments and front-line workers had made courageous decisions to resume campaigns, and the programme welcomed that spirit of resilience.

Mr. O'Leary's presentation aimed to develop a shared understanding for all attendees of the new strategy, the status of the programme and integration. He started by outlining the revised strategy and it's two goals: (i) to permanently interrupt poliovirus transmission in endemic countries, and (ii) to stop transmission of circulating vaccine-derived poliovirus (cVDVP) and prevent outbreaks in non-endemic countries. To achieve these goals, the revised organigram of the GPEI emphasizes partnerships, performance and accountability.

Mr. O'Leary delved into some of the specifics of the strategy, such as the need to operate with an emergency tempo, and to re-establish polio eradication as a public health emergency of the highest priority. Moreover, he outlined that the strategy emphasizes collective engagement, particularly with communities, through which the GPEI commits itself to better reflect the needs, voices and capabilities of the broad spectrum of stakeholders on whom eradication depends, and to rebalance capacity and decision-making between WHO headquarters and regional and country teams.



bOPV = bivalent oral polio vaccine; cVDPV2 = circulating vaccine-derived poliovirus type 2; IPV = inactivated polio vaccine; nOPV2 = novel oral polio vaccine type 2; PCS = Post-Certification Strategy; PQ = prequalification; WPV1 = wild poliovirus type 1.
Source: WHO.

Polio Eradication Strategy 2022-2026 planning and budgeting timeline, 2021-2027+.

Expanding on some operational elements of the strategy, Mr. O'Leary outlines some of the key objectives of the strategic framework: generating vaccine acceptance through context-adapted community engagement, expediting progress through extended integration and unified partnerships, improving front-line success through changes to campaign operations, enhancing detection and response through sensitive surveillance, and creating urgency and accountability through advocacy to generate greater political will.

Mr O'Leary outlined that, at the time of the meeting, the environmental surveillance findings for both endemic countries present a unique opportunity. The challenges, however, include risks of

resurgence due to mobile populations, persistently missed children in reservoirs in Pakistan, and seasonal variation. The new Government of Afghanistan has made a commitment to ensure safety and independence but is facing economic collapse and an acute humanitarian crisis. In Pakistan, there is a high level of political engagement in polio vaccination.

Cases due to WPV type 1 (WPV1) and cVDPV appear to be decreasing. In 2021, supplementary immunization activities (SIAs) with both the Sabin and Novel oral poliovirus vaccines type 2 (mOPV2 and nOPV2) were conducted, while preparations for use of novel oral poliovirus (nOPV2) type 2 vaccine are completed or ongoing in 85% of countries at high risk for cVDPV2, of which 38% are verified and 47% are preparing for verification. Post-deployment monitoring requirements will remain; each country must meet the requirements for use of nOPV2; the WHO Prequalification team (PQ), the Global Advisory Committee on Vaccine Safety (GACVS) sub-committee and the Strategic Advisory Group of Experts on Immunization (SAGE) will continue to monitor and/or evaluate nOPV2 performance in the field; and the WHO PQ can withdraw the emergency use listing (EUL) at any time. The “essential initial use criteria” will no longer be required, i.e., countries will not have to provide evidence of functional environmental surveillance or minimum non-polio acute flaccid paralysis and stool sample adequacy before use, the standard interval between OPV campaigns will be four weeks, and the number of required training sessions and documentation will be reduced.

The SAGE re-emphasized that countries must be cautious in considering switching from bivalent OPV (bOPV) to only an inactivated poliovirus vaccine (IPV) schedule, and recommended either a three- or a four-dose schedule at an early age, or a two-dose schedule at a later age, before moving to IPV-only schedules during pre-eradication. The SAGE agreed that whole-cell pertussis hexavalent vaccine could be used in any of the early primary series of IPV only. For nOPV2, the SAGE endorsed a transition from initial to wider use under an EUL and considered that additional studies should be conducted with nOPV2. It endorsed use of nOPV2 with other vaccines, with no limitation on vaccines other than OPV, but retained a one-month interval between campaigns of nOPV2 and other OPV vaccines.

In finishing, Mr. O’Leary emphasised that the current global stockpile of OPV2-containing vaccines is adequate for outbreak response; however, there are significant challenges with the nOPV2 supply, and the situation remains fluid, evolving and unpredictable in the context of COVID.

2. Interrupting poliovirus transmission

Supply of bOPV: SIA calendar and long-term projections – Ann Ottosen and Jason Thompson (UNICEF)

Ann Ottosen’s presentations had the objectives of providing an update on current supply and future projections. She began by outlining that securing the right vaccines to achieve global eradication requires close collaboration with manufacturers and regulators.

The procurement objectives from the 2016 tender remain relevant, i.e., to sustain a sufficient supply of OPV for polio eradication certification and to withdraw OPV from the market responsibly while maintaining the affordability. The demand for bOPV was lower forecast in 2019 and 2020, and this has required adjustments to supply plans and greater flexibility on the part of manufacturers. The demand was 15% below forecast in 2019, due to the cancellation of some campaigns in endemic countries together with the delayed implementation of planned activities and cancellation of some activities in low- to medium-risk countries due to GPEI budget constraints.

In 2020 due to the COVID pandemic there was a dramatic decrease in demand in March, with a slower than expected recovery due to cancellation and postponement of campaigns in many countries resulting in a build-up of ageing stocks both with manufacturers and in countries. There were considerable efforts made in order to align supply and demand in order to mitigate the risk associated

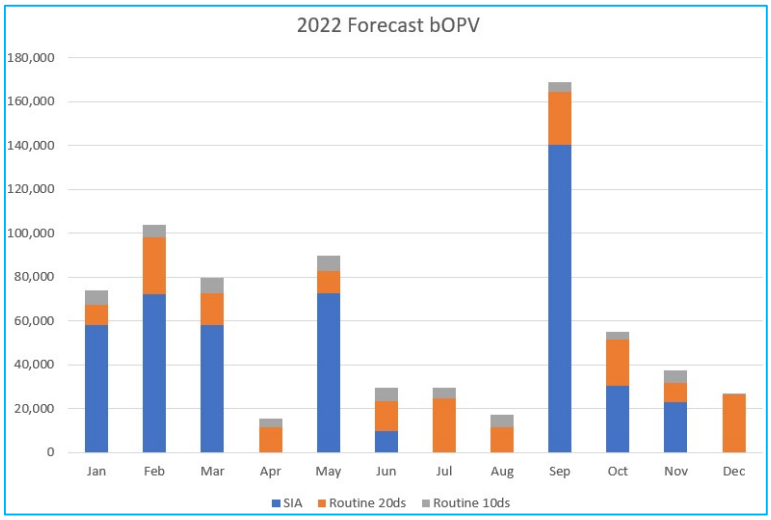
with suppliers holding large stocks in inventory, with UNICEF facilitating the postponement of production with many manufacturers and the release of supplies to third parties. UNICEF also worked closely with countries to ensure acceptance of doses with a short shelf-life, in line with WHO/UNICEF interim guidance issued in March 2021.

The demand forecast for bOPV in 2021 has been implemented to 95% as of September 2021. Requirements for routine vaccination for 2021 had been forecast at an unprecedented high of 241 million doses but has materialized at the usual level of around 190million doses.

The demand for SIAs continued to be affected by COVID-19 in the first half of the year, UNICEF considers it likely that demand will reach the forecasted level as countries look to resume immunization activities in the last quarter of 2021 and the first quarter of 2022. UNICEF's preliminary demand forecast for bOPV in 2022 is estimated to be in the region of 700 million doses. The GPEI calendar for SIA campaigns in 2022 is in the final stages of approval but will continue to be impacted by COVID-19. The UNICEF annual forecasting exercise in ongoing and will factor in unused doses in stock in countries. and will have an impact on the total volumes forecast for the 2022 year.

An additional awards of 20-dose vials for supply in 2022 is in the process of being made, the need for this additional award was due to some manufacturers shifting production capacity to other polio vaccines and to COVID-19 vaccines.

To achieve eradication, GPEI's preliminary demand forecast through to cessation is for 600-700 million doses annually. This volume will be required in order to ensure an uninterrupted supply of bOPV for preventive SIAs and routine demand as well as buffer stock to meet short-term surges in vaccine demand.



The bOPV forecast for 2022.

The calendar for 2023 and beyond has been approved in principle, and GPEI is working to finalize a multi-year budget by end of Q1 2022.

The demand assumptions for the 2022-27 demand forecast are outlined below:

1. that funding is available to implement the GPEI SIA calendar,
2. the governments of China, India and other countries that use domestic or bilateral funds continue to self-finance bOPV supply,
3. the 85 countries supplied by UNICEF will continue to source bOPV for routine programmes through UNICEF.

In addition to bOPV, since 2016, about 900 million doses of type 2-containing vaccines have been procured to respond to cVDPV type 2 outbreaks.

In order to ensure sufficient supply of OPV through to cessation UNICEF continues to work closely with partners as below in order to ensure that the appropriate vaccine supply is available in the coming years will continue to be critical, and a high level of flexibility, transparency and collaboration will continue to be required from suppliers as we work closely to find solutions for supply:

1. the GPEI to forecast current and future vaccine requirements and to ensure recognition of the opportunities, constraints and requirements on the supply side;
2. with countries on their requirements, timelines, funding and supply acceptability; and
3. with suppliers to ensure uninterrupted, timely provision of affordable, quality-assured vaccines of the required type.

The current supply agreements for bOPV are valid until the end of 2022. UNICEF will review its procurement strategy in the first quarter of 2022, including the possibility of extending supply agreements for one year.

A market note will be issued in the coming months providing an update on how UNICEF assesses the current state of bOPV supply and demand market.

During the discussion, questions were asked about the availability of nOPV to replace Sabin OPV. It was suggested that future demand for bOPV might be better understood by a better understanding why some countries abandon its use and adopt an IPV-only regimen. Ms. Ottosen replied that an adequate supply of bOPV has not yet been an issue and that there may be other reasons that countries move to IPV-only. Martin Eisenhawer said the question of whether nOPV1 and 3 would replace bOPV for routine use is under discussion; however, its use and the policy have not yet been established.

Several questions were posed about containment requirements for manufacturing Sabin OPV2 and whether UNICEF would consider that manufacturers should comply with GAPIII for proper containment or could receive one-time approval. Ms. Ottosen replied that proper containment is part of good manufacturing production requirements. Proposals to UNICEF are all reviewed by WHO PQ, the Containment Committee and national containment and regulatory authorities.

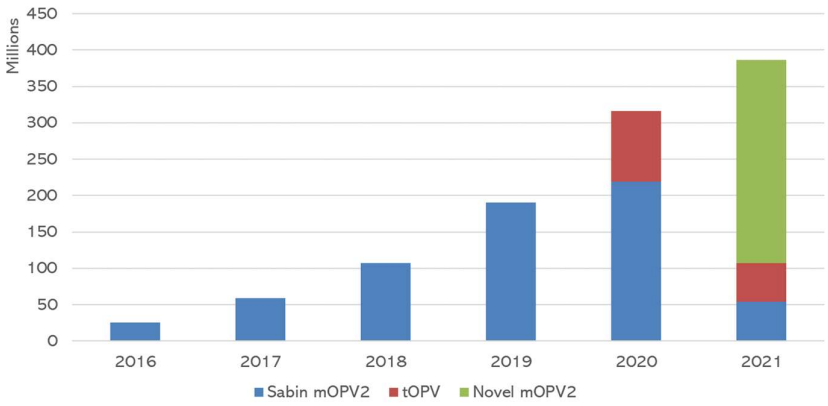
In answer to a question about whether technology transfer was available to permit other manufacturers in countries that produce bOPV to produce IPV or nOPV, Mr. Eisenhawer said that WHO had no programme for technology transfer; however, WHO would be willing to support initiatives between contractors. The Gates Foundation has initiated a project to extend the supplier base of nOPV2 by encouraging such initiatives, and similar projects might be started in the future for OPV1 and OPV3.

Global OPV Stockpile: Mechanism for the supply of vaccines for outbreak response after OPV cessation – Vachagan Harutyunyan (WHO)

Vachagan Harutyunyan made a presentation on the Global OPV stockpile with the objective of developing a shared understanding amongst the attendees of the status of the stockpile, including OPV1 and 3, the trends observed and the latest vaccine requirements. In doing so, Dr. Harutyunyan presented the strategic milestones of the programme over the course of the new strategy, starting from initial use of nOPV2 in 2021 to wider use, provision of second IPV dose and prequalification of nOPV2 in 2023. It was outlined that the timeline projects the reporting of the last isolate of cVDPV2 as forecast for the end of 2023, when the 2022-2026 strategy will be reviewed. Certification of

eradication of WPV1 and validation of the absence of cVDPV2 is forecasted for the end of 2026, with an entry into the post-certification era and phasing-out of bOPV in the following year.

Dr. Harutyunyan outlined that the global stockpile is a mechanism for equitable supply of OPV2-containing vaccines to respond to poliovirus outbreaks and events and is an essential component of the strategy to sustain a polio-free world after global certification of WPV eradication, ensuring the capacity to respond to a potential re-emergence of poliovirus from any source. Between 2016 and 2020, over one billion doses of OPV2-containing vaccines were released to countries, and the strategy for 2022-2026 includes contingency plans that aim to ensure an uninterrupted supply of OPV2 for the response to cVDPV2 outbreaks, whilst also establishing preparedness for the prepositioning of stockpiles of types 1 and 3 OPVs and new products.



Over 1 billion doses of OPV2 released to countries between 2016 and 2021.

Dr. Harutyunyan noted that important decisions must be made at each stage of the strategy in the event of possible failures, risks and delays. The demand scenario for OPV2 in 2021-2026 includes the base demand, a 50% buffer and a rolling stockpile, with a supply of Sabin vaccine in case of nOPV2 failure. The objectives of the 2022-2026 global stockpile strategy are therefore to ensure a sufficient supply of the right mix of OPV2 and of OPV1, 2 and 3 after withdrawal of all Sabin OPVs from routine immunization programmes. It is assumed that nOPV2 will continue to be successful and will receive WHO prequalification in 2023, with maintenance of a supply of Sabin OPV2 in the interim; that Member states with GPEI support will conduct timely, high-quality SIAs with OPV2 to prevent the spread and stop transmission of type 2 poliovirus; that vaccine shelf life is not considered significant in planning due to expected rapid movement of stocks; and that nOPV1 and nOPV3 will potentially be available by 2025-2026.

In answer to a question about the stockpiles for OPV1 and OPV3, Dr.Harutyunyan said that sources of supply of types 1 and 3 OPV are available, but, with development of nOPV1 and 3, planning must remain flexible. A switch from Sabin to Novel OPV could be made if nOPV was available before the end of the strategy, with Sabin vaccine pre-positioned while preparing to introduce nOPV. With regard to when nOPV could be considered definitely to be genetically stable and, therefore, when a decision could be made about a switch, he said that a switch could be considered only when nOPV has been prequalified, probably in 2023. Martin Eisenhawer added that extensive environmental monitoring has been conducted in areas of response with nOPV2, and, with data from clinical trials on genetic stability, shows less reversion to neurovirulence and no recombinants. Genetic stability must nevertheless be monitored over time, especially for mutations. In answer to a question about the stockpiles of bulk and finished OPVs in post certification period, Dr.Harutyunyan said that some supply of finished product will be kept to respond to potential outbreaks quickly; however, most of the OPV supply will be kept as bulk.

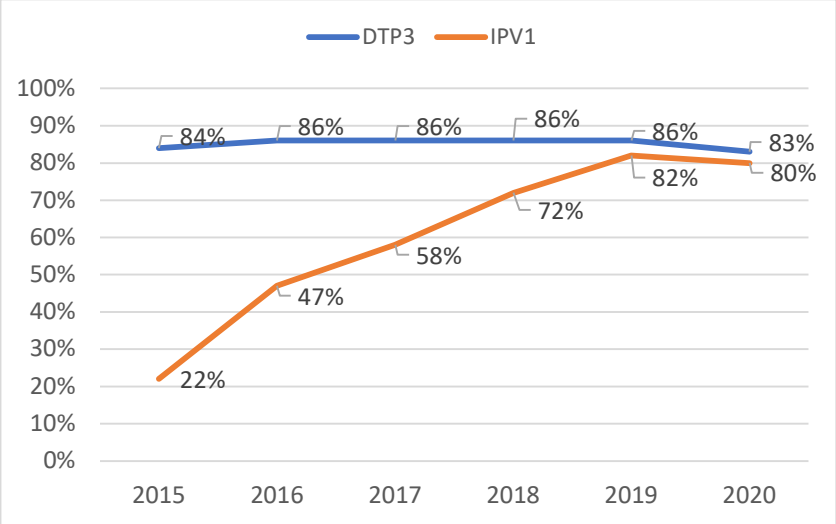
Essential immunization: Supply of IPV (including tender update), second dose, progress in IPV catch-up campaigns and Gavi 5.0 – Ian Lewis (UNICEF), Alejandro Ramirez Gonzalez (WHO), Yann Folly (Gavi, the Vaccine Alliance)

Yann Folly presented an overview of Gavi support for the provision of first and second doses of IPV (IPV1 and IPV2) in the 73 Gavi-eligible countries, with the exceptions to co-financing and eligibility policy. Catch-up immunization was conducted in 33 countries targeting children that did not receive a dose of IPV due to global supply constraints between 2016-2019 and extension of catch-up vaccination beyond 2020.

In October 2020, the SAGE recommended that the best immunogenicity was achieved with IPV1 at 14 weeks and with IPV2 at least four months later, with either a full or a fractional dose; an early dose of IPV1 at 6 weeks and IPV2 at 14 weeks of age could be considered in certain epidemiological circumstances. Globally, 99 countries are targeted for IPV2 introduction out of which 63 Gavi-supported countries.[1] Of these Gavi supported countries, 41 have applied to Gavi, 28 are approved. There are nine countries that have introduced IPV2, either through fIPV or switched to an acellular pertussis hexavalent product. IPV1 catch-up activities were conducted for over 43 million children in 37 countries. Although COVID-19 affected planned catch-ups in 2020, most campaigns have now been implemented, reaching about 10 million children. Nine countries have yet to vaccinate five million missed children, of which six have yet to request Gavi support.

The priorities are to ensure sufficient supplies to Gavi supported countries of their preferred vaccine mix, minimize the cost implications to Gavi and countries, while ensuring sustainable prices for manufacturers and clear guidance and policies for provision of hexavalent vaccine.

Alejandro Ramirez Gonzalez (WHO) said that the supply and demand for IPV in 2021 was dramatically different from previous years. Enough IPV is now available for all countries to introduce a second dose and to complete catch-up immunization.



Global coverage estimates 2016-2020.

Ian Lewis (UNICEF) said that the rapid change in the IPV market in 2020 was due to reduced demand because of delays in catch-up vaccination due to COVID-19 and increased supply availability from both the current manufacturers and with two new suppliers having entered the market. Under the current tender, established manufacturers increased their prices, whereas prices are becoming more

[1] This number excludes the 10 Gavi IPV eligible countries that have already adopted a 2-dose schedule with fractional IPV.

affordable as new manufacturers enter the market. The weighted average price for 2022 is US$ 2.00 per dose, but it is expected to be lower in 2023. The expectation is that 2021would probably end with under-utilization of long-term arrangements.

The current tender is for the period 2019-2022 with an option for a 12-month extension if the offers contribute to achieving the tender objectives. Awards were made to five manufacturers to cover the full forecasted demand up to 2022. For 2023, awards were made to two manufacturers.

For the nest tender, the main objectives as presented during the pre-tender consultation with manufacturers and the consultation with the Procurement Reference Group are to ensure that the health of the market continues to improve and supports countries that decide to continue using IPV-standalone to protect their populations from all types of poliovirus. The specific objectives are to ensure access to an affordable vaccine for those countries and to ensure that the manufacturers of the vaccine can serve the market, up to 10 years after withdrawal of bOPV.

In answer to a query, it was confirmed that Gavi funding would cover 100% of the cost of IPV1 and 2 for the 73 IPV-eligible countries until cessation of OPV use. IPV1 and 2 coverage has always been a priority of the GPEI, despite fluctuations in IPV1 coverage in 2020, particularly in the WHO African Region but also in WPV1-endemic countries and in cVDPV outbreaks; however, supply has been an issue. Gavi now provides support for IPV2 and has initiated active, direct advocacy with all countries, especially those at high risk, to ensure that they are aware of the importance of IPV2 in the current epidemiological context. Despite the challenges of COVID-19, nine countries have already introduced IPV2, including Afghanistan and Pakistan. In answer to a question about the IPV strains used in Sabin vaccine and plans for its introduction, it was stated that two manufacturers are licensed nationally, one of which is prequalified by WHO.

The forecast for the necessary vaccine supplies to give a second dose was based on various considerations and does not include countries such as in India and those in the Americas that buy their own supplies. In answer to a question about whether the roadmap for penta-IPV would be updated in view of the new SAGE position on hexa-IPV, which might increase demand, Yann Folly replied that the new position applies only to new schedules, such as 3 or 3 + 1 IPV schedules, which would also be applicable for hexavalent vaccine. Furthermore, a three-dose schedule is not supported by the Gavi Board. The GPEI does not have a target coverage rate, and it might be useful to consider setting one.

Summary comments and wrap-up – Aidan O'Leary (WHO)

Aidan O'Leary thanked all the participants for their useful presentations, comments and remarks, noting the importance of ensuring a common understanding that is built on common information, and that there were another range of important sessions upcoming during Day Two.

3. New product developments and innovations with potential to impact supply

nOPV2: Update on rollout and transition into wider use – Simona Zipursky (WHO)

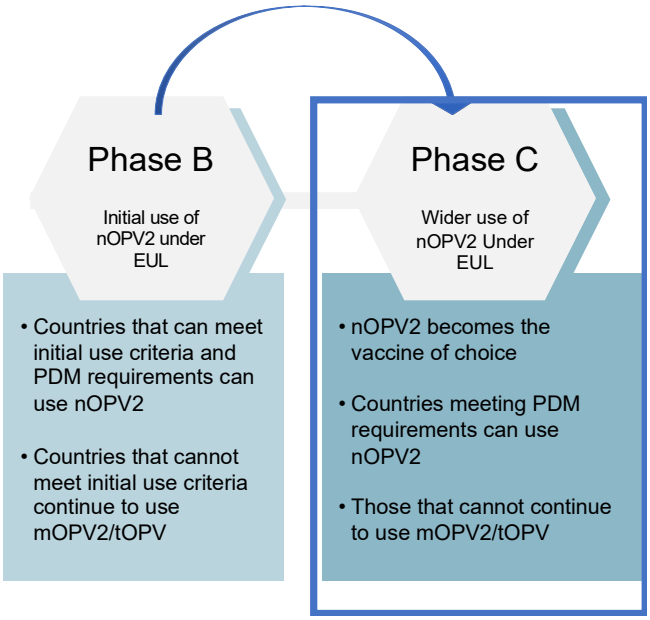
Simona Zipursky (WHO) presented an update on the use of nOPV2 thus far under an Emergency Use Listing, recalling that development of nOPV2 had taken 10 years. The GPEI conducted and consulted molecular and evolutionary studies of the determinants and mechanisms of viral virulence and epidemiological studies to understand the molecular basis of attenuation and the genetic instability of OPVs and how the genetic mutations that accumulate during cVDPV epidemics increase the replication fitness of poliovirus and increase its virulence. It concluded that the major determinant of attenuation is in the 5′ noncoding region and that adaptation and virulence are driven by the high error

rate and recombination capacity of the viral polymerase. These findings were used to engineer a vaccine strain that preserves the antigenic and immunogenic characteristics of the Sabin 2 strain while increasing its safety by stabilizing determinants of attenuation. The nOPV2 genome carries five modifications of the Sabin 2 genome, each of which contributes to genetic stability and attenuation and the combination of which prevents detectable reversion to neurovirulence by reducing the capacity of the virus to acquire mutations that increase replication fitness in neuronal tissues.

nOPV2 received WHO's first recommendation for an EUL for a vaccine in November 2020. nOPV2 is a next-generation version of Sabin OPV2, the cVDPV2 outbreak response vaccine. All countries using nOPV2 under an EUL recommendation must meet requirements for readiness before the vaccine is shipped to the country. Clinical trials show that nOPV2 provides comparable immunity against PV2 but is more genetically stable and therefore less likely to revert to a form that can cause paralysis in under-immunized communities. nOPV2 can therefore help stop the spread of cVDPV2 outbreaks. To date, over 100 million doses of nOPV2 have been used in seven countries for outbreak response; a further 19 countries are accredited to use nOPV2 if necessary, and 14 other high-risk countries are preparing for nOPV2 use. In October 2020, the SAGE endorsed prioritization of use of type 2 vaccines for cVDPV2 outbreak response, in three phases, from initial use under an EUL through to licensure of the vaccine.

The GACVS, at its meeting on 17 September 2021, concluded that there were no obvious warnings or safety concerns to be notified to the SAGE. They noted the substantial quantity of data available and that vaccine doses had been successfully administered in the field. They noted three causally associated cases (one anaphylaxis, one potential case of vaccine-associated paralytic polio and one diagnosis of fever, pending additional information) but concluded that there was inadequate case documentation and clinical diagnostic data for 12 cases regarded as indeterminate.

To date, no events of concern have been reported in clinical studies, and the SAGE has endorsed the transition from initial to wider use of nOPV2. The main considerations for moving beyond initial use were data on safety; furthermore, the GACVS nOPV2 sub-committee concluded that preliminary data on genetic stability support the decision to move beyond initial use. In full-genome sequencing, the primary attenuation site was unchanged in all isolates, and none of the nOPV2 isolates was recombinant. In the wider-use phase, nOPV2 will still be used only for outbreak response but with fewer restrictions, including fewer readiness verification requirements, use in campaigns with other vaccines and with other interventions, administration with IPV (although not usually recommended) and a delay of only four weeks between use of nOPV2 and other OPVs in campaigns.



SAGE endorsed the transition from initial to wider use of nOPV2.

The move towards full licensure is on schedule. It requires timely completion of phase-III studies and studies in naïve infants, with coordinated submission of clinical data (from new and previous studies) to WHO PQ. The main risk to timely completion of the studies is COVID-19. Additional clinical studies are being planned on administration at a shorter interval, to a wider age group and in outbreaks.

In reply to questions, Ms. Zipursky said that, if cVDPV continues to circulate widely, nOPV2 could potentially be introduced into routine schedules. It would be replaced by the new trivalent formulation, which is, however, several years away. Furthermore, the effectiveness of nOPV2 in resolving outbreaks is not yet known, although the results of the trial should be available in the first half of 2021. nOPV2 would have to be fully licensed before its introduction into routine schedules.

In response to a question about whether enough nOPV2 is available to respond to cVDPV outbreaks, she replied that there is no shortage of type 2-containing vaccine for countries to respond to such outbreaks. The most important considerations are the timeliness and quality of the response, with mOPV2 or nOPV2 or even trivalent OPV (tOPV). The company has adjusted its planning to ensure that the most nOPV2 possible will be available next year, and another manufacturer will be added in 2023.

In answer to a question about whether the nOPV may replace bOPV or IPV for routine immunization, Ms. Zipursky recalled that nOPVs reduce the risk of reversion but do not eliminate it. Therefore, it would not be used instead of IPV, which is associated with zero risk, if polio is under control globally. Furthermore, as different regions have different risks of poliovirus circulation, a choice for one region might not be suitable for another. In answer to another question, she said that nOPV2 had been isolated in the stool of one AFP case in Nigeria, where about 70 million doses have been used. Classification of the case still under discussion by the national regulatory body. In answer to a further question, she confirmed that a four-week gap is recommended before and after administration of an OPV.

Research and product development priorities – Martin Eisenhawer (WHO)

Martin Eisenhawer (WHO) presented with the objective of enabling manufacturers to plan their research and development and production, including updates on nOPV1/3 development, Sabin IPV, and virus-like particles.

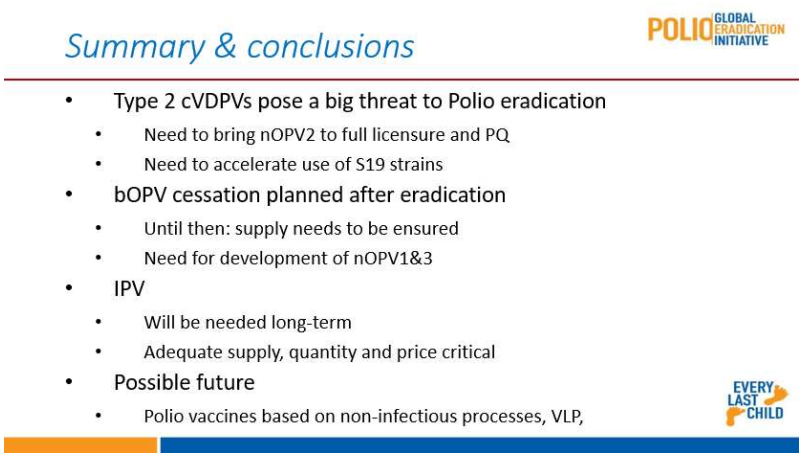
Dr. Eisenhawer outlined that the priorities for research are vaccine development, laboratory assays, antiviral therapies and clinical trials of different vaccine schedules. Vaccine development so far has resulted in several generations of OPV and IPV, development of virus-like particles (VLPs), Sabin IPV and NIBSC S19. Future possibilities are RNA, DNA or vector vaccines. He mentioned the availability of poliovirus strains and development on microarray patches and dmLT-adjuvanted IPV. The history of OPVs started with licensing of tOPV in 1963 and continued through mOPV1, 2 and 3 and bOPV to the most recent nOPVs. nOPV2 is the first vaccine listed under a WHO EUL. More than 100 million doses have been administered in seven countries, and it will be used more widely following SAGE recommendation for wider use. Full prequalification of nOPV2 is expected in 2023. nOPV1 and 3 are being developed by the same consortium as nOPV2 with similar genetic constructs to ensure comparable immunogenicity but greater genetic stability than Sabin vaccines. The timeline of clinical development of nOPV1, nOPV3 and nOPV multivalent projects phase-II trials was mentioned.

VLPs are being developed to obtain a non-infectious polio vaccine with no containment requirements, to be used after eradication. Research and development are being led by a consortium headed by the University of Leeds (United Kingdom) based on a yeast expression system, with baculovirus as the back-up. The yields and purity are improving, and encouraging results have been obtained. After a call for expressions of interest for commercialization in July 2019, discussions are underway with various manufacturers and will be considered by the WHO VLP advisory panel at its next meeting, in November 2021.

With regard to Sabin IPV, under the WHO technology transfer project, two manufacturers have obtained national licensure, one has obtained WHO PQ, and one expects national licensure by the end of 2022. Sabin strains suitable for OPV and sIPV are SO+1 types 1 and 2 and RSO type 3. S19 is suitable only for IPV as it is non-infectious for humans. The stains are held by NIBSC, with a limited amount of pre-GMP seeds. The intellectual property owner is the Health Security Agency in the United Kingdom (former Public Health England), which will provide it to small number of companies.

The idea of RNA, DNA and vector vaccines is to explore the potential of technology used for COVID-19 vaccines for polio as an incentive for manufacturers to broaden their portfolio of products based on the same technology in a favourable funding environment. The challenge for use against polio is that the antigenic entity is the whole poliovirus capsid with four structural proteins (VP1–4). Its RNA is approximately 7500 NTs. GPEI seeks feedback from stakeholders.

Type 2 cVDPVs threaten polio eradication, and nOPV2 must be fully licensed and prequalified. Use of S19 strains should be accelerated, and cessation of bOPV after eradication should be planned. Until then and beyond, the supply must be ensured. nOPV1 and 3 and IPV should continue their development, as they will be required in the long term, with an adequate supply and an accessible price. The possible future is polio vaccines based on non-infectious processes such as VLP.



Summary and conclusions slide to the Research and product development priorities presentation.

In answer to the question about technological transfer, Dr. Eisenhawer said that it would depend on the product in question. The programme for Sabin IPV is now closed. Manufacturers interested in technology transfer for VLPs could contact him, and it would be determined whether they had already produced prequalified products and whether they had experience in working with yeast expression systems. Usually, contractual agreements are made between the primary developer of the technology and the manufacturer. For VLPs, there would be an obligation to make available to the United Nations markets products that are cost-effective and can be used in low- and middle-income countries under prequalification. Engagement will be maintained with NRAs with regard to technology transfer to ensure comparable methods.

In answer to another question, Dr. Eisenhawer said that, in principle, work to develop an even more stable strain of nOVP2 would be conceivable. The timeline would, however, be long and he alluded to the available nOPVs and S19. In order to coordinate production of new vaccines with containment, he said that that he would continue collaboration with both the Containment Advisory Committee (CAG) and WHO staff working on containment.

Next generation sequencing (NGS) – An alternative to animal based neurovirulence testing (NVT) of polio vaccines – Kutub Mahmood, PATH

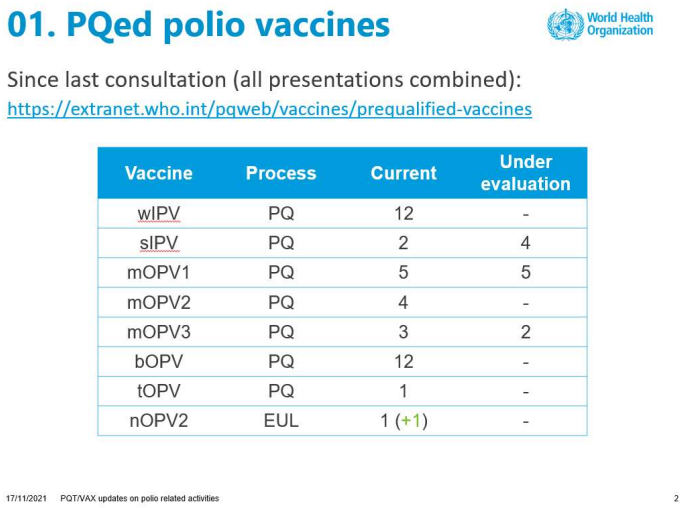
Kutub Mahmood described a programme for testing live attenuated Sabin OPV, nOPV and IPV for neurovirulence by next-generation sequencing rather than in monkeys or in poliovirus receptor transgenic mice. The use of monkeys is restricted in some countries, and there is only one supplier of these transgenic mice. Tests in animals are expensive, and highly-trained technicians are required for intra-spinal inoculations. Furthermore, few laboratories are licensed for GAPIII containment. In the mid-1990s, an attempt was made to replace animal testing partly with in vitro assays; however, only limited genomic loci could be assayed, and mutations at other sites were missed. Replacement of animal testing by in vitro molecular surrogate assays is therefore highly desirable.

The main activities of the programme are testing of Sabin type 1, 2 and 3 vaccine materials that have passed quality control tests for batch release by next-generation sequencing (NGS) to establish whole-genome profiles and the consistency of production runs. NGS results obtained with a bio-informatics software tool will be compared with those of standard animal neurovirulence tests. A collaborative study is planned to assess the usefulness of the method for testing Sabin polioviruses types 1, 2, and 3, and a workshop will be held to discuss the results of the study, validation of the assay and development of pass–fail decision criteria. The method will then be submitted to the WHO Expert Committee on Biological Standardization for review to determine whether it could replace

animal testing. The work is being conducted in collaboration with OPV and IPV manufacturers and national laboratories and with support from WHO.

Update from the vaccine prequalification team on polio-related activities – Mathias Janssen (WHO)

Mathias Janssen (WHO) presented with the objective of providing a briefing on key regulatory developments in polio vaccines. Mr. Janssen listed the polio vaccines that had been prequalified since the previous consultation. With regard to poliovirus vaccine stockpiles, the PQ team has assessed the compliance of artwork samples with approved packaging requirements set out with UNICEF, compared the quantities submitted with those purchased and the expiry date with the approved shelf life. It has also monitored data for conformity, consistency and trends. mOPV2 is provided by three suppliers, with shelf lives of nine, five and two years; 354 batches have been included after review. tOPV is provided by one supplier, with a two-year shelf life, and 103 batches have been included; nOPV2 is provided by one supplier, with a 12-year shelf life, with 61 batches included. Bulk stocks of mOPV2 are available from one supplier, with a 20-year shelf life, and of nOPV2 from one supplier with a shelf life still being assessed.



Vaccine	Process	Current	Under evaluation
wIPV	PQ	12	-
sIPV	PQ	2	4
mOPV1	PQ	5	5
mOPV2	PQ	4	-
mOPV3	PQ	3	2
bOPV	PQ	12	-
tOPV	PQ	1	-
nOPV2	EUL	1 (+1)	-

Overview of prequalified polio vaccines.

nOPV2, a live viral vaccine from a genetically modified type 2 Sabin strain, is available as a ready-to-use liquid in a 50-dose presentation, a 12-month shelf life at –20 °C and a three-month storage period at 5 ± 3 °C. It was the first vaccine approved under EUL, in November 2020. He described the steps leading up to EUL, from final clinical and non-clinical studies and quality control with post-listing commitments, inspections for compliance with good manufacturing practice, discussions with WHO on lot release and a protocol review and testing. Since EUL, post-listing commitments include additional clinical data for confirmation of safety and immunogenicity, a report on genetic stability and responses to pending questions on quality, with no major impact on the overall quality of the vaccine. Since EUL, workshops have been held on authorization for use in countries and for manufacturers' agreement to share the dossier and generate additional data.

In the future, the shelf life will be extended and the incubation temperature for virus culture will be changed from 33.3 ±0.5 °C to 33.3–34.0 °C, the latter being under review. Full prequalification will follow the requirements of the EUL procedure.

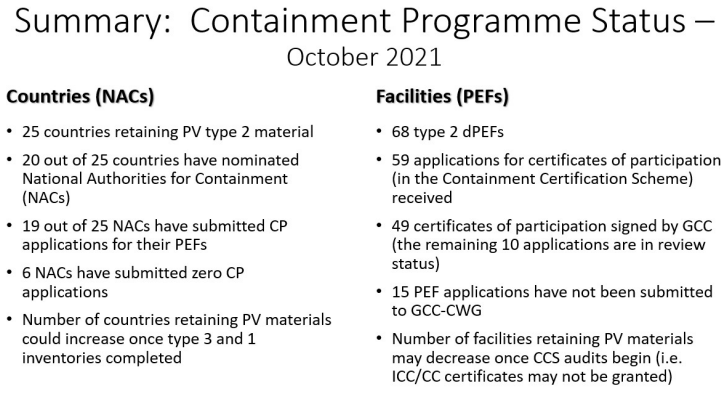
In answer to a question, Mr. Janssen confirmed that whole-cell and acellular pertussis hexavalent vaccine, including IPV, would be on the list of prequalified vaccines and those are under evaluation.

4. Containment and certification

Global containment update – Arlene King (Global Certification Commission)

Arlene King (Chair, Containment Working Group, Global Certification Commission) presented the global containment update. Dr. King recalled World Health Assembly Resolution WHA71-16 of 2018, which urges all Member States to accelerate certification of poliovirus containment, to make inventories of polioviruses, destroy unneeded materials and ensure immediate reporting of any confirmed breach in poliovirus containment. Member States that retain polioviruses were also urged to reduce to a minimum the number of facilities designated for retention of polioviruses, to appoint, no later than the end of 2018, a competent national authority for containment (NAC) and to request facilities designated to retain poliovirus type 2 to formally engage in the Containment Certification Scheme (CCS) no later than 31 December 2019. Containment oversight and advisory bodies have remained the same. The number of countries with "designated poliovirus essential facilities" (dPEF) has remained constant at 25 since 2019, while the number of NACs decreased in 2021, such that 20% of countries that retain poliovirus materials do not have an NAC, which is non-compliant with WHA 71.16.

Since 2018, the number of dPEFs has decreased from 89 to 68 (~24%), while 49 of 60 certificates of participation (CPs) have been awarded, although 15 requests were not submitted from six countries. In October 2021, 25 countries were retaining poliovirus type-2 material, 20 of 25 countries have nominated NACs, and 19 of the 25 NACs have submitted CP applications for their dPEFs. The number of countries that hold poliovirus materials might be higher once the inventories of types 1 and 3 are completed. There are 68 type 2 dPEFs, and 59 applications (note: this has increased to 60, at the time of writing (10 December 2021)) for participation in the CCS have been received, of which 49 have been signed by the Global Certification Commission (GCC), and the remaining 10 are under review. The number of facilities retaining poliovirus materials may be lower once CCS audits begin, as interim containment certificates (ICCs) and containment certificates (CCs) may not be granted.



Summary of the Containment Programme Status (as of October 2021).

COVID-19 has affected poliovirus containment, as many WHO focal points have been reassigned for months, and most NACs have been reassigned to their national response to the pandemic. Surveys and validation of type 1 and 3 infectious and potentially infectious material have been delayed. Nevertheless, progress in the CCS continues, some NACs have stated their intention to present

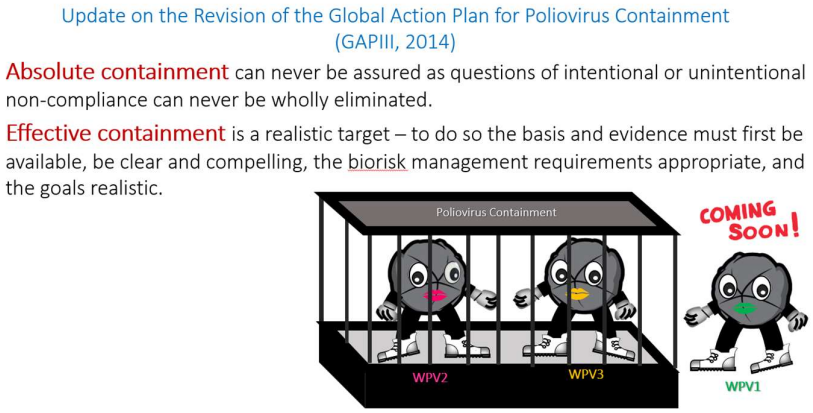
applications for interim certificates of containment in 2022, and standardized tools and an Internet platform for such applications have been prepared. The Containment Working Group has reviewed 60 CPs since 2018 and awarded 50. The GPEI Containment Management Group has initiated the development of a Containment Strategic Plan for 2022-2026.

In July 2021, the GCC recommended extension of the validity of current CPs to the end of December 2022 (from the current expiration date of April 2022) upon receipt of a formal request from an NAC. Guidance on potentially infectious material has been revised and updated. Although revision of GAPIII began in September 2020, the current version remains the reference.

The challenges to containment are: the five countries that have not managed to initiate certification; continued use of mOPV2 for outbreak response, which creates a continuous cycle of surveys and inventories, as will reintroduction of tOPV; lack of priority for poliovirus containment during the COVID-19 pandemic; and the variable readiness of countries to move to the next steps in certification. Investigations of vaccine "contamination" and reported facility breaches underscore the importance of vigilance in containment. Containment programmes require long-term global oversight but risk loss of political will in a competing environment.

Containment Advisory Group recommendations, GAPIII revision and implementation, and TRS amendments – Harpal Singh (WHO)

Harpal Singh (WHO) recalled that the Containment Advisory Group (CAG) in 2018 had welcomed the transfer of containment oversight and documents from SAGE, and had recommended that the Secretariat coordinate a detailed revision, with a public consultation. Although absolute containment can never be assured, as intentional or unintentional noncompliance can never be wholly eliminated, effective containment is a realistic target when based on evidence, appropriate biorisk management and realistic goals. The current version of GAPIII was published in 2015, and the international landscape of both poliovirus eradication and biosafety best practices continue to evolve.



Containment and the revision of GAPIII.

Since publication, several guidance documents have been published by WHO to refine the concepts of biorisk management, some of which were at odds with GAPIII. A stakeholder solicitation of technical comments on Annexes 2 (biorisk management standard for facility retaining WPV/VDPV) and 3 [biorisk management standard for facility retaining OPV/Sabin (no WPV)] of GAPIII was organized between September and October 2020, and 399 comments were received. The issues raised most frequently were: facility physical requirements, lack of clarity, cumbersome structure, redundancy of many requirements, lack of harmonization among guidance documents and difficulty of

meeting both performance and prescriptive requirements within one standard. Meetings are being held with stakeholders to discuss the sections, subsections or chapters that should be removed, replaced or added to provide guidance on the overall organization of the revised GAPIII, which is expected to be ready for endorsement by the CAG in February 2022.

The main changes made are in harmonization and language to reduce redundancy, improve clarity and flow and distinguish requirements from guidance. Stakeholders' roles, activities involved in inventory and destruction and in containment, novel poliovirus strains and criteria for determining containment requirements have been added. Safeguards have been categorized as "laboratory" and "community", which allows a risk-based approach, in addition to vaccination requirements. The new approach to implementation separates inventory and destruction from containment and assigns the GCC to set the global containment status of strains, in addition to a trigger-based approach. Annexes two and three have been combined to reduce redundancy, with clear requirements for WPV after global certification. The presentation has been revised for better readability, and the introduction now includes a section describing the structure, organization and intended use of the standard. The requirements have been harmonized with relevant standards, and requirements for which evidence was lacking have been replaced by risk-based language; risk assessment is emphasized in all elements.

In the ensuing discussion, Dr.Harutyunyan noted that the topic of containment had received the most comments from participants before the consultation. In response to a question about whether dPEfs in a country without a designated NAC could proceed with containment certification, Arlene King said that dPEFs should contact their national government with respect to establishment of a NAC and advocate for such a body; they could also contact WHO.

It was confirmed that WHO is supporting qualification of GAPIII auditors and additional options are being addressed by the GCC. Dr. King said that the GCC- CWG may consider countries to pursue the ICC application phase in the absence of qualified GAPIII auditor if justification and relevant documentation can be provided to demonstrate the national auditor e.g., GMP meet the intent of the CCS and AQAS. Nicoletta Previsani said that training for candidate auditors was begun many years ago and is continuing, and auditor qualification activities have now started.

It was noted that PQ inspections of facilities do not address the safety of production as described in TRS 1016 and TRS 1028. Additional information was requested on the commencement of containment for WPV3 and containment implementation of WPV1, Sabin 1 and 3. Dr. King said that countries are being asked through regional certification commissions whether they retain or intend to retain those materials. Dr. Previsani added that, currently, there is no containment requirement to contain Sabin 1 or 3, as they are widely used in vaccines around the world, and, as WPV1 is not yet eradicated, there is also no requirement for containment. As WPV3 was eradicated several years ago, work is under way to commence the containment of WPV3.

5. Interactive breakout groups

For this session, the participants were divided up into one of three interactive breakout groups, each facilitated by members of the GPEI. The following provides a summary of the discussions, as reported back to plenary by the various facilitators.

Group 1: Containment matters and GAPIII: Ondrej Mach (WHO) and other WHO staff reported that most of the comments during the discussion had been on the practicalities and operationalization of containment, extending the current CPs and initiating work on ICCs. It had been noted that communication between dPEfs and NACS was not always optimal. The meeting of NACs next week would discuss the timeline and process of extension of CPs, which will also be applied to ICCs, with

the required communication between NACs and the CWG concerning ICC documentation. Various activities for qualifying auditors were described, and further questions were asked about the revision of GAPIII, to which the CAG has not yet provided input.

Group 2: Challenges to polio vaccine manufacturing: Ian Lewis (UNICEF) noted that, with regard to bOPV, the market would be closed down in a responsible manner. What is important is that no-one takes unilateral action to jeopardize continued availability of vaccine until it is no longer used. Manufacturers must have forecasts of at least two years, as bOPV manufacturing takes at least 18 months and several months more are required to order the raw materials before they start bulk production. Shorter-term forecasting is also necessary to ensure that manufacturers do not overproduce.

For IPV, forecasting is also required to account for uptake of a second dose, which is not occurring as rapidly as was expected, partly due to country decisions and partly, when they have the vaccine, to the COVID-19 pandemic. Both the accuracy and the length of forecasting will be improved by both the GPEI and Gavi. Several manufacturers have experienced lack of raw materials, which have been prioritized for COVID-19 vaccines and also, in some countries, prioritized for national vaccine manufacture. Longer forecasting will also be necessary to account for the two-year lead time required for obtaining some raw materials.

Group 3: Research: Current and future priorities: During this breakout session, it was stressed that developing vaccines, diagnostics, and other tools to eradicate polio is a time-consuming and resource-intensive endeavour. Therefore, to facilitate the research for the polio programme GPEI and WHO should:

- Establish the objectives of the polio product research
- Set polio product research planning horizons that are aligned with eradication and post-certification strategies and plans
- Provide guidance on priority products that need development in the coming years
- Define whether the scope of the polio product research should expand beyond vaccines

In response to the question of what WHO and GPEI partners could do to facilitate polio-related research, the group concluded that industry must have a strong investment case for developing a new product. To minimize business risks, a clear demand forecast is required from GPEI of when and which type of vaccine is necessary. It was emphasized that the vaccine market is shaped by GPEI partners and not by the manufacturers. The industry also pointed out that, for hexavalent vaccines with clear usefulness, it would be difficult and time-consuming to change a component, such as an antigen, both operationally and to meet regulatory requirements.

Vachagan Harutyunyan added that a number of requests had been made for stronger leadership from the GPEI, more transparent planning, clearer objectives, more consultation, more information-sharing and agreement on parameters.

Summary comments and closure of the meeting

Summary comments and wrap-up – Aidan O'Leary (WHO)

Aidan O'Leary thanked all participants for their active involvement in the consultation, which had been particularly informative. He welcomed the comments made throughout the consultation on the importance of accurate forecasting and the refinement of the research agenda. The vaccine manufacturers had also clearly defined their interests and what they are prepared to do, and the GPEI would align its programmes as closely as possible with those views. The field of poliovirus containment had been clearly presented, and he welcomed further interaction with the NACs in the coming days. The frameworks, plans, strategic direction and approaches to containment must be as

clear, concise and concrete as possible. As the world reaches zero cases of polio, all aspects of the programme must be aligned. Although one aim of the consultation was to bring specific issues to the fore, it was also an opportunity to strengthen the collaboration. The team would now work to ensure that the issues raised are addressed.

Mr. O'Leary encouraged participants to raise any issues that they considered had not been addressed to their focal points to ensure that GPEI had the clearest picture possible of their views. The deliberations of the consultation and any other feedback would be communicated to the GPEI Strategy Committee and to the Polio Oversight Board before its next session, in early December.

Annex I: Agenda

AGENDA

Consultation between the GPEI and Poliovirus Vaccine Manufacturers, NACs and NRAs

Date: 12-13 October 2021

Time: 10.00-14.15 [approximately] (CET / Geneva time)

Online: Zoom

Chair	Aidan O'Leary (Director of Polio Eradication, WHO; Chair, GPEI Strategy Committee)
Goal	Enable polio vaccine manufacturers to optimally plan their production over the span of the poliovirus eradication strategy
Objectives	Apprise attendees on the new 2022-26 polio eradication strategy, and changes to GPEI governance and management Develop a shared understanding of the epidemiology, the status of the programme towards eradication and stopping outbreaks, and the projected demand for polio vaccines over the span of the strategy Bring attendees up-to-date on new vaccine technologies, regulatory pathways for the licensing of poliovirus vaccines, and poliovirus containment updates and requirements (including GAPIII revision and its implementation)

Tuesday, 12 October	
10.00-10.30 **Introduction**	
Welcome and opening remarks	Aidan O'Leary (WHO)
Housekeeping and feedback on survey	David Woods (WHO)
10.30-11.30 **SESSION I: Update on strategy and epidemiology**	
Update on the new strategy, epidemiology, progress towards eradication and stopping outbreaks *Develop a shared understanding of the new strategy, the status of the programme and integration*	Aidan O'Leary (WHO)
11.30-11.45 Break	
11.45-13.30 **SESSION II: Interrupting poliovirus transmission**	
Supply of bOPV: SIA calendar and long-term projections *Update on current supply and future projections*	Ann Ottosen and Jason Thompson (UNICEF)
Global OPV Stockpile: Mechanism for the supply of vaccines for outbreak response after OPV cessation *Develop a shared understanding of the status of the stockpile, including OPV1 and 3, trends and vaccine requirements*	Vachagan Harutyunyan (WHO)
Essential Immunization: Supply of IPV (including tender update), second dose, progress on IPV catch-up campaigns and Gavi 5.0 *Objective: Brief on the status of polio eradication in EPI, supply of IPV and Gavi 5.0*	Ian Lewis (UNICEF), Alejandro Ramirez Gonzalez (WHO) Yann Folly (Gavi)
(Placeholder – in case some additional presentations required)	
13.30-13.40 **Wrap-up**	
Summary comments and wrap-up	Aidan O'Leary (WHO)

Wednesday, 13 October	
10.00-10.05 **Introduction**	
Welcome and opening remarks	Aidan O'Leary (WHO)
10.05-11.20 **SESSION III: New product developments and innovations with potential to impact supply**	
nOPV2: Update on rollout and transition into wider use *Update on nOPV2 use under an Emergency Use Listing*	Simona Zipursky (WHO)
Research and product development: Update on GPEI's priorities *Enable manufacturers to plan their R&D and production, including updates on nOPV1/3 development, Sabin IPV, virus-like particles*	Martin Eisenhawer (WHO)
Update from Vaccine Prequalification Team on polio-related activities *Brief on key regulatory developments in polio vaccines*	Mathias Janssen (WHO)
11.20-12.20 **SESSION IV: Containment and certification**	
Global Containment update *Update on status of Containment certification*	Arlene King (Global Certification Commission)
Containment Advisory Group recommendations, GAPIII revision and implementation, and TRS amendments *Update on the revision and recommendations with potential impact on manufacturers, and the timelines*	Harpal Singh (WHO)
12.20-12.40 Break	
12.40-14.10 **SESSION V: Interactive breakout groups** *(running in parallel)*	
Interactive breakout groups (45 minutes each): Group 1: Containment matters and GAPIII Group 2: Challenges to polio vaccine manufacturing Group 3: Research: Current and future priorities *Discuss specified challenges and potential solutions*	Ondrej Mach (Containment) Ian Lewis (Manufacturing) Martin Eisenhawer (Research)
Return to plenary: Facilitators report back (for 7-10 minutes each) on their group	Facilitators
14.10-14.20 **Wrap-up**	
Summary comments and wrap-up	Aidan O'Leary (WHO)

Annex II: Registered organizations

AJ Vaccines

L'Agence nationale de sécurité du médicament et des produits de santé (France)

Australian Department of Health

Batavia Biosciences

Beijing Biological Products Institute Co., Ltd.

Beijing Minhai Biotechnology Co., Ltd

Bharat Biotech International Limited

BIBP of Sinopharm

Bill and Melinda Gates Foundation

Bilthoven Biologicals (Serum Institute of India)

Biological E Ltd.

Bio-Manguinhos

Cadila Healthcare Limited

Centers for Disease Control and Prevention (USA)

Central Drugs Standard Control Organisation (India)

Autoridad Reguladora de Medicamentos, Equipos y Dispositivos Médicos de la República de Cuba (NAC)

Central Institute for Experimental Animals (Japan)

Centre for Biosecurity and Biopreparedness (Denmark)

China CDC

Chumakov Federal Scientific Center for Research & Development of Immune-and-Biological Products of Russian Academy of Sciences

China National Biotec Group

Containment Working Group (GPEI)

Dalla Lana School of Public Health, University of Toronto

EPI-Government (Pakistan)

Federal Agency for Medicines and Health Products (Belgium)

Federal Budgetary Institution of Healthcare "Federal Center for Hygiene and Epidemiology" of the Federal Service for Surveillance (USA)

Federal Hygienic and Epidemiological Center (Rospotrebnadzor)

Federal Service for Surveillance on Consumer Rights Protection and Human Well-Being (Rospotrebnadzor)

FSASI “Chumakov FSC R&D IBP RAS”

Gavi, the Vaccine Alliance

GlaxoSmithKline

Gryphon Scientific

Haffkine Bio Pharmaceutical Corporation Limited

Health Canada

ICMR-National Institute of Virology, Pune (India)
Iran Food and Drug Administration
IMBCAMS
Indian Council OF Medical Research
Indian Council of Medical Research, Delhi
Indonesian FDA/BPOM
Institute of Medical Biology Chinese Academy of Medical Sciences
Intravacc.
Jansen Vaccines / J&J
KM Biologics Co., Ltd.
Korea Disease Control and Prevention Agency
Korea NAC
LGChem
Ministry of Health, Labour and Welfare of Japan
Ministry of Health of Iran
National Authority for Containment (United Kingdom)
National Center For Global Health And Medicine (Japan)
National Emergency Operation Center Pakistan
National Institute for Viral Disease Control and Prevention (China)
National Institute of Health (Pakistan)
National Institute of Hygiene and Epidemiology (Vietnam)
National Institute of Infectious Diseases (Japan)
National Institutes for Food and Drug Control (China)
National Public Health Center, Hungary
National Institute for Biological Standards and Control (United Kingdom)
National Institute of Health (Pakistan)
National Institute of Health Research and Development (Indonesia)
Pan American Health Organization (PAHO)
Panacea Biotec Ltd.
PATH
PharmaJet
Polyvac
PT Bio Farma (Persero)
Public Health Agency of Canada
Public Health Agency of Sweden
Razi Vaccine and Serum Research Institute
Republican Research and Practical Center for Epidemiology and Microbiology (Belarus)
Riskren Pte Ltd
Rotary International
Sanofi Pasteur

Serum Institute of India
Sinopharm BIBP
Sinovac Biotech Co., Ltd.
Service Publique Fédéral - Santé publique, Sécurité de la Chaîne Alimentaire et Environnement (Belgium)
Stellenbosch University
Taconic Biosciences, Inc.
Temptime Corporation
Tropical Medicine Institute Pedro Kouri, Cuba
UK Health Security Agency
UNICEF
University of Belgrade (Serbia NAC)
University of Leeds
U.S. Food and Drug Administration Office of Vaccines
Vabiotech
Valneva Sweden AB
Viroclinics Biosciences
World Health Organization
Zydus Cadila Health Care Ltd