Note for the Record

GPEI Consultation with OPV/IPV Manufacturers, National Authorities for Containment and National Regulatory Authorities

Virtual meeting, 12-13 October 2020

POLIO GLOBAL ERADICATION INITIATIVE

Contents

Abbreviations

AFP	Acute Flaccid Paralysis
bOPV	Bivalent Oral Poliovirus Vaccine
CAG	Containment Advisory Group
COVID-19	Coronavirus disease 2019
cVDPV	Circulating vaccine-derived poliovirus
EUL	Emergency Use Listing
Gavi	Gavi, the Vaccine Alliance
GPEI	Global Polio Eradication Initiative
IPV	Inactivated Poliovirus vaccine
MAP	Microassay patch
mOPV	Monovalent Oral Poliovirus Vaccine
nOPV	Novel Oral Poliovirus Vaccine
SAGE	Strategic Advisory Group of Experts
SIA	Supplementary immunization activity
tOPV	Trivalent Oral Poliovirus Vaccine
VLP	Virus-like particle
WPV	Wild poliovirus

1. Interrupting poliovirus transmission

Update on new strategy: Polio Eradication, Integration and Certification Endgame Strategy 2019-23 – Michel Zaffran (WHO)

The meeting was opened by Michel Zaffran, Director of Polio Eradication, WHO, and Chair, Global Polio Eradication Initiative's (GPEI) Strategy Committee, who welcomed the 190+ participants from around the world. He presented a map of cases of polio due to wild poliovirus (WPV) type 1 and circulating vaccine-derived poliovirus (cVDPV) in the previous 6 months, showing that cases due to WPV1 are occurring only in Afghanistan and Pakistan; five cases due to VDPV1 have been reported in Yemen, and outbreaks due to VDPV2 are being seen from West to East Africa, and in Afghanistan and Pakistan.

He informed the participants of the aims and the process of revision the strategy for GPEI, in which the main barriers to eradication worldwide and gaps in the current strategy had been evaluated and prioritized. Solutions will be identified with partners and stakeholders, and associated costs, resources and the timeline to reach eradication will be estimated. Better communication with stakeholders was emphasized. The strategy is to be finalized early next year for presentation to the World Health Assembly in May 2021.

Financing for activities in 2021 has been challenging. The approved budget for 2021 was US$ 929 million, while the anticipated available resources are US$ 800 million, and the estimated financial requirement is US$ 1.27 billion. The solutions being explored are fund-raising by advocacy and resource mobilization with donors and with recipient countries. Another approach includes adjusting the size of the vaccine stockpile, which is currently large in order to mitigate the possible risk of failure of the novel oral poliovirus vaccine (nOPV).

He welcomed the achievement of the African Region, which had been certified free of WPV on 25 August 2020.

Image: African Region Wild Polio Virus Eradication Certified in August 2020.

The coronavirus 2019 (COVID-19) pandemic had resulted in halting of all polio supplementary immunization activities (SIAs) globally. GPEI is supporting the pandemic response through surveillance, the global polio laboratory network, data management and community networks of more than 31,000 staff and contractors, at significant cost. Many have been infected with SARS COV-2, with two reported deaths. Vaccines supplies worth US$ 6 million were already in countries at the time

of suspension of SIAs, and 100 million procured doses had their delivery delayed due to reduced air freighting options.

The pandemic has also had a widespread, significant effect on surveillance, with decreased case detection in many areas, including high-risk countries. Resumption of SIAs was encouraged in May, after a risk-benefit analysis and with precautions for the safety of front-line workers, and supply of vaccines was resumed in late June to countries that could conduct campaigns. Outbreaks due to cVDPV2 had occurred in 90 additional districts in the African Region by the end of July, and a 200% increase is foreseen if SIAs are not resumed. Simulation of the impact in Afghanistan and Pakistan indicated an exponential rise in cVDPV2 cases if a response is not initiated.

In October 2020, the Strategic Advisory Group of Experts (SAGE) endorsed the introduction of a second dose of inactivated poliovirus vaccine (IPV) in all countries that currently administer one IPV dose in addition of bivalent oral poliovirus vaccine (bOPV) to their routine polio immunization schedule. They endorsed use of Novel monovalent OPV2 (nOPV2) as the vaccine of choice for the response to cVDPV2 outbreaks, pending the granting an emergency use listing (EUL) for that vaccine, review of the initial use period and verification that all requirements for its use have been met. SAGE did not recommend IPV for use in poliovirus outbreak response.

The priorities for the next 6 months are to finalize transformation of the programme in Pakistan and resume SIAs as advised by technical advisory groups. Countries with outbreaks will be advised that they should resume outbreak response SIAs with monovalent OPV2 (mOPV2) with an emphasis on ensuring the safety of front-line workers and communities and introduce nOPV2 as soon as the EUL is granted. GPEI will advocate with donors to secure additional funds and with recipient countries for greater ownership and accountability, ensure that all planned expenditure is aligned with available resources, implement the recommendations of the governance review and complete revision of the strategy.

Update on epidemiology, progress towards eradication & stopping outbreaks – Arshad Quddus (WHO)

Arshad Ouddus, Coordinator, Detection and Interruption Unit, Polio Eradication Department, WHO, described the current epidemiology of polio and progress towards eradication and stopping outbreaks. The African Regional Certification met in August 2020 and concluded that transmission of indigenous wild polio virus (WPV) has been interrupted in all the 47 countries and the eradication of WPV in WHO's African Region is certified. The WPV transmission is restricted to Pakistan and Afghanistan where country-wide transmission continues with increase in incidence of cases during 2020. He said that the co-circulation of cVDPV2 alongside WPV1 is further complicating the epidemiological situation in Afghanistan and Pakistan. The main challenges to eradication in those two countries are inaccessibility in Afghanistan and, in Pakistan, lack of community mistrust and refusal to vaccinate, especially in Pashtun-speaking communities. It is essential to ensure community ownership, restore the motivation of vaccinators and to ensure their safety and quality of vaccination campaigns through improved national, provincial and district level political leadership and programme management and coordination.

The emergence of cases due to cVDPV in the previous 6 months is of particular concern for type 2, with a sharp exponential increase in cVDPV2 cases in 2019-20, which can be attributed largely to the pause in SIAs during the COVID-19 pandemic and sub-optimal quality of vaccination campaigns. Most of the recent outbreaks resulted from seeding after use of mOPV2 although the virus is also emerging in places where mOPV2 had not been used. Following an interval of pause due to the pandemic, the SIAs are being resumed and were conducted recently in 10 countries, in some cases integrated with the measles vaccine, Vitamin A, and deworming tablets in a few countries. Dynamic

planning is under way in 12 countries in the African Region; responses to new outbreaks are planned in Sudan and Yemen; and Afghanistan and Pakistan are planning to use trivalent OPV (tOPV).

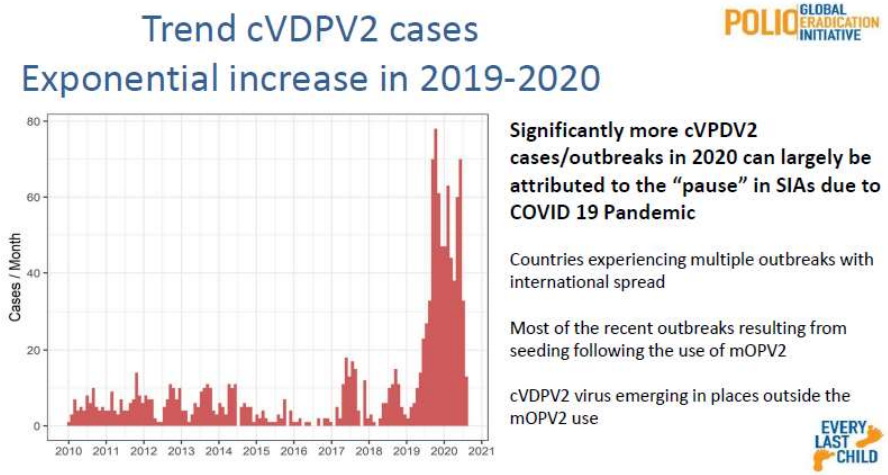

Image: Trend cVDPV2 cases, exponential increase in 2019-2020

The pandemic has demonstrated the importance of coordination between polio and COVID-19 strategic and management bodies in aligning messages and providing guidance and resources to countries. Well-coordinated, transparent national decision-making based on risk-benefit analyses, observance of infection prevention and control, use of personal protective equipment, and effective community engagement and communication are essential. Innovative approaches such as using local vaccinators, hand-washing and other COVID-19 prevention messages have increased community trust and confidence.

The main epidemiological risks are the effect of the COVID-19 pandemic, especially on the quality of SIAs; further extension of cVDPV2 geographically; intensive WPV1 transmission in Afghanistan and Pakistan, with the risk of international spread; and the risk of stockouts of Sabin OPV2. In order to address these risks and challenges, 2020 had been designated the "year of transformation" in stopping poliovirus transmission in Afghanistan and Pakistan, by ensuring the quality of SIAs, improving communication and community ownership and addressing broader health needs by providing integrated services. Measures to address the risk of cVDPV2 include monitoring the impact of COVID-19 and ensuring adequate global stocks of Sabin mOPV2 and tOPV. Use of the novel OPV2 in large-scale campaigns is expected to minimize new emergences of cVDPV2. Regional rapid response teams are being formed, preparedness for new cVDPV2 outbreaks is being strengthened, and methods for direct detection of poliovirus are to be introduced, with an earmarked budget for preparedness in 2021.

Responding to questions, Dr Ouddus said that, after declaration of COVID-19 as a Public Health Emergency of International Concern, the National Emergency Operation Center and provincial chief ministers in Pakistan had made a political commitment to resume SIAs, although some problems were still being encountered in Karachi. He said that the likelihood of country-wide cVDPV2 transmission can't be ruled out. In answer to another question, he confirmed that poor accessibility due to lack of security is the main issue in Afghanistan, although the quality of campaigns with regard to field operations and coordination also remain suboptimal. Negotiations are under way, but the political situation has deteriorated with the gradual withdrawal of US Army forces. As part of COVID-19 response, the PEI network in Afghanistan distributed soaps, awareness materials and baby blankets, which helped build some confidence in the polio programme. Moreover, some progress has

been seen in Taliban-controlled areas, and they recently allowed house-to-house vaccination in the south-east for the first time.

Global stockpile: Update, new plan & forecast of needs (Sabin & Novel type 2 polio vaccines) – David Woods (WHO)

David Woods, Technical Officer, Detection and Interruption Unit, Polio Eradication Department, WHO, described the global stockpile and forecasting of requirements for Sabin and novel vaccines. The purpose of the stockpile is to ensure an uninterrupted supply of type 2-containing OPV for outbreak response. He recalled that three bulk Sabin OPV stockpiles were established in 2009, and the first new finished product (Sabin mOPV2) was added in April 2016 and released in May, for use in Nigeria. A graph of the current status of the stockpile showed an increasing rate of release, in particular, since May 2018 and a balance as of 12 October 2020 of -35.9 million doses of mOPV2 and 5 million doses of tOPV. Of the 649 million doses that had been supplied to 28 countries, over half had been to Nigeria and Pakistan. tOPV had so far been used only in Afghanistan and Pakistan. The rate of release of vaccine had almost doubled each year since 2016.

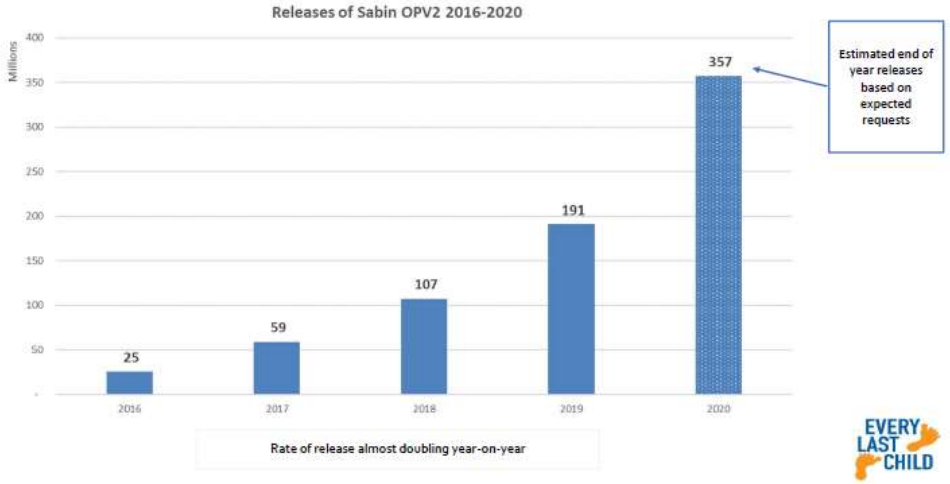

Image: Releases of Sabin OPV2 2016-20 almost doubling year-on-year.

The global stockpile plan aims is to supply sufficient quantities of OPVs to stop the spread of outbreaks. The supply will consist of a combination of novel and Sabin OPV type 2 containing vaccines, with phasing out of Sabin OPV2 use targeted by 2022. The assumptions for 2021, on the basis of current trends, include the requirement for vaccinating up to 600 children with OPV2 , that EUL will be granted on time and will not substantially delay the introduction of nOPV2, that the entire production capacity of 140 million doses of tOPV in 2021 will be utilised, and that full financing will be available to provide the proposed OPV2 supply. Vaccine shelf life is considered not to be a significant factor in view of fast-moving stocks. Establishment of stockpiles of mOPV1 and mOPV3 will be postponed because of financial constraints.

In terms of 2022, the plan assumes the high likelihood of successful nOPV2 rollout; and therefore, the moderate need for contingency planning for an event of nOPV2 failure. The plan assumes that a limited supply of finished Sabin mOPV2 will be needed in 2022 to supply Member States that decline Novel OPV2 before its full prequalification.

In terms of the quantities contained in the Global Stockpile Plan, for 2021, the plan aims at the procurement of 400 mds of Novel OPV2 and 500 mds of finished Sabin OPV2. It is probable that

there will be about 180 mds of Novel OPV2 carried-over from this year into next, so it is therefore probable that 580 mds of Novel vaccine will be available next year. On Sabin OPV2, the plan aims to secure 140 mds of tOPV and 360 mds of mOPV2 in 2021. It is not anticipated that there will be Sabin carryover into 2021 given the current rates of release for outbreak responses. In terms of 2022, under the plan, 1 billion doses of Sabin OPV2 bulk is to be tendered for. This procurement would be a contingency measure in case of novel OPV2 failure and would be delivered by the end of 2022. Finally, the procurement of 600 mds of nOPV2 bulk is planned for 2022.

SIA calendar: Options and bOPV projections – William Mbabazi (WHO)

William Mbabazi, Epidemiologist, Polio Eradication Department, WHO, presented an overview of the SIA calendar and estimates of bOPV supply. He noted that the 2019-23 Polio End-game Strategy, approved by the World Health Assembly in May 2019, is the basis for current programming but is being revised, as the critical milestones of interrupting WPV transmission and prevention and control of cVDPV outbreaks have been missed.

The objectives of a multi-year SIA calendar are to interrupt endemic circulation of WPV1 and then maintain polio-free status; boost population immunity in countries at risk to prevent WPV1 outbreaks in case of importation and reduce the risk of emergence of VDPV types 1 and 3; help estimate the requirements for vaccines needed for SIAs and projections of the bOPV market for manufacturers. The SIA projections in 2019 were based on interruption of WPV transmission in 2021, which is increasingly unlikely. The annual SIA calendar is based on risk rating of countries, calculated supplemental immunizations required to generate at least 80% with 3 doses of OPV for all children, and the multi-year SIAs projections and budget ceilings. The 2021 SIA calendar proposals have been discussed by task teams and WHO and UNICEF regional advisers, and the agreed upon option was approved by the Eradication and Outbreak Management Group. Notably, the risk of types 1 and 3 vaccine-derived polio outbreaks has reduced in more countries, and in turn, the SIAs planned have been reduced based on sub-national estimates of immunity generated from the vaccination status of AFP cases. Measles incidence has also been used as a tracker of risk for poliovirus types 1 and 3, as immunity to measles mirrors low poliovirus type 1 immunity in Africa. Subsequently, GPEI will explore integration of bOPV with measles outbreak response SIAs as a strategy to raise population immunity in measles affected geographies.

The prospects for 2020 demand against supply indicate that the year will end with an over-supply of about 320 million doses of bOPV. The low bOPV demand is due to a) increased needs for cVDPV2 outbreak response that pulled additional budget or required shifting from bOPV to tOPV in countries with co-circulation of type 1 and 3 polioviruses; b) disruptions due to COVID-19 pandemic; and c) GPEI cash gaps. Globally, the bOPV projections for 2021 foresee a cumulative supply surplus of 190 million doses or 205 million doses, if the contingency scenario is used. It is important to note that this contingency scenario is built on the assumption that there will likely be country hesitancy to conduct preventive bOPV SIAs during the COVID-19 pandemic and that the GPEI cash gap is likely to continue. The SIA Task Team proposes that domestic financing of bOPV campaigns should be explored to complement GPEI financing.

In conclusion, preventive bOPV SIAs will remain part of the polio eradication strategy as long as routine polio vaccination coverage remains at current levels, and the programme is exploring all means possible to reach more children by a) increasing the eligible age groups targeted; b) co-delivery of bOPV in other vaccine-preventable diseases SIAs; c) introduction of bOPV to measles outbreak response SIAs and d) integration of bOPV in all planned COVID-19 immunization recovery interventions.

Supply of IPV & OPV: Current status & demand forecasts – Ann Ottosen (UNICEF)

Ann Ottosen, Senior Manager, Vaccine Centre, UNICEF Supply Division, presented the current status and the forecast demand for supplies of IPV and bOPV. While overall projected demand for 2020 had increased from 88 to 92 million doses, the timing had been considerably delayed due to the effect of COVID-19 on catch-up campaigns for 42 million children who had missed the first dose; 10 of 17 countries in which catch-up had been planned are still completing applications or awaiting approval from Gavi, the Vaccine Alliance (Gavi). The 2020 demand might therefore be changed to early delivery of 2021 allocations to make up low stocks, with deliveries for introduction of a second dose of IPV in early 2021 or later. The demand for volume of about 4 million doses set aside for outbreak response in 2020 is not materializing.

For 2021, routine requirements make up 97% of the forecasted demand of 102 million doses. It is assumed that 29 countries would introduce a second dose of IPV, with supplies procured through UNICEF, although further applications might be made. The applications are under review by Gavi, and endorsement is expected at the end of October. The SAGE recommended that there be no IPV allocation for use in outbreak response. Consultations with all manufacturers indicate that the projected demand is expected to be fully met and that an additional supply could be secured if necessary, if the lead times are respected. She said that, in line with the IPV tender, all bidders that had made an offer had been asked to confirm whether they would extend their offer for 12 months to cover the period January-December 2023. Offers would be reviewed against the original tender objectives, which were: to ensure a sufficient supply of IPV for all countries that procure through UNICEF, to achieve a price that is affordable for countries and donors and to extend the supplier base to stimulate a healthy market and improve vaccine security. Awards might be made if any of the offers was deemed to contribute to those objectives.

Demand is projected to increase by one third annually in 2021-23 to cover introduction of the second dose of IPV into routine schedules, for a total of 140 million doses through UNICEF. The next steps under the tender are to confirm the number of countries that will introduce the second dose of IPV, the dose requirements and the timing of introduction. The demand and supply balance will be monitored continuously to ensure that any additional requirements for 2021 are met by additional awards. Award scenarios and recommendations will be reviewed with the Procurement Reference Group. If any requirements for 2023 remain unawarded, UNICEF will make awards in mid-2021. If all the quantities for 2023 have been awarded, UNICEF will make awards for supplies in 2024 in mid-2022.

The main reasons for the changes in demand for bOPV in 2019 were cancellation and delay of activities in endemic countries, cancellation of activities in low- and medium-risk countries due to GPEI budget constraints and an approximately 15% decrease in actual demand from that forecast. Adjustments to the supply include postponing production of the awarded quantities to 2020 and reallocating capacity to mOPV2. In the context of the global COVID-19 pandemic, the GPEI recommended temporary postponement of campaigns until the second half of 2020. In those countries with active polio transmission that are planning campaigns, the safety of health workers and communities must be considered paramount. There was an immediate decrease in demand in March due to cancellation and postponement of campaigns, and stocks have built up in countries. As the initial forecast was for 900 million doses, a considerable volume of doses has had to be carried over to 2021. The GPEI is reviewing the 2021 calendar for SIAs, and UNICEF is conducting annual forecasting, factoring in unused doses in stock. The scale and scope of catch-up campaigns will depend on the continued effect of COVID-19. Demand for 2021 is fully awarded, and the demand forecast for 2022 and beyond depends on an updated GPEI calendar. UNICEF will consult with industry before making awards.

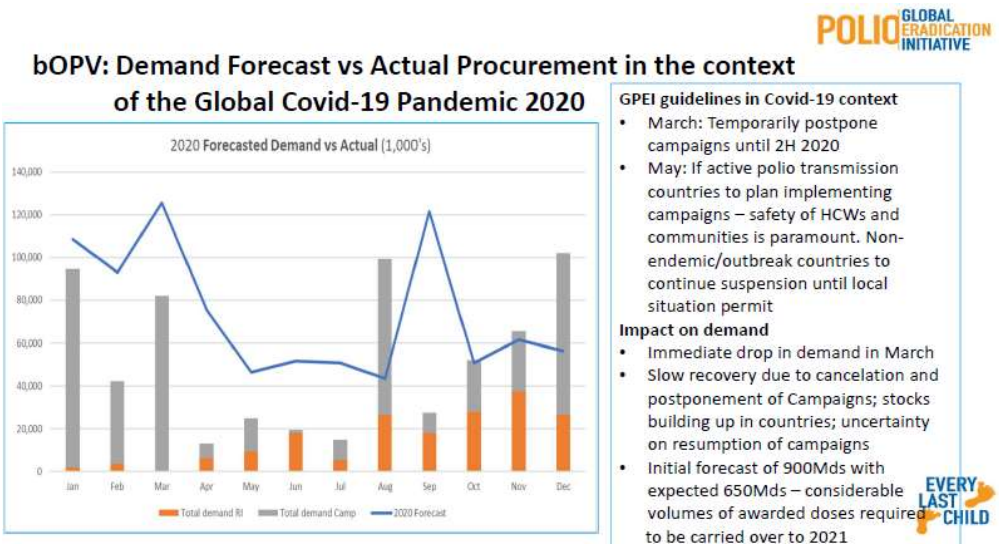

Image: bOPV: Demand Forecast vs Actual Procurement in the context of the Global Covid-19 Pandemic 2020.

To secure sufficient OPV up to cessation, UNICEF continues to monitor demand and supply, working with the GPEI to ensure that the programme recognizes the impact on suppliers, with countries to ensure acceptability and with suppliers to ensure an appropriate supply. UNICEF is reviewing bOPV requirements up to the end of 2020 with suppliers, discussing the carry-over supply within "good faith" agreements and discussing production plans for 2021 to ensure the best use of capacity and mitigating risks on both sides while maintaining affordability, flexibility and access. A market note will be issued shortly on the status of bOPV supply and demand.

The supply of therefore IPV is improving and is projected to be sufficient to meet programme requirements for catch-up campaigns and introduction of a second dose; new suppliers are entering the market, improving its health and the security of vaccine availability. Affordable prices will be an important consideration in awarding supplies for 2023. The demand for bOPV continues to be volatile due to COVID-19, and the requirements for 2021 will depend on the SIA calendar and forecasts of routine demand. Awards have been made though to 2022, and additional awards will be made in 2021 to secure the supply for 2023 and beyond.

In answer to a question, she said that fractional doses were supplied only to Bangladesh and India; the assessment was based on full doses.

Essential Immunization: Update on integration, second dose, progress on IPV catch-up campaigns – Alejandro Ramirez Gonzalez (WHO) and Steven Sosler (Gavi)

Alejandro Ramirez Gonzalez, Technical Officer, Department of Immunization, Vaccines and Biologicals, WHO, summarized progress in coverage of IPV catch-up campaigns among children, noting that the COVID-19 pandemic had affected implementation of nine approved or planned campaigns in 2020. Nevertheless, 13 million children have been vaccinated since February 2020, and additional catch-ups are planned, covering 8.5 million children. The SAGE working group reinforced the recommendation to complete IPV catch-up campaigns when safe and feasible and to encourage countries to take opportunities to integrate activities. WHO, UNICEF and Gavi prepared overviews of the effect of COVID-19 on immunization services in April and June 2020, which indicated partial disruption in all 25 indicator services and particularly in routine vaccination in communities and health services. WHO has proposed a common framework for decision-making in mass vaccination

campaigns, evaluation of the risks and benefits of conducting campaigns to respond to vaccine-preventable and high-impact diseases and considerations and recommendations for mass vaccination campaigns in the context of COVID-19. WHO guidance on maintaining health services during COVID-19 stresses immunization as a core health service, maintaining routine vaccination and planning catch-up vaccination as soon as possible in parallel with other services.

With regard to the introduction of a second dose of IPV, SAGE had recommended that immunogenicity is best achieved with IPV1 at 14 weeks and IPV2 at least 4 months later. IPV1 at 6 weeks and IPV2 at 14 weeks could be considered under certain epidemiological circumstances. A total of 94 countries are targeted for introduction of IPV2, and Gavi has extended support from 2021. Risk assessment would be used to prioritize doses if necessary.

The objectives of the interim Programme of Work of the GPEI and the Essential Programme on Immunization for integrated action in the context of the COVID-19 pandemic up to December 2021 are to accelerate alignment and coordination among agencies working on polio and immunization, to identify immediate, innovative, adaptive, integrated action to meet the challenges and to provide proof of concept for further integration into broader strategic plans. The primary audience is global and regional partner agencies. The programme will engage and inform other stakeholders, such as donors and national governments, especially of countries endemic for polio or with acute outbreaks and vulnerable countries.

The four strategic priorities of the programme are comprehensive surveillance for vaccine-preventable diseases, integrated laboratories and community engagement and service delivery, including demand promotion and ensuring coverage, equity, capacity-building, training, monitoring of impact and risk assessment for vulnerability. For acute outbreaks, the programme includes planning and preparedness, response and recovery and management and coordination. The actions and primary responsibility will be finalized at the end of the first quarter of 2021 and coordinated resumption of disrupted or suspended immunization activities at the end of 2021, when additional actions will be considered for a revised GPEI Endgame Strategy.

Steve Sosler, Gavi, the Vaccine Alliance, gave an overview of Gavi support for IPV introduction, which includes routine immunization in 73 eligible countries. They are exempt from co-financing and the eligibility policy until cessation of OPV; the Board will review the IPV co-financing approach in 2022. Between 2016 and 2020, populations that had been missed because of supply constraints received IPV catch-up doses, and Gavi support was extended. A second dose of IPV is to be made available in 2021, also with exemption from co-financing and the eligibility policy, and support would be provided for changes in schedules to introduce the second dose.

Gavi makes in-principle decisions on introduction of a hexavalent vaccine containing whole-cell pertussis, defining the conditions to be met. The objective is to include the hexavalent vaccine as an option with pentavalent vaccine and IPV. Co-financing for hexavalent vaccine will be finalized when the Board opens a funding window in 2022. The priorities for pentavalent, IPV and hexavalent vaccines are to ensure a sufficient supply and flexibility in the vaccine mix to cover countries' preferences; mitigate risks to ensure uninterrupted supplies to Gavi-eligible countries; minimize the cost of the vaccines to Gavi and countries while ensuring sustainable prices for manufacturers; and provide clear guidance and policies for use of hexavalent vaccine.

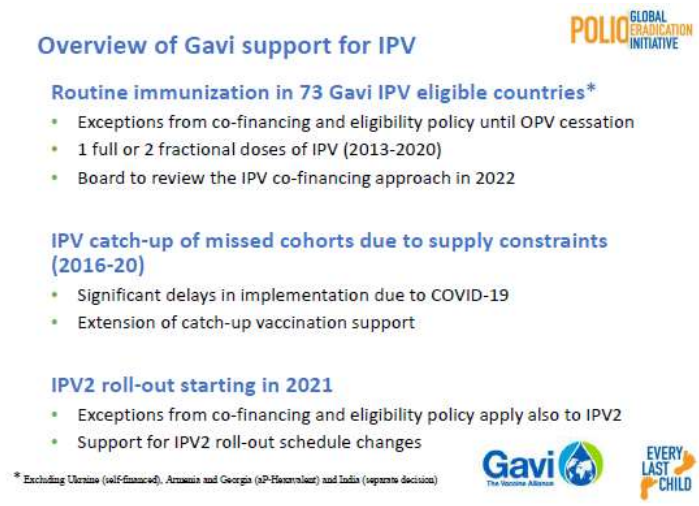

Image: Overview of Gavi support for IPV.

In response to a question about support for other IPV-based combinations, Mr Sosler confirmed that only hexavalent vaccine containing whole-cell pertussis was being considered. Responding to queries about Gavi support for introduction of the second dose of IPV, he said that issues of the dose schedule had been resolved and discussions were now concentrating on cost. Price increases might compromise the programme, and ways would have to found to minimize the risks.

2. Pre-tender consultation on OPV2 bulk

Pre-tender consultation on OPV2 bulk – Vachagan Harutyunyan (WHO) & Ian Lewis (UNICEF)

Vachagan Harutyunyan, Team Leader, Detection and Interruption Unit, Polio Eradication Department, WHO, and Ian Lewis, Contract Specialist, Vaccine Centre, UNICEF Supply Division, led a discussion on the upcoming tender that would be issued for the production of 1 billion doses of bulk Sabin OPV2 for delivery in 2022.

Questions were asked about the technical requirements for the tender, the vaccine vial monitor to be affixed to the finished product and whether a valid containment certificate would be sufficient. Daphne Moffett replied that the requirements of the 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 (GAPIII) were being updated. If a facility had revised the packaging appropriately, the national authorities for containment should support the application. She said that no change had been made to containment conditions for formulation, filling and quality control. Containment inspectors will be experienced experts who are familiar with the risks and will check compliance with GAPIII during inspection of IPV manufacturing facilities.

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

nOPV2: Update, Emergency Use Listing, initial use and scale-up – Simona Zipursky (WHO)

Simona Zipursky, Advisor to the Director, Polio Eradication Department, WHO and co-chair of the GPEI nOPV2 Working Group, described EUL, initial use and scale-up of nOPV2. The new vaccine is essential in view of the recent spread of cVDPV2; in 2020, cVDPV2 outbreaks spread to 19 countries.

cVDPV2 outbreaks continue to occur, because of insufficient routine immunization coverage in weak health systems and constrained global vaccine supply, decreasing mucosal immunity to cVDPV2 among children born after the switch from tOPV to bOPV, regional migration patterns that lead to children being missed in vaccination campaigns, low-quality outbreak response and use of mOPV2 in outbreak responses, which risks seeding new outbreaks in areas of low immunization coverage.

nOPV2 is a modification of mOPV2 has been shown in clinical trials to provide comparable protection against poliovirus but to be more genetically stable and less likely to revert to a form that could cause paralysis or seed new cVDPV2 outbreaks. The trials show a favourable general profile of safety and reactogenicity and less or comparable shedding to mOPV2; cessation of intestinal mucosal viral replication and shedding might actually occur earlier in infants.

The GPEI strategy for control of cVDPV2 includes accelerated development of nOPV2 and improved outbreak response with mOPV2, which is currently the best available vaccine against type 2 vaccine-derived polio. Routine immunization will be strengthened by GPEI technical staff to optimize immunization delivery systems in high-risk areas, and a sufficient supply of OPV2 will be ensured to reach every child at risk, with innovative strategies when necessary.

nOPV2 will be used under a WHO EUL recommendation, a regulatory pathway that involved careful, rigorous analysis by the WHO prequalification team and independent experts of the available data for early, targeted use of unlicensed products for a public health emergency of international concern such as polio. An initial recommendation for use of nOPV2 under an EUL is imminent. WHO has urged Member States to expedite authorization for the importation and use of nOPV2 on the basis of its impending EUL recommendation. When it is first used under EUL, additional essential criteria, endorsed by SAGE, are applicable to monitor safety and effectiveness during an initial use period that will last approximately 3 months. Enhanced monitoring is required throughout use of nOPV2 under an EUL to assess and ensure safety, surveillance, performance and other factors that affect the validity of the listing. Countries must have detected VDPV2, have the capacity to acquire and distribute the vaccine in a timely manner, to respond to unanticipated findings and for surveillance; it should not be used for 12 weeks after the last use of mOPV2 in the area and 6 weeks after a bOPV campaign. The vaccine must be accepted, and access must be reasonable.

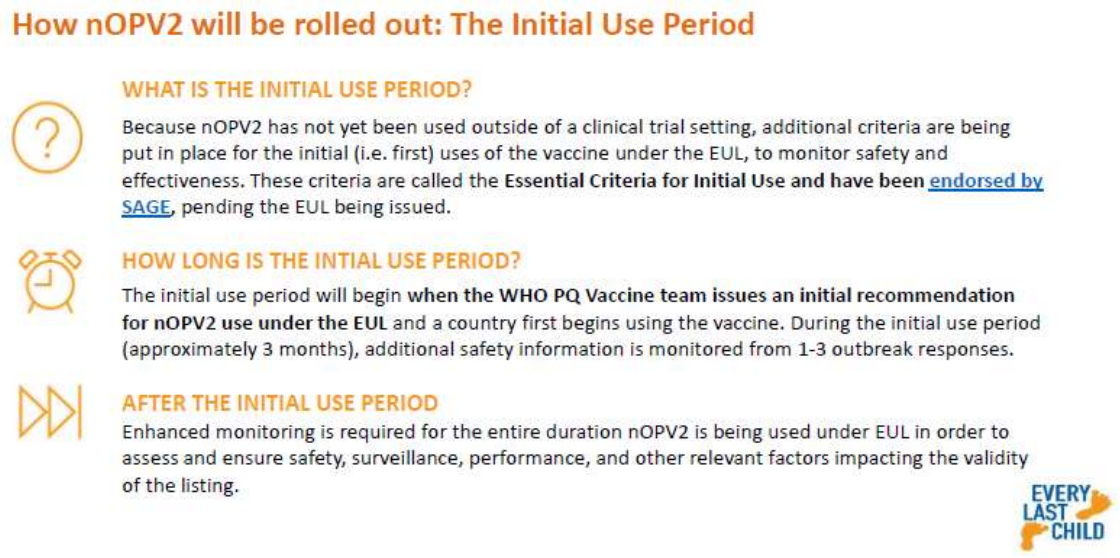

Image: How nOPV2 will be rolled out: The Initial Use Period.

GPEI has created a “readiness process” and tools to help countries meet all the criteria. Each country must complete all 20 in the “readiness checklist” and 7 additional requirements for the initial use

phase. Countries will be supported by national nOPV2 focal points and facilitators, regional nOPV2 focal points and other regional and global experts, and their readiness will be assessed by a multi-disciplinary GPEI team. Although the interim recommendation for an EUL is anticipated very soon, it will take 5-8 weeks before nOPV2 will be available for the first time in a country (i.e. end November/December 2020 at earliest). Prior to nOPV2 use, each country will have to meet all the readiness requirements, and the vaccine supply will have to be cleared and available in the country.

Full licensure and prequalification of nOPV2 are not expected before end 2022, and therefore all countries at risk of cVDPV2 outbreak should consider preparing for nOPV2 use under an EUL now. Countries considered at high risk are those with VDPV2 detected currently or in the previous 6-12 months and neighbouring countries; countries in which cVDPV2 has been detected but which do not meet these criteria might also wish to prepare for VDPV2 detection and a subsequent response with nOPV2. The presentation of the vaccine was to be in 50 dose vials, to maximize the number of doses available due to limited fill/finish capacity. The wastage rate with the 50-dose vials will be assessed; one advantage of the preparation is that its size differentiates it from other polio vaccines.

In the ensuing discussion, it was confirmed that a second manufacturer, Bio E in India, will be the recipient of the nOPV2 technology transfer, which will help ensure an adequate and secure supply of the vaccine. After the 3-month period of initial use under the EUL, the safety and relevant surveillance data that has been collected will be reviewed by an independent safety group. Their assessment will be presented to SAGE, and if data is supportive, SAGE will endorse the end of the initial use phase. Countries will still need to meet EUL requirements to use the vaccine but will no longer also need to meet the initial use criteria. High-priority laboratories in the Global Polio Laboratory Network in all WHO regions have receive training in detection of nOPV2 with a specific, highly sensitive PCR test, and all nOPV2-related samples will, at least for the initial use phase, be shipped to NIBSC or CDC laboratories for whole-genome sequencing. Andrew Macadam, National Institute for Biological Standards and Control, confirmed that S19 strains for vaccine development are available through relevant agreements.

GPEI's research & product development priorities – Martin Eisenhawer (WHO)

GPEI's priorities for research and product development were summarized by Martin Eisenhawer, Product Development and Research, Polio Eradication Department, WHO, as vaccine development, laboratory assays and antiviral therapies. He described the evolution of OPVs since 1963 through to nOPV in 2020 and of IPVs since 1955 through to a potential DNA or RNA vaccine; the breakthrough had been vaccines that give mucosal immunity. As the poliovirus genome changes by mutation and recombination, the advantages of nOPV2 are genetic stability and less neurovirulence. He described the genomic background of the candidate nOPV2 strain C1. Virus-like particle (VLP) vaccines are under development in a quest for a non-infectious polio vaccine that does not require containment, for use post-eradication. A research and development consortium has made important progress in manufacturing stable, immunogenic VLPs on several expression systems, such as yeast and baculovirus, and purification, characterization, immunogenicity and stabilization are under way.

A call for expressions of interest for commercialization of the vaccine was issued in July 2019, with an extensive response. WHO's IPV advisory panel included VLP vaccines in November 2019 and made recommendations on the selection of candidates, which were being evaluated. Micro-assay patches (MAPs), which are being developed for use in house-to-house campaigns, have shown good antigen recovery and immunogenicity. Negotiations with one manufacturer are under way for IPV supply for the MAPs, and a clinical trial is planned. Pseudovirus is being developed for use in a neutralization assay.

The Containment Advisory Group (CAG) decided that some genetically modified poliovirus strains could be handled outside containment, which might replace Sabin or WPV neutralization testing and thus exempt those testing facilities from the list of polio-essential facilities. The antiviral therapies being developed are for treatment with a single drug or a combination or with monoclonal antibodies (mAbs). The candidates in development are Pocapavir (V-073), a capsid Inhibitor, and V-7404, a 3C protease inhibitor; ViroD7000 is a combination of the two. When used as an adjunct to polio antiviral agents, mAbs could contribute to clearing chronic polio infection. Substantial work has been done over the past decade, with seed funding from the Polio Research Committee. Promising candidate mAbs have been identified, including one that neutralizes all three poliovirus serotypes. The next steps are to find a pilot or commercial producer to produce mAbs according to good manufacturing practice and conduct a phase-I trial to assess safety and effect on excretion after an OPV challenge.

Work should be accelerated on both nOPV2 and pseudovirus, with surveillance and therapy for patients with primary immunodeficiency disorder. Research should include assessment of the behaviour of nOPV2 is intended to be rolled out under EUL in populations and additional vaccine solutions.

Clarifications were made in response to questions. The expected therapeutic outcome of potential therapeutics is not only stopping virus shedding but also clearing the virus as quickly as possible. No studies have yet been conducted on whether S19 strains could be used in MAPs. Increased availability of IPVs would reduce the risk of paralytic polio, although it would not stop circulation of the virus.

Update on pre-qualification of poliovirus vaccines – Mathias Janssen (WHO)

Regulatory pathways for poliovirus vaccines were summarized by Mathias Janssen, Vaccines and Immunisation Devices Assessment Team, WHO. He highlighted that the normal process is prequalification (PQ) for international supply after an extensive review by independent experts of the quality, safety and efficacy aspects of the vaccine and its suitability for programmes. Post PQ activities include fulfilling of commitments by manufacturer, reassessment and potential requalification. The usual sequence of events leading to PQ is evaluation of quality, safety and efficacy of the product and licencing at national level, subsequent policy recommendation in line with conditions of use in low- and middle-income countries and finally prequalification.

Emergency Use Listing (EUL), initiated in 2015, is a risk-benefit based pathway leading to time limited recommendation for use, initiated only during public health of international concern events. Quality, safety and efficacy data are reviewed on a rolling-based submission process by independent experts in collaboration with national regulatory authority of oversight. Development of the vaccine should continue for final marketing authorisation and PQ. Both regulatory processes can be abbreviated under oversight of mature regulatory agencies, with evaluation and monitoring of programmatic aspects by WHO.

A genetically modified OPV2 vaccine (nOPV2) has been developed and is supported by a multi-partner collaboration. It is believed to better address polio outbreaks resulting from reversion mutations in mOPV2 as it should be more genetically stable. SAGE endorsed the initial use criteria of nOPV2 in principle in April 2020. The manufacturer was inspected for good manufacturing practice and the vaccine is currently in the final steps of review for quality aspects by independent experts under EUL procedure, as initial safety and efficacy assessment was found satisfactory.

The next steps are granting of Emergency Use Approval by NRA of oversight and recommendation of use under EUL by WHO. Guided by the risk management plan, consolidation of safety profile and confirmation of the effectiveness of nOPV2 is required post EUL along with commitment to an observational study of the safety of nOPV2 in pregnant women exposed by shedding. Coordination of

GPEI activities will enable rapid, effective roll-out of nOPV2, facilitation of country decisions for initial use, post-EUL monitoring and communication.

4. Containment and certification

Global poliovirus Containment update – Arlene King (Global Certification Commission)

Arlene King, Chair of the Global Certification Commission, Containment Working Group, described the status of containment certification. She recalled World Health Assembly resolution 71-16 of 28 May 2018, which urged all Member States to take adequate measures to contain poliovirus, with goals to reduce the number of containment facilities and to establish national authorities for containment. She reported that 25 countries retained poliovirus type 2 material, of which 22 had nominated national authorities. Of those, 20 have submitted plans for their poliovirus-essential facilities. The number of countries that retain poliovirus materials will increase once the inventories of types 3 and 1 are completed. Of the 73 facilities containing type 2 polioviruses, 60 have applied for certificates of participation in the containment certification scheme, and 32 certificates of participation have been signed by the Global Commission for the Certification of the Eradication of Poliomyelitis; 13 facilities have not submitted applications. The number of facilities that retain poliovirus materials might decrease if certificates are not granted.

WHO headquarters and regional containment focal points have been engaged in COVID-19 work, some for several months, as most of them also advise on global disease containment issues. Surveys of infectious material have been delayed, and discontinuation of international and domestic flights and other transport has affected work. Despite COVID-19, a global network of national authorities for containment was launched in February 2020, the certification scheme continued, and consultations with some national authorities for containment have moved forward. A time-bound, costed audit and country support strategy during the pandemic has been developed. Containment advisory and working groups continue to meet to review applications, make recommendations on nOPV1 and nOPV3 use and containment and review containment during COVID-19 recovery.

WPV3 materials must now be destroyed or contained in a facility, with explicit methods. A World Health Assembly resolution proposed for 2021 will specify requirements for all poliovirus types entering containment. The Global Certification Commission has provided guidance on poliovirus containment and extended the validity of current containment certificates for 1 year; guidance on potentially infectious materials is being revised. A revised auditing and country support plan was shared with national authorities in May 2020 and will be reviewed.

The challenges facing containment are a global lack of qualified auditors; continued use of mOPV2 for outbreak response, which creates a continuous cycle of surveys and inventories, as will reintroduction of tOPV; and the prioritization of poliovirus containment, particularly during the COVID-19 pandemic. Investigations of vaccine “contaminants” and reported breaches in facilities underscore the importance of vigilance in containment. The sustainability of the containment programme will require long-term global oversight and continuing political will.

Containment Advisory Group recommendations, GAPIII & TRS amendments – Daphne Moffett (WHO)

Daphne Moffett, Containment Team, Polio Eradication Department, WHO, reported on the CAG recommendations, GAPIII and revision of requirements and recommendations that might affect manufacturers. With respect to type 2 poliovirus, the goal remains the eradication of all live type 2 poliovirus from the world. mOPV2, tOPV and nOPV2 all contain live, attenuated type 2 poliovirus and can be used only in outbreak response. The EUL for nOPV2 poses additional requirements for its introduction and use, and the vaccine will have limited availability during the first 3 months of initial

use. nOPV2 is highly attenuated Sabin OPV2, which appears to maintain its attenuation phenotype; however, its performance in producing population immunity and its reversion potential are still unknown. The CAG recommendations for nOPV2 containment are contained in GAPIII. The only recommendation so far is with regard to Annex 3, Biorisk management standard for poliovirus-essential facilities holding only OPV/Sabin poliovirus materials, from which nOPV2 is temporarily waived for vaccine production and quality control, clinical trials and outbreak response. CAG will review the waiver once it has received the results of phase-III clinical trials and surveillance data.

The CAG recommendations for nOPV1 and nOPV3 are that novel OPV strains be defined by their capsid regions, and chimaeric viruses with non-structural regions from Sabin-2 or nOPV2 but a type 1 or 3 capsid should be defined as type 1 or 3 for containment purposes and not be subject to type 2 containment. Although Sabin 1 and 3 are still used in routine vaccination, once containment guidelines are issued, GAPIII guidance for Sabin viruses will apply. Exclusion of the development and production of nOPV1 and nOPV3 strains from GAPIII is being considered, as the discussions on the construct are similar to those on nOPV2, the main difference being insertion of capsid sequences from types 1 and 3. Types 1 and 3 will be contained at some time in the future after cessation of use of OPV. The recommendation represents a pre-emptive step to address concerns raised by regulators. CAG agrees that the four candidate strains (1 and 2 for types 1 and 3) could be handled outside GAPIII containment for the purposes of production, quality control and clinical trials. Handling of infectious materials in facilities is subject to national and international regulations, and national regulations maintain primacy.

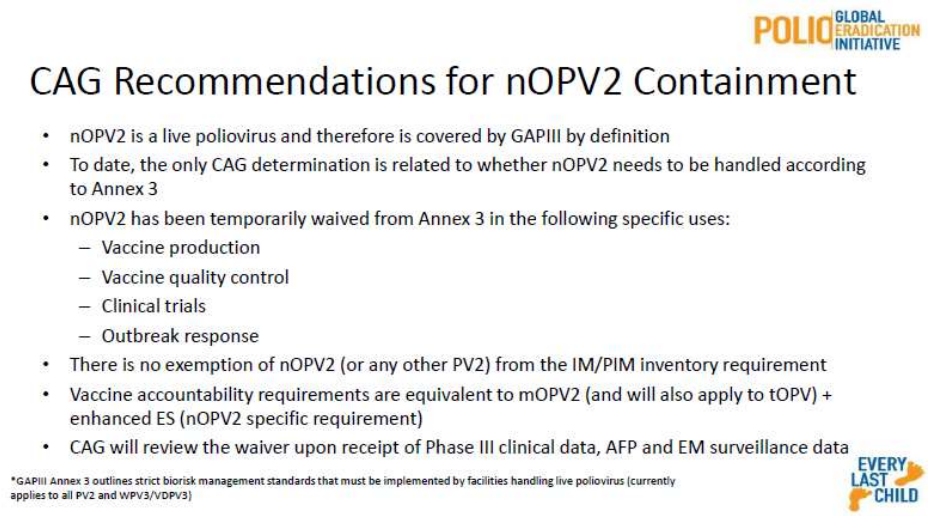

Image: Containment Advisory Group (CAG) Recommendations for nOPV2.

Annex 4 to the sixty-ninth report of the WHO Expert Group on Biological Standardization (WHO TRS No. 1016), Guidelines for the safe production and quality control of poliomyelitis vaccines, was amended in August 2020 to resolve difficulties in implementing current GAPIII guidelines. This amendment was conducted in consultation and agreement with CAG for interpretation and application of GAPIII. Companies that contribute to the GPEI through production, stockpiling and supplying polio vaccines have been challenged to ensure the right level of containment while maintaining the continuity of supply and rationalizing investment and operational costs. In a quality control laboratory where several biological agents are tested, “campaign testing” is not feasible. Industry’s biocontainment infrastructure and stringent, documented biosafety procedures are largely effective in minimizing the risk of poliovirus release, and they consider that routine showering when leaving a production or quality control area does not add to biosafety and would affect industry’s ability to supply GPEI. The proposed revision would specify that a full-body shower facility be available in the

personnel exit airlock from the containment facility. The use of a shower upon exit should follow the established procedure supported by the risk assessment and be consistent with the policies established by the latest version of GAPIII and with the most recent CAG recommendations."

The second issue is whether non-dedicated facilities (e.g. quality control laboratories) should be used in the final phase of containment. The TRS drafting group considered that non-dedicated laboratories could be used in that phase, with additional precautions, comprising location of the laboratories within the containment facility, adherence of all non-poliovirus-related activities and all personnel admitted to the laboratories to all applicable containment procedures and a risk assessment that complies with the requirements in GAPIII to identify any additional controls. The third issue is handling of samples outside containment, as GAPIII requires that all samples from manufacturing facilities be tested in containment laboratories. All samples received from the containment production facility should be handled using established procedures to prevent the release of live poliovirus. Procedures used to decontaminate sample containers or packaging materials should be validated and shown to have no impact on sample integrity. The packaging materials should be decontaminated prior to disposal. All samples received from the containment production facilities – with the exceptions described below in sections 11.5.1 and 11.6 – should be tested in containment laboratories. All test procedures using reagents containing live poliovirus should also be performed within the containment laboratories.

> "11.5.1 On the issue of handling samples outside the containment facility, certain samples (i.e. those for water or environment monitoring) taken from within the containment perimeter may be tested outside the containment laboratories if a risk assessment concludes that they are unlikely to contain live poliovirus, based on facility design, equipment used (especially closed systems) and sampling locations (3) provided all sample-handling, transportation and disposal processes adhere to GAPIII."

The Global Certification Commission has recommended extension of the validity of current certificates of participation in the containment certification scheme to 30 April 2022. Regional certification commissions have encouraged countries to identify facilities holding WPV3 materials and include them in their surveys and inventories and then to either destroy unnecessary material or place it in designated poliovirus-essential facilities. The guidance on potentially infectious materials is being revised and updated, and a revised GAPIII Containment Certification Scheme auditing and country support plan is being prepared. As auditors are not necessarily aware of the background of GAPIII, a plan is also being prepared for qualification of auditors and support for audits, which makes provision for remote activities during the period of travel restrictions due to COVID-19.

In answer to a question about vaccine contaminants or facility breaches, Dr Moffett said minor issues had arisen in a few countries, such as leakage around a seal and accidental release, with no consequences; one issue was being analysed. Guidance is being issued on how to report such incidents to WHO. She urged manufacturers to examine the changes to the GAPIII requirements and their effect on risk and to contact WHO if they had any questions. In reply to a question about whether resistance had been met to containment measures, she said that any perceived resistance was to WHO's application of the requirements. She said that efforts had been made to ensure no new inconsistency between the TRS and GAPIII requirements in the latest revision. In response to another question, she said that the modifications to the TRS would initially apply only to manufacturers but might apply to laboratories in the future.

5. Updates on vaccine development and manufacturing

Public-private collaboration: Development of Novel OPV2 – Ananda Bandyopadhyay (Bill & Melinda Gates Foundation)

Ananda Bandyopadhyay, Bill & Melinda Gates Foundation, described the development of nOPV2 through public-private collaboration. He said that, in view of the spread of cVDPV2 between January 2019 and June 2020, accelerated manufacturing and clinical development of nOPV2 had been undertaken to reduce the risk of vaccine-associated paralytic poliomyelitis and cVDPV. Two nOPV2 candidates were designed by a global scientific consortium supported by the Gates Foundation to improve genetic stability and decrease the risk of loss of attenuation relative to the parental Sabin 2 strain.

The first human study was initiated in 2017, and phase-II studies in adults in Belgium and in children and infants in Panama were completed in 2019. The first candidate had been prioritized for manufacture at-risk, given the global public health emergency, and a decision on EUL was expected in 2020. Clinical development was accelerated by the involvement of global agencies and vaccine experts, and a decision was made to pursue an accelerated manufacturing plan to ensure a stockpile of 200 million doses within 10 months. Bio Farma had undertaken an aggressive production schedule to ensure that a stockpile of doses would be ready as soon as possible. A 50-dose vial presentation had been decided in order to reduce the number of filling cycles. The accelerated schedule required scaling-up of a commercial facility before the original production facility became available, and a facility for production of measles vaccine had been converted to produce the maximum possible number of doses as early as possible, while fill-finish capacity was limited.

Thus, a cross-cutting global partnership had enabled timely preclinical and clinical development and large-scale manufacturing of a vaccine considered to be critical. A global consortium of preclinical research organizations, GPEI partners, PATH, clinical trial sponsors, Bio Farma, regulatory authorities and policy bodies such as SAGE had built a strong partnership. The next steps are continued at-scale production, approval of use through the EUL, country use and generation of further field and clinical data for widespread use and eventual prequalification of the vaccine.

Production Polio Vaccines: Strategy and Planning – Erman Tritama (Bio Farma)

Bio Farma's role in producing polio vaccines was described by Erman Tritama. He said that the company is committed to producing mOPV, bOPV and nOPV2 for global demand and also IPV for Indonesia. The company has separate personnel and facilities for producing components and products for Sabin and novel polio vaccines. nOPV2 development starting since 2015. The research seed arrived in 2015 and was tested at their good laboratory practice-compliant facility. Clinical lot material for phase 1 was produced in GMP clinical lot facility and clinical trial phase 1 conducted in 2016-2017, seed was characterized in 2017, and working seed and clinical lot material for phase 2 was produced in 2018 at the good manufacturing practice-compliant clinical lot facility. In 2019, activity was increased at both the manufacturing and the commercial production facility. To accelerate the manufacturing at the commercial scale, the unit for measles virus production was repurposed for production of nOPV2 substances, and the facility for measles and rubella vaccine production was changed to nOPV2 production.

Industrial perspective related to polio vaccines in COVID-19 time – Jim Dillman & Alain Dutilleul (Sanofi Pasteur)

Alain Dutilleul and Jim Dillman, Sanofi Pasteur, discussed the industrial perspective of poliovirus vaccines in the time of COVID-19. They said that their company acknowledged the disruption of

programmes caused by COVID-19 and is committed to support the recovery plan, including provision of polio vaccines. Organization of manufacture and supply and networks adapts continuously to ensure no disruption by close, continuous dialogue with national and international stakeholders and procurement bodies to anticipate potential bottlenecks especially on batch release, clinical & regulatory plans implementation, and supply reagents for local testing.

Sufficient anticipation is essential for both OPV and IPV in view of the significant lead time between production and delivery, as vaccines produced in 2020 can be delivered only in 2022-23. That highlights the risks of last-minute demand and programme shifts for suppliers and vaccine supplies and stocks, which was the case for bOPV in 2020. Sanofi Pasteur had adjusted its 2020 bOPV supply plan several times to double the supply despite the challenging conditions to produce during the times of the COVID-19 pandemic and on top of the numerous other vaccines it manufactures in the fight against other vaccine preventable diseases; however, now, only half is required. Although a certain volume would probably be used, for which they are working with UNICEF, some might be unused, and manufacturers bore the economic risks.

Sanofi Pasteur remains strongly committed to support WHO and the GPEI in the fight against polio, and in view of the numbers of countries in which campaigns in 2020 had been postponed because of COVID-19, all stakeholders should maintain close and routine communications and make a commitment to secure the vaccine ecosystem in 2021 and beyond.

Manufacturing challenges for OPV & IPV, & suggestions to overcome – Rajeev Dhere (Serum Institute of India) & Maarten Manders (Bilthoven Biologicals)

Rajeev Dhere, Serum Institute of India, described the effect of COVID-19 on supply and demand of OPV. He said that bulk OPV1 and OPV3 are procured from Bio Farma, and the fill-finish facility is dedicated to OPV. Formulation, filling, visual inspection, labelling and packaging at –20 °C are done online. Under normal circumstances, a balance is maintained between receiving bulk OPV from Bio Farma and dispatching OPV product. A 3-month stock of filled product, representing 120-150 million doses, is kept at a storage temperature of -20 °C, and filling is undertaken according to the dispatch rate. A decrease in OPV demand has a cascading effect on cold storage capacity and the bulk bought under a volume-based contract from Bio Farma; filling capacity remains unused. With regard to contractual obligations, the bulk price is based on predicted volumes, and the price of the final product is based on volumes allocated by UNICEF. The impact on the manufacturer is therefore choked cold storage, leading to stoppage of production and an unused workforce.

The difference in the volume of OPV in long-term agreements and actual demand was about 95 million doses in 2018, 31 million doses in 2019 and 171 million doses on 2020. The forecast for 2020 received from UNICEF was for 83.81 million doses, which would result in a deficit of 88 million doses. COVID-19 has caused a considerable decrease in supplies of OPV, resulting in a huge stockpile. Dr Dhere suggested a number of solutions, including evaluation of use of the facility for production of similar products, which would, however, require discussion and negotiations with regulators; and additional cold storage, such as refrigerated mobile vans or hiring outside cold storage, which would also require permissions from regulators and significant validation and qualification. He asked whether a price correction mechanism could be developed that kept both the manufacturer and the buyer in a safer position and reduced the risks for both. In view of the factors that affect the demand and supply of OPV, a different mechanism should be designed, whereby risk is shared equally by the manufacturer and the buyer.

Maarten Manders, Bilthoven Biologicals, said that, until 2019, there had been a chronically insufficient supply of IPV, and nongovernmental agencies had urged increased IPV manufacturing capacity, particularly to permit countries to provide a second injection of IPV in their routine immunization programmes. After the Serum Institute of India purchased Bilthoven Biologicals in 2012, IPV

production output increased by 10 times. The supply of IPV, however, ground to a halt in March 2020 with the advent of COVID-19 due to flight cancellations and airport and country closures, which led to the stoppage or reduction of vaccination activities, with competing resources in order to fight COVID-19.

The decreased IPV supply made it increasingly difficult to secure orders, with decreased global demand in the short term. The implications for Bilthoven Biologicals in 2020 were an increasing stock of finished product with insufficient storage capacity on site; external storage capacity, which incurs transport costs; and discontinuation of filling (limited to a 3-month safety stock). The lack of IPV, with COVID-19, is increasing the number of missed vaccinations. In this situation of increasing missed vaccinations and zero vaccination children together with the SAGE recommendation for a routine second IPV dose, overall demand has not substantially increased. Discussions are under way with partners to drive supply. Shorter payment terms are helpful but are not a lasting solution, and additional measures to support stable and predictable processes are required. Security of demand is as important as security of supply.

Mr Zaffran said that he had taken note of the suggestions of Dr Dhere. He said that issues of procurement should be discussed with the Supply Division. Although programme projections had been clear, COVID-19 had affected all vaccine activities.

Dr Harutyunyan asked manufacturers what reasonable lead times they would require to change plans and minimize risk, how communication could be increased and their priorities.

The representatives of Sanofi Pasteur answered that meetings should be held at least twice a year between WHO and manufacturers to discuss release and testing of vaccine and short-term decisions on allocation. Additional impromptu meetings should be organized for any dramatic event, such as COVID-19, that might affect demand or supply. Their company had continued production of IPV and OPV.

The representative of Bio Farma said that his company had not been obliged to close down production.

6. Summary comments and closure of the meeting

Mr Zaffran stressed that continuous communication was essential to progress in polio eradication. He realized that COVID-19 caused particular difficulties for the private sector and containment mechanisms. Those challenges require close collaboration, access to information and answers to questions. He looked forward to the continued valuable interaction with vaccine manufacturers. Many problems had been overcome in the past; COVID-19 was one more hurdle, but he was confident that the goal of polio eradication would be met. Dr Harutyunyan thanked everyone for their work and manufacturers for securing supplies of vaccine for the Polio Eradication.