



Fifth Meeting of the Containment Advisory Group

2, 4 and 9 March 2022
1400 – 1700 (CEST)
Virtual Meeting

Note for the Record

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List of Abbreviation

AQAS	GAPIII Auditor Qualification and Audit Support Plan 2021–2023
AAT	Advanced Auditor Training
CEV	Country Engagement Visit
BRM	Biorisk management
CAG	Containment Advisory Group
CAG – ESG	CAG – Expert Support Group for Novel Poliovirus Strains
CAG1	First Meeting of the CAG, 19-20 June 2017
CAG2	Second Meeting of the CAG, 28-30 November 2017
CAG TC1	Teleconference of the CAG on Showers, 25 January 2018
CAG TC2	Teleconference of the CAG on Novel Poliovirus Strains, 8 March 2018
CAG TC3	Teleconference of the CAG TC3 on nOPV2 candidate vaccines and S19 – poliovirus type 2 strains, 7 June 2018
CAG TC4	Ad hoc Teleconference of the CAG on Tertiary Safeguards, 14 August 2018
CAG3	Third Meeting of the CAG, 13-14 December 2018
CAG4	Fourth Meeting of the CAG, 15-16 July 2019
CAG TC5	Teleconference of the CAG on the Definition of Novel OPV strains and GAPIII Containment Requirements for nOPV1 and nOPV3 Development and Production, 20 March 2020
CAG5	Fifth Meeting of the CAG, 2, 4 and 9 March 2022
CAVA	Cold-Adapted Viral Attenuation (CAVA) - Poliovirus strains
CCS	Containment Certification Scheme to support the WHO Global Action Plan for Poliovirus Containment
CP	Certificate of Participation
ICC	Interim Certificate of Containment
CC	Certificate of Containment
CMG	Containment Management Group
COVID-19	Coronavirus disease 2019
CEN	European Committee for Standardization
CWA	CEN Workshop Agreement
EB	Executive Board
EUL	WHO Emergency Use Listing
GAPI	WHO Global Action Plan for laboratory containment of wild polioviruses (1st ed., 1999)
GAPII	WHO Global Action Plan for laboratory containment of wild polioviruses (2nd ed., 2004)
GAPIII	WHO global action plan to minimize poliovirus facility-associated risk after eradication of wild polioviruses and cessation of routine OPV use (3rd ed., 2009)
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 or WHO Global Action Plan for Poliovirus Containment (3rd ed., 2015) (version undergoing revision)
Annex 2	BRM standard for poliovirus-essential facilities (PEFs) holding wild poliovirus (WPV) materials
Annex 3	BRM standard for PEFs holding only OPV/Sabin poliovirus materials (no WPV)
Annex 6	BRM standard for safe handling of new samples potentially containing poliovirus material in poliovirus-non-essential facilities
GCC	Global Commission for the Certification of the Eradication of Poliomyelitis
GCC – CWG	GCC – Containment Working Group
RCC	Regional Commission for the Certification of the Eradication of Poliomyelitis
NCC	National Committee for the Certification of the Eradication of Poliomyelitis
GPEI	Global Polio Eradication Initiative
IHR	International Health Regulations (3rd ed., 2005)
ISO	International Organization for Standardization
IPV	Inactivated poliovirus vaccine

List of Abbreviations

LBM	WHO Laboratory Biosafety Manual
LBM2	WHO Laboratory Biosafety Manual (2nd ed.,1993)
LBM3	WHO Laboratory Biosafety Manual (3rd ed., 2004)
LBM4	WHO Laboratory Biosafety Manual (4th ed., 2020)
LOC	Loss of containment event
MOH	Ministry of Health
NAC	National authority for containment
NPCC	National Poliovirus Containment Coordinator
NTFC	National Task Force for Containment
OPV	Oral poliomyelitis vaccine
bOPV	Sabin bivalent oral poliomyelitis vaccine serotypes 1 and 3
mOPV2	Sabin monovalent oral poliomyelitis vaccine serotype 2
nOPV2	Novel oral poliomyelitis vaccine serotype 2
OPV1	Sabin oral poliomyelitis vaccine serotype 1
OPV2	Sabin oral poliomyelitis vaccine serotype 2
OPV3	Sabin oral poliomyelitis vaccine serotype 3
tOPV	Sabin trivalent oral poliomyelitis vaccine serotypes 1, 2 and 3
PEF	Poliovirus-essential facility
PHEIC	Public health emergency of international concern
PIM	Potentially infectious materials, poliovirus
PIM Guidance	Guidance to minimize risks for facilities collecting, handling or storing materials potentially infectious for polioviruses (2nd ed., 2021)
PIM Tool	Potentially Infectious Materials, Poliovirus Identification Tool (Digital version of the PIM Guidance (2nd ed., 2021)
PVSRIPO	Neuro-attenuated recombinant poliovirus consisting of live attenuated Sabin poliovirus serotype 1 with heterologous internal ribosomal entry site (IRES) of human rhinovirus type 2
S19	S19 with the structural (capsid) protein encoding P1-region (of Wild poliovirus or Sabin polioviruses; serotypes 1, 2 or 3)
S19/N18S	S19 with the structural (capsid) protein encoding P1-region (of Wild poliovirus or Sabin polioviruses; serotypes 1, 2 or 3) with mutation (substitution) of asparagine (N) by serine (S) at amino acid 18 of the non-structural protein 2A for better growth in Vero cells.
SAGE	Strategic Advisory Group of Experts on immunization
TRS	WHO Technical Report Series
VDPV	Vaccine-derived poliovirus
VDPV1, 2, 3	Vaccine-derived poliovirus serotype 1, serotype 2 and serotype 3
cVDPV	Circulating vaccine-derived poliovirus
cVDPV1, 2, 3	Circulating vaccine-derived poliovirus serotype 1, serotype 2 and serotype 3
VLP	Virus-like particle
WHA	World Health Assembly
WHO	World Health Organization
WPV	Wild poliovirus
WPV1, 2, 3	Wild poliovirus serotype 1, serotype 2 and serotype 3

Summary of Recommendations

The Fifth Meeting of the Containment Advisory Group was held virtually on 2, 4 and 9 March 2022. The main agenda items for this meeting were presentations and discussions on the ongoing revision of the WHO Global Action Plan for Poliovirus Containment, 3rd edition, 2015 (GAPIII, 2015), and follows the critical review of the revised GAPIII draft by CAG. The following are the recommendations:

Session 1: Update on Polio Eradication and Poliovirus Containment Programme

Implementation of the Containment Certification

- CAG commends the Global Commission for the Certification of the Eradication of Poliomyelitis - Containment Working Group (GCC – CWG) for the work, time and effort being invested in the review of facility' containment certification applications received by the National Authorities for Containment (NAC) and the ongoing work in line with the latest recommendations made by the GCC on progressing with containment certification despite the challenges brought about by the COVID-19 pandemic and associated delays with implementation of Containment Certification Scheme (CCS)..
- In line with the terms of reference of CAG specifically on 'Guidance on the identification of acceptable alternative containment solutions in the interim period, before full eradication', CAG offers its support, as needed to the GCC – CWG as progress is made towards the interim containment certification (ICC) phase and recommends that the Secretariats of CAG and CWG work closely as needed.

Session 2: Update on the Progress with the Revision of GAPIII

Overview of the Process Undertaken for the Revision of GAPIII

- CAG commends the Secretariat for its work in engaging relevant stakeholders in the various inputs used for the revision process and encourages the Secretariat to ensure sufficient time and extensive outreach is implemented during the public consultation period.

Issues for Consensus or Recommendation by CAG

Containment Perimeter

- Anterooms and personnel airlocks are to be considered within the containment perimeter and must meet the requirements of spaces within the containment perimeter.
- Kill-tank rooms or equivalent must meet all construction, sealing, and Heating, Ventilation and Air-Conditioning (HVAC) requirements of the primary containment space and are required to have an anteroom/personnel airlock for controlled entry as described above.

Operator Inactivated Poliovirus Vaccine (IPV) Immunization and Poliovirus Antibody Titer Determination Requirements

- Individuals associated with the poliovirus-essential facility must demonstrate established immunity to poliovirus through evidence of poliovirus antibodies prior to accessing the facility
- Subsequent need for IPV vaccination and antibody titre testing should be determined by a local risk assessment and should be consistent with national occupational health guidelines.

Risk-based Approach for Walk-through Exit Shower from the Containment Perimeter in line with the Most Recent CAG Recommendation.

- Exit shower requirement should be replaced with performance-based language which would generally be more applicable to the range of poliovirus-essential facilities (PEFs) – this should emphasize the need for a facility-specific risk assessment which should be approved by the NAC.
- Additional measures should be considered when exiting from the containment perimeter to prevent exposure to contaminated PPE or personnel.

Risk-based Approach for Storage of Poliovirus Materials Outside of GAPIII Containment.

- The current version of GAPIII does not address storage of polioviruses outside of the containment perimeter. Therefore, the biorisk management element associated with ‘poliovirus inventory and information’ should be expanded to include storage procedures for polioviruses outside of the containment perimeter including conditions to be met e.g., leak-proof containers, dedicated freezers, proper labelling and other biosecurity measures, etc. as determined by a facility-specific risk assessment with the approval from the NAC.

Alternative Measures for Gaseous Decontamination and Guidance for Use.

- The containment perimeter for existing facilities must be an area sealable for gaseous decontamination. For new facilities or facilities undergoing renovation, retrofitting or refurbishing, alternative methods of decontamination e.g. physical decontamination, etc. may be considered provided it is guided by the performance of a comprehensive risk assessment.

High-Efficiency Particulate Air Filtration (HEPA) on Exhaust Side As Requirement Prior to Final Containment of all Wild Polioviruses.

- The use of supply-side HEPA filters directly on the containment barrier if and when correctly maintained would functionally meet the intent of a dedicated HVAC system.
- This requirement i.e., HEPA filter on exhaust or its functional equivalent, is to be maintained for facilities retaining WPV polioviruses in the containment phase of all WPV serotypes.

Changes Made in Primary, Secondary and Tertiary Safeguards as Described in GAPIII

Replacement of GAPIII Jargon ‘Primary, Secondary and Tertiary Safeguards’ with Technical Language or Definition

- Replace the term ‘primary safeguards’ to ‘facility safeguards’, ‘secondary safeguards’ to ‘immunization coverage safeguards’ and ‘tertiary safeguards’ to ‘environmental control safeguards’.

Operationalization of Population Immunity Safeguards Within the Context of SAGE Current Recommendations

- Based on the Polio Eradication Strategy 2022 – 2026: Delivering on a Promise, the complete phase out of all oral poliomyelitis vaccine (OPV) is anticipated in 2030+ and this provides sufficient time for countries hosting PEF to achieve these requirements i.e., two-IPV doses and IPV2 coverage.
- In line with the recommendation made by the Strategic Advisory Group of Experts (SAGE) on immunization which permits countries-hosting PEFs to implement this requirement no later than time of all OPV cessation, the approach to be taken in the revised GAPIII should be adjusted to make it more globally implementable and pragmatic based on data availability and local circumstances. In the interim period (before complete phase out of all OPV), the immunity requirements should consider the current IPV supply, IPV in routine immunization, and availability of IPV coverage data, etc. with the goal of achieving the recommendation made by SAGE by the time of all OPV cessation. [Therefore, two options are recommended for the operationalization of these safeguards: (1) pre-OPV cessation period and (2) post-OPV cessation period. The post-OPV cessation period is to be considered the deadline for countries hosting PEFs to meet this requirement, but CAG encourages an early compliance with this requirement.

	OPV/Sabin	WPV/VDPV
Population Immunity Safeguards		
IPV1 or IPV2 coverage during the pre-OPV cessation period	= DTP3 coverage or ≥90%	= DTP3 coverage or ≥90%
IPV2 coverage during the post-OPV cessation period	≥90%	≥90%

Operationalization of Population Immunity Safeguards Within the Context of SAGE Current Recommendations

Depending on the country context and location of the PEF, coverage data may represent national level or subnational level, whichever appropriate.

Local Risk-based Approach for Environmental Control Safeguards

- The requirement for PEFs to be located in areas with closed sewage systems with secondary or greater treatment of effluents in the community should be replaced with risk-based language that maximizes the utilization of local environmental parameters that reduces the risk of poliovirus transmission (R_0).
- Consideration should also be provided for the implementation of additional environmental safeguards by the NAC e.g., environmental surveillance for communities living close to the PEF.
- Thus, the definition is to be expanded to include local context in the determination of the R_0 of poliovirus and risk-based in approach tailored to local situations i.e., 'The environmental, sanitation and hygiene conditions (e.g., good personal, domestic, and environmental hygiene standards; closed sewage systems with secondary or greater effluent treatment; low population density in surrounding areas) that minimize the risk of re-establishing the circulation of highly transmissible wild poliovirus in the event of reintroduction'

Revision Made in the Survey, Inventory and Destruction Activity Section of GAPIII.

- CAG noted that the revision of this section was based on the outputs from the 'Kick-off' meeting held on 15 April 2021 (Table 1) and consented to the following recommendations:
 - Definitions (previously Annex 1) moved to the beginning of the revised document
 - Revision and update of the introductory text
 - Addition of the 'Roles and Activities' section to describe poliovirus containment stakeholders and their terms of reference in the context of this document
 - Addition of 'Containment Requirements for Novel Poliovirus Strains' section based on previous CAG requirements
 - Complete removal of the 'Phases' approach from GAPIII
 - Replaced with 'Inventory and Destruction' and 'Containment' phase
 - 'Inventory and Destruction' is described as ongoing and in-effect for all strains, WPV and Sabin/OPV, globally
 - 'Containment' requirements to be implemented in stages by strain as determined by GCC based on eradication progress and involves four parts:
 - 'Establishment' (as needed),
 - 'Verification' (in-transition for all strains),
 - 'mOPV stockpiles' (in-transition for all OPV strains), and
 - 'Final Containment' (in-transition for WPV2 and WPV3)

Containment Requirements for Potentially Infectious Materials, WPV/vaccine-derived polioviruses (VDPV)

- CAG noted the concerns raised by the NACs of the need for facilities retaining for potentially infectious materials, WPV/VDPV to implement the containment requirements in GAPIII, undergo compliance verification as per CCS which places an additional burden on the NACs in countries with numerous facilities retaining only such materials.
- CAG recommends the following:
 - In line with the strategy for the implementation of GAPIII i.e., risk elimination, the concerned NACs should encourage these facilities to destroy such materials.
 - The containment requirements for the retention of potentially infectious materials, WPV/VDPV will remain in line with the requirements of GAPIII or its revised version for now. A more in-depth review of the containment requirements of potentially infectious materials, WPV/VDPV in regards to the applicability of GAPIII or its revised version, will be undertaken by the Potentially Infectious Materials, Polioviruses Guidance Development Group

Containment Requirements for Potentially Infectious Materials, WPV/vaccine-derived polioviruses (VDPV)

(previously established and tasked with the development of the PIM Guidance, 1st edition) in 2022.

- In addition, CAG also highlighted several issues associated with the retention of potentially infectious materials, polioviruses which require resolution and encourages the Secretariat to coordinate with the Potentially Infectious Materials, Polioviruses Guidance Development Group to deliberate on the following:
 - The compliance verification mechanism, which the Potentially Infectious Materials, Polioviruses Guidance (PIM Guidance) currently lacks, for facilities retaining potentially infectious materials, Sabin/OPV materials against the risk mitigation strategies described in the PIM Guidance.
 - In line with the current goal of eliminating the use of all type 2 polioviruses (including Sabin serotype 2 poliovirus and OPV2), the longer-term containment requirement for the retention of potentially infectious materials, Sabin specifically in the post-OPV cessation period should be discussed.

Updated Recommendations from the CAG - Expert Support Group (CAG-ESG) on Novel Poliovirus Strains.

In line with the submissions received by CAG on the use of specific novel poliovirus strains for specific uses, CAG recommends the following:

1. CAG – ESG through the CAG Secretariat to request for access to genetic stability data after first year use of novel oral poliomyelitis vaccine serotype 2 (nOPV2) at scale from the nOPV2 Working Group.
2. The following specific uses are granted a temporary waiver* to be exempt from the containment requirements of Annex 3 of GAPIII:
 1. trivalent formulation of novel oral poliomyelitis vaccine serotype 1 (nOPV1), nOPV2, and novel oral poliomyelitis vaccine serotype 3 (nOPV3).
 2. nOPV (all four) formulation studies and tnOPV clinical trials
3. For specific research purposes, the following novel poliovirus strains are granted a temporary waiver* from the containment requirement of Annex 2 or 3 of GAPIII, whichever applicable as follows:

Strains

- nOPV2 candidate 1 (aka nOPV2-c1, or S2/cre5/S15domV/rec1/hifi3/S2P1)
- nOPV3 candidate 1 (aka nOPV3-c1, or S2/cre5/S15domV/rec1/hifi3/S3P1)
- nOPV1 candidate 2 (aka nOPV1-c2, or S2/cre6/S15domV/CpG30/rec1/hifi3/S1P1)
- nOPV2 candidate 2 (aka nOPV2-c2, or S2/S15domV/CpG40)
- nOPV3 candidate 2 (aka nOPV3-c2, or S2/cre6/S15domV/CpG30/rec1/hifi3/S3P1)
- nOPV2 candidate 3 (aka nOPV2-c3 or S2/cre6/S15domV/CpG40/rec1/hifi3)
- S19S1
- S19S2
- S19S3
- S19S1_N18S
- S19S2_N18S
- S19S3_N18S
- S19Mah
- S19MEF1
- S19Skt
- S19Mah_N18S
- S19MEF1_N18S

Specific Uses

- Laboratory activities to support clinical trials and ongoing monitoring of continued use
- Viral concentration from environmental samples
- Development or refinement of methods for viral concentration and detection from environmental samples
- Frozen storage of stool specimens from clinical trials
- Determination of D-antigen content
- Determination of viral titer
- Stability studies, including for alternative nOPV formulations
- Characterization of aliquots from stability studies (e.g., pH, aggregation assays, HPLC)
- Immunogenicity assays in mice and rats
- Detection of nOPV and mucosal antibodies to nOPV in stool samples
- Neutralization assays
- Isolation of antibodies and virus from stool samples (human, mouse, rat)
- Mass spectroscopy
- Small-scale propagation
- Nucleic acid extraction

Updated Recommendations from the CAG - Expert Support Group (CAG-ESG) on Novel Poliovirus Strains.

- S19Skt_N18S
 - Sequencing
 - Potency testing for immunoglobulin (human) lot control and release
 - Testing effectiveness of inactivation and disinfection methods
 - Sterility studies to confirm inactivation and disinfection methods
 - Spiking biosolids (sewer sludge) or wastewater to demonstrate effectiveness of treatments
4. Deliberation by the CAG-ESG should be initiated as soon as possible to address outstanding issues associated with the temporary waiver granted for the use of novel poliovirus strains for specific uses including:
- CAG recommendation on the compliance monitoring of relevant facilities with the terms of the temporary waiver as there currently is no mechanism to do so.
 - The duration of validity of the temporary waivers as there are implications to the CCS and the containment requirements for the handling of novel poliovirus strains, after the end-validity of these waivers.
 - Related to the point mentioned above, the role of CAG in resolving the exemption from the containment requirements of novel poliovirus strains for specified uses in the post-OPV cessation period when all live poliovirus are expected to be fully contained.

List of abbreviations: (Wild-type): Mah1: Mahoney serotype 1; MEF1: Middle East Forces serotype 2; Sau3: Saukett serotype 3; (Sabin strains): S1: Sabin serotype 1; S2: Sabin serotype 2; S3: Sabin serotype 3; P1: region of the poliovirus genome encoding the structural (capsid) polypeptides and N18S is a mutation (substitution) of an asparagine by a serine at amino acid 18 in the non-structural protein 2A to allow better growth in Vero cells.

*The issuance of a temporary waivers for the specified uses indicated is not to ease oversight but has been granted to facilitate the eradication programme's response to the ongoing cVDPV2 outbreaks and failures of outbreak response campaigns. Temporary waivers only cover specific viruses and specific uses and cannot be generalized to other novel poliovirus strains or other uses. The duration of validity of the temporary waivers and the containment requirements for the handling of novel poliovirus strains, after the end-validity of these waivers, is currently being discussed by the CAG – ESG. The exemption granted will be extended to the containment requirements of the revised GAPIII, upon its publication.

Session 3: Other Issues Associated with the Revision of GAPIII

Timelines and Remaining Steps in GAPIII Revision

- CAG agreed to the proposed processes and timelines, including dates for the TC, to complete the revision of GAPIII by end of Q2/2022, should they remain appropriate.

Naming of the Revised GAPIII

CAG recommends the following: WHO Global Action Plan for Poliovirus Containment (full- and short-titles) and GAPIV (abbreviation).

Other issues:

In line with these issues raised, CAG has requested the Secretariat to present at the next CAG TC a summary document with the supporting evidence for safeguards in the revised GAPIII as well as a brief study proposal utilizing the most appropriate methodology to address these medium- and longer-term issues raised by CAG. In addressing some of these broader issues, the Secretariat should collaborate with Secretariats of other containment supporting groups, as needed e.g., GCC, GCC – CWG, SAGE, etc.

Note for the Record

Background

The Fifth Meeting of the Containment Advisory Group¹ (CAG5) was held virtually on 2, 4 and 9 March 2022 (1400 – 1700 CEST). The main agenda items for this meeting were presentations and discussions on the ongoing revision of the WHO Global Action Plan for Poliovirus Containment, 3rd edition, 2015 (GAPIII, 2015)², and follows the critical review of the revised GAPIII draft by CAG. At this meeting, CAG members deliberated on the proposed revisions made in GAPIII for consensus and recommendations. More broadly, the objectives of this meeting were:

1. To provide CAG with an update on:
 - a. Polio Eradication Strategy 2022 – 2026: Delivering on a Promise and develop a shared understanding of the epidemiology, the status of the programme towards eradication, etc.;
 - b. Implementation of containment programme (survey, inventory and destruction activities for poliovirus and poliovirus containment certification) including ongoing work to support countries;
 - c. Progress with the revision of GAPIII including process, proposed revisions and basis for change for consensus or recommendations by CAG and to address associated issues, etc.
2. To discuss administrative issues related to the work of CAG e.g., membership, meetings, etc.

CAG5 was attended by the following:

CAG: Professor David HEYMANN (Chair of CAG), Dr Jagadish DESHPANDE, Dr Atef EL-GENDY, Professor George E GRIFFIN [also member of CAG-Expert Support Group for Novel Poliovirus Strains (CAG - ESG)], Dr Vibeke HALKJÆR-KNUDSEN, Dr Janice LO, Dr Stephen MCADAM (also member of CAG - ESG), Dr Mark PALLANSCH (also Chair of CAG - ESG and Co-Chair of the Containment Management Group (CMG)), Dr Åsa SZEKELY BJÖRNDAL, Professor Shahina TABASSUM and Mr Kenneth UGWU.
Unable to attend: Mr Neil GODDEN

Representative of other containment supporting groups: Dr Arlene KING, Liaison Member of the Containment Working Group of the Global Commission for the Certification of the Eradication of Poliomyelitis (GCC-CWG) to the CAG and Chair, GCC – CWG

Invited participants (Observers): 2, 4 and 9 March 2022: Gryphon Scientific LLC, Takoma Park, MD, USA: Dr Rocco Casagrande, Dr Ryan RITTERSON, Ms Erin LAUER, Dr Adam FLEMING, Ms Kelly KIM and Mr Rob DETTMANN.
4 March 2022: Presentation of Studies Conducted on GAPIII Walk-Through Exit-Shower Requirement: Perseus BVBA, BELGIUM: Dr Karen VAN DER MEULEN, Dr Patrick RÜDELSHEIM and Mr Toon DE KESEL and U.S. National Authority for Containment of Poliovirus, Atlanta, GA, USA: Dr Christy OTTENDORFER.

¹Containment Advisory Group. Terms of Reference. Available at: <http://polioeradication.org/wp-content/uploads/2016/12/CAG.TOR.122016.pdf> and Meeting Reports of the CAG. Available at: <http://polioeradication.org/tools-and-library/policy-reports/advisory-reports/containment-advisory-group/>

²WHO Global Action Plan to minimize poliovirus facility-associated risk after type-specific eradication of wild polioviruses and sequential cessation of oral polio vaccine use or WHO Global Action Plan for Poliovirus Containment, 3rd ed (GAPIII, 2015). Available at: <https://polioeradication.org/polio-today/preparing-for-a-polio-free-world/containment/containment-resources/>

WHO Secretariat Poliovirus Containment Team, Department of Polio Eradication, WHO headquarters in Geneva, SWITZERLAND: Mr Aidan O'LEARY, Team Lead *a.i.* and Director, Department of Polio Eradication; Dr Nicoletta PREVISANI, Technical Officer; Ms Liliane BOUALAM, Technical Officer and Secretariat, GCC - CWG; Dr Harpal SINGH, Technical Officer and Secretariat, CAG; Mr Joseph SWAN, Communications Officer and Ms Caroline NAKANDI, Assistant to the Team. Detection and Interruption Unit, Department of Polio Eradication, WHO headquarters in Geneva, SWITZERLAND: Dr Graham TALLIS, Senior Scientific Adviser and Secretariat, GCC.

WHO Regional Containment Coordinators: WHO - Regional Office for Africa: Dr Jacob Samson BARNOR; WHO - Regional Office for the Americas/Pan American Health Organization: Ms Gloria REY; WHO - Eastern Mediterranean Regional Office: Dr Humayun ASGHAR and Dr Salmaan SHARIF; WHO – European Regional Office: Dr Eugene Victor SAXENTOFF and Dr Maria IAKOVENKO and WHO – Western Pacific Regional Office: Dr Varja GRABOVAC.

Unable to attend: WHO – South-East Asia Regional Office: Dr Sigrun ROESEL.

All CAG members submitted a signed declaration of interest (DoI) form and were requested to inform the secretariat of any change in situation or circumstance requiring the need for new disclosure at this meeting. All DoI were assessed as per WHO Guidelines for Declaration of Interests (WHO Expert) with no CAG member identified as having any relevant real or perceived conflict of interest.

The agenda and list of participants are included in Annexes 1 and 2.

Session : Introduction
Context and expected outcomes of the meeting

Absolute poliovirus containment may never be assured as questions of intentional or unintentional facility-associated release of poliovirus will always remain. Nonetheless, effective containment is a realistic target - in achieving so, the basis and evidence must be clear and compelling and the biorisk management (BRM) requirements appropriate, and the goals realistic.

The implementation of the revision of GAPIII undertaken till date has been consistent with the recommendations made by CAG at its third meeting in December 2018³:

1. Oversight function for issues related to containment and containment documents e.g., GAPIII, GAPIII – Containment Certification Scheme (CCS), Guidance to minimize risks for facilities collecting, handling or storing materials potentially infectious for polioviruses (PIM guidance), etc., previously held by the Strategic Advisory Group of Experts (SAGE) on immunization is now a function of CAG as deliberated by the Polio SAGE Working Group;
2. CAG Secretariat coordinates a detailed review meeting of CAG recommendations, its implications on other requirements, taking into consideration all applicable recommendations, coordinate a detailed review of the draft revised GAPIII by CAG to ensure consistency of approach to all safeguards;
3. A period of public consultation for the revised GAPIII is implemented.

The expected outcomes from this meeting are consensus or recommendations from CAG on the proposed revisions made in GAPIII and deliberations on outstanding issues associated with the revision process.

³ Meeting Reports of the Containment Advisory Group. Available at: <http://polioeradication.org/tools-and-library/policy-reports/advisory-reports/containment-advisory-group/>

Session 1: Update on Polio Eradication and Poliovirus Containment Programme

Polio Eradication Strategy 2022 – 2026: Delivering on a Promise
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The Polio Eradication Strategy 2022 – 2026: Delivering on a Promise⁴ has two goals: (1) permanently interrupt poliovirus transmission in endemic countries and (2) stop circulating vaccine-derived poliovirus (cVDPV) transmission and prevent outbreaks in non-endemic countries. It aims to achieve interruption of wild poliovirus serotype 1 (WPV1) transmission and reporting of the last isolate of cVDPV serotype 2 (cVDPV2) by end-2023, followed by certification of WPV1 eradication and validation of the absence of VDPV2 by end-2026, transition to an inactivated poliovirus vaccine (IPV) - exclusive essential immunization a year after i.e., end-2027, stop the transmission of cVDPV1 and cVDPV3 transmission by end- 2028, etc. These milestones would imply that poliovirus survey and inventory activities will need to be dynamic, repetitive in several instances and will likely persist for years.

The epidemiological situation in 2021 and 2022 (till date) shows a curtailment in WPV1 cases and environmental isolates detected in the two remaining endemic countries i.e., Pakistan and Afghanistan compared to previous years. Till date, only one WPV1 case has been reported in Afghanistan with no environmental isolates reported in both countries. In February 2022, a WPV1 was isolated from a child in Malawi who developed acute flaccid paralysis (AFP) with genetic analysis indicating linkages to a WPV1 detected in Sindh Province, Pakistan in October 2019. The WPV-free certification status of the WHO African Region declared in August 2020 remains unaffected as there is no evidence of local transmission.

Novel oral poliomyelitis vaccine serotype 2 (nOPV2), the first vaccine to be granted WHO Emergency Use Listing (EUL) in November 2020 was endorsed by the Strategic Advisory Group of Experts (SAGE) on immunization on 5 October 2021 to transition from initial to wider use based on its independent safety and genetic stability assessments. This makes nOPV2 the vaccine of choice for responding to outbreaks in countries meeting the post-deployment monitoring requirements.

At the 17th GCC meeting⁵ in 2018, the criteria for the certification of eradication of WPV were updated to include safe and secure containment of WPV⁶. While in the context of cVDPV to include non-detection of persistent cVDPV2 outbreaks in the previous 18 months and of cVDPV1 or cVDPV3 outbreaks of any source in the previous six months. In recognition that polio eradication has taken more time than anticipated with certification occurring sequentially i.e., WPV2 in 2015, WPV3 in 2019 and WPV1 in five of the six WHO Regions since 2020 and improved and expanded environmental surveillance to complement AFP surveillance, the GCC at its 21st meeting⁵ in 2021 recommended the establishment of a working group (GCC

⁴Polio Eradication Strategy 2022 – 2026: Delivering on a Promise. Available at: <https://apps.who.int/iris/bitstream/handle/10665/345967/9789240031937-eng.pdf> is the result of the revision of the Polio Endgame Strategy 2019-2023: Eradication, Integration, Containment and Certification. Available at: <https://polioeradication.org/who-we-are/polio-endgame-strategy-2019-2023/>

⁵ Meeting reports of the Global Commission for the Certification of Eradication of Poliomyelitis (GCC). Available at: <https://polioeradication.org/tools-and-library/policy-reports/certification-reports/global-certification-commission/>

⁶ The criteria include: (1) No WPV transmission detected from any population source for the previous three years; (2) adequate global poliovirus surveillance; and (3) safe and secure containment of WPV retained in facilities, such as laboratories and vaccine manufacturing facilities which would include: facilities retaining WPV having in-place a GCC-countersigned Containment Certificate (CC), or an Interim Certificate of Containment (ICC); and the biorisk management status of facilities retaining potentially infectious materials, poliovirus and facility readiness to respond to breaches in poliovirus containment.

Reference Group) to deliberate on the criteria to determine with certainty the interruption of WPV1 transmission in Pakistan and Afghanistan and interruption of cVDPV2 transmission.

WHO Containment Programme Update (Update on Survey and Inventory Activities, Containment Certification Update and Containment Country Support Activities)

Ms Liliane BOULAM, Technical Officer, Poliovirus Containment, Department of Polio Eradication, WHO headquarters in Geneva, SWITZERLAND and Secretariat, Global Commission for the Certification of the Eradication of Poliomyelitis - Containment Working Group (GCC – CWG) on behalf of the Poliovirus Containment Team, Department of Polio Eradication, WHO headquarters in Geneva, SWITZERLAND

The current governance for poliovirus containment oversight and functions of the different containment advisory bodies i.e., GCC, GCC – CWG, CAG, SAGE, Polio SAGE WG, Expert Committee on Biological Standardization (ECBS), etc. will remain in place with the implementation of the Polio Eradication Strategy 2022 – 2026: Delivering on a Promise. The World Health Assembly (WHA) resolution 71.16 (2018)⁷ adopted by all WHO Member States aims to accelerate progress in poliovirus containment and provides a timeline for the completion of national inventories of poliovirus materials and for the certification of facilities retaining poliovirus materials as described in the Containment Certification Scheme (CCS). There are currently 67 facilities in 25 countries designated for the continuation of critical functions requiring the retention of needed poliovirus serotype 2 (PV2). 64 of the 67 facility' applications to be recognised as suitable candidates to become poliovirus-essential facilities (PEFs) [i.e., Certificate of Participation (CP)] have been received by the GCC - CWG through the NACs of which 51 have been awarded a GCC-countersigned-CP.

GAPIII – CCS⁸ (2017) describes the recommended mechanism for certification of PEFs associated with global confirmation of poliovirus containment. Due to limitations of candidate auditors achieving the qualifying requirements of GAPIII auditors as described in the CCS, the GAPIII Auditor Qualification and Audit Support Plan (AQAS) 2021–2023⁹ was published in 2021 to provide flexibility and to ensure continuity of containment certification by providing sustainable activities for the qualification of auditors and certification of PEFs remotely due to the COVID-19 pandemic. Despite this, by end-2021 there were no GAPIII qualified auditors globally.

The poliovirus containment programme priorities for 2022 are: certification of facilities retaining polioviruses, advocacy to decrease the global number of PEFs; revision of containment reference documents e.g., GAPIII, CCS, etc. and national capacity building for the implementation of surveys and inventories of all poliovirus serotypes, implementation of the Global Polio Eradication Initiative (GPEI) Strategy for Global Poliovirus Containment and Suggested Activities 2022-2026, increasing visibility of poliovirus containment and future integration of the containment programme within WHO.

⁷ Resolution WHA71.16 (2018) Poliomyelitis – containment of polioviruses. Available at: http://apps.who.int/gb/ebwha/pdf_files/WHA71/A71_R16-en.pdf

⁸ GAPIII Containment Certification Scheme (CCS). Available at: <https://polioeradication.org/polio-today/preparing-for-a-polio-free-world/containment/containment-resources/>

⁹ GAPIII auditor qualification and audit support plan (AQAS) 2021–2023. Available at: <https://polioeradication.org/polio-today/preparing-for-a-polio-free-world/containment/containment-resources/>

Global Commission for the Certification of the Eradication of Poliomyelitis – Containment Working Group (GCC – CWG) Update on Containment Certification Processes, Challenges, and Progress.

Dr Arlene KING, Liaison Member of the Global Commission for the Certification of the Eradication of Poliomyelitis - Containment Working Group (GCC-CWG) to the CAG, Chair, GCC – CWG and Member, GCC, Toronto, Ontario, CANADA

The GCC is the global oversight body to confirm global containment of polioviruses. At the 15th GCC meeting⁵ in 2016, the GCC endorsed the proposed oversight structure for poliovirus containment, including the establishment of the GCC –CWG and agreed to delegate its day-to-day responsibility for the review of CCS applications submitted by PEFs through their NACs to the GCC – CWG. The review process adopted by the GCC – CWG for the CP-application phase is standardized and harmonized in line with the terms of the reference of the GCC – CWG¹⁰. To facilitate the review process, standardized CP-application forms have been made available, together with guidance on the relevant supporting documentation needed e.g., description of facility current containment conditions, facility time-bound action plan to achieve an ICC, etc. Submission of CCS applications are done through a dedicated and secure IT platform. The development of a similar process is nearing completion for the ICC phase.

There is an overall acknowledgement that the current COVID-19 pandemic has presented challenges to the NACs to progress to the ICC phase e.g., staff reassignment to COVID-19 pandemic response and PEF audits hindered by government restrictions on travel; misalignment between national legislation and CCS requirements; absence of qualified GAPIII auditor as per CCS at country level, etc. This lack of progress has delayed NACs from having the capacity to issue an ICC to facilities. This places CP-holding facilities at risk of not being able to be awarded an ICC before or by the CP end-validity date of 30 April 2022¹¹. Following the intention expressed by a NAC in May 2021 to pursue the ICC phase through a request for exemption from certain aspects of CCS and AQAS e.g., qualification requirements, etc., and supported by documentation consistent with meeting the intent of CCS, the GCC at its 21st meeting⁵ in July 2021 recommended that to sustain global containment progress, NACs may request for extension of facility CP end-validity of 30 April 2021 or pursue the ICC-phase in the absence of national-level qualified GAPIII auditors as per CCS with the necessary supporting documentation submitted and pre-approved by the GCC – CWG. Till date, 16 of the 20 established NACs have requested for the extension of the CP end-validity for 38 facilities – of which 29 of these facilities, which includes most of the polio vaccine producers, have expressed intention to pursue the ICC-phase.

In summary, the poliovirus containment programme has: observed a reduction in the global number of facilities designated for the continuation of critical functions requiring the retention of needed PV2 materials (owing to advocacy to countries to weigh the risk and benefits of hosting a PEFs; further reductions are anticipated through the widespread use of the S19 poliovirus strains which are highly attenuated and genetically stable developed as alternatives to the use of live polioviruses once available, destruction or the transfer of PV2 materials, cessation of work with PV2 by the CP end-validity, etc); countries readiness for CCS implementation [fewer CP applications from NACs for newly designated facilities planning to retain poliovirus serotype 3 (PV3) materials with some of such facility' CP applications already submitted to their NACs] and associated with the work of GCC – CWG in compliance verification (maintains the need for independence, autonomy and neutrality in performing quality and consistent compliance verification against the containment requirement), etc.

¹⁰ Terms of Reference of the Global Commission for the Certification of the Eradication of Poliomyelitis Containment Working Group (GCC – CWG). Available at: http://polioeradication.org/wp-content/uploads/2016/10/TOR_GCC-CWG.pdf

¹¹ Communication: Letter from Chair, Global Commission for the Certification of the Eradication of Poliomyelitis to National Authorities for Containment on COVID-19 pandemic impacts on implementation of CCS activities. Dated: 8 October 2020.

CAG Recommendation:

- CAG commends the GCC – CWG for the work, time and effort being invested in the review of facility' containment certification applications received by the NACs and the ongoing work in line with the latest recommendations made by the GCC on progressing with containment certification despite the challenges brought about by the COVID-19 pandemic and associated delays with implementation of the CCS..
- In line with the terms of reference of CAG specifically on 'Guidance on the identification of acceptable alternative containment solutions in the interim period, before full eradication', CAG offers its support, as needed to the GCC – CWG as progress is made towards the ICC phase and recommends that the Secretariats of CAG and CWG work closely as needed.

Session 2: Update on the Progress with the Revision of GAPIII

Overview of the Process Undertaken for the Revision of GAPIII and Outline of Issues
 Dr Harpal SINGH, Technical Officer, Poliovirus Containment, Department of Polio Eradication, WHO headquarters in Geneva, SWITZERLAND and Secretariat, Containment Advisory Group (CAG)

The process taken throughout the revision of GAPIII has been in line with the recommendations made by CAG at the Third Meeting of the CAG, 13 – 14 December 2018, as previously described³. The revision process was implemented as two workstreams consistent with the strategy for GAPIII implementation (Table 1):

1. Risk elimination i.e., survey of all facilities that may possess poliovirus materials, encourage destruction of unneeded materials, preparation of national inventory of facilities planning to retain needed polioviruses post-eradication.
2. Risk mitigation i.e., BRM requirements for facilities retaining polioviruses post-eradication¹².

Table 1: The process for the revision of GAPIII

Revision of BRM requirements for facilities retaining polioviruses post-eradication ¹²	
Inputs	Stakeholder solicitation of comments on Annexes 2 and 3 ¹² : <ul style="list-style-type: none"> • Initiated on 14 September 2020 – deadline extended upon request • 336 comments received from more than 17 stakeholder groups • Comments categorized by GAPIII BRM elements and prioritized based on availability of evidence or justification to support recommended change • Repeatedly cited issues: need for harmonization with other relevant documents, requirements repetitive and redundant, annex structure (tabular presentation) cumbersome, and combination of performance-based and polio-prescriptive requirements in a single standard is challenging for facilities to comply with, etc.
	Previous CAG recommendations
	Review of relevant standards such as but not limited to: <ul style="list-style-type: none"> • GAPIII – Containment Certification Scheme (GAPIII – CCS) • Guidance to minimize risks for facilities collecting, handling or storing materials potentially infectious for polioviruses (PIM Guidance) – 2nd, 2022. • WHO Laboratory Biosafety Manual and Associated Monographs, 4th edition (2020) • Guidelines for the safe production and quality control of poliomyelitis vaccines, Annex 4, WHO TRS No 1016 and Annex 3, WHO TRS No 1028 (Amendment to Annex 4 of WHO TRS No 1016) • ISO 35001: Biorisk management for laboratories and other related organisations (2019) • European Committee for Standardization (CEN), CEN Workshop Agreement CWA15793 – Laboratory biorisk management (2011)

¹² Annex 2 (Biorisk management standard for poliovirus-essential facilities holding wild poliovirus) and Annex 3 [Biorisk management standard for poliovirus-essential facilities holding OPV/Sabin (no wild)] of the current version of GAPIII. Available at: https://polioeradication.org/wp-content/uploads/2016/12/GAPIII_2014.pdf

	Review of relevant literature and scientific studies
	Research studies performed on GAPIII requirements e.g., walk-through exit shower, etc.
Output	Proposed changes made in the draft of the BRM standard for facilities retaining polioviruses post-eradication (technical e.g., new or revised requirements and non-technical e.g., document structure and organization) were based on the analysis of the different inputs.
	GAPIII requirements setting meeting (14 April 2021): to discuss the proposed structure of the revised GAPIII. The discussion involved members from CAG, CMG and NACs, WHO HQ and Regional Offices' Containment Team Members and WHO Global Polio Laboratory Network (GPLN), etc. Outputs: Note for the record and proposed draft of the table of contents of the revised GAPIII which was shared with the participants for feedback.
	Revision of activities involving survey of facilities that may possess poliovirus materials, encourage destruction of unneeded materials, preparation of a national inventory of facilities planning to retain needed polioviruses post-eradication.
Inputs	'Kick-off' meeting (15 April 2021): to identify, discuss issues and challenges faced in the implementation of activities as is currently described in GAPIII, to propose solutions in line with the terms of reference of other relevant containment stakeholders. This meeting involved members from CAG, CMG and National Poliovirus Containment Coordinators (NPCC) and WHO HQ and Regional Offices' Containment Team Members, etc.
Output	Note for record with the discussion points raised which formed the basis of the proposed changes made in this section. Revised section draft shared with participants for feedback.
	Draft outputs from both workstreams were consolidated into a single document for: <ul style="list-style-type: none"> • Detailed review and discussion by WHO • Critical review by CAG, as was requested, for feedback, comments and used as basis for deliberation at this meeting. .

The proposed consolidated revised GAPIII draft is, among others: in in line with other relevant documents and standards, it clarifies the basis of facility-based containment requirements, and emphasizes the use of a local risk-based approach for the application of risk mitigation strategies that can be applied across a range of PEFs that vary by location, size, and purpose, etc. These resulted in major changes to both the structure and the technical contents of GAPIII. A summary list of proposed changes made in the revised GAPIII for deliberation by CAG at this meeting, not to be construed as final requirements or endorsed by CAG, is included in Annex 3.

Issues for Consensus or Recommendation by CAG

Containment Perimeter

Dr Harpal SINGH, Technical Officer, Poliovirus Containment, Department of Polio Eradication, WHO headquarters in Geneva, SWITZERLAND and Secretariat, Containment Advisory Group (CAG)

Relevant Section or Text in GAPIII:

- The containment perimeter is a defined working area sealable for gaseous decontamination and with sealed penetrations to prevent uncontrolled outward airflow. The containment perimeter is required irrespective of the choice of primary containment.
- Controlled exit from the containment perimeter is via a walk-through exit shower. Showering out is mandatory except for facilities employing fully functional Class III biosafety cabinets (BSCs) or similar isolators (in such facilities, showering out is required in the event of an uncontrolled breach of the primary containment equipment).

Issue Raised :

Are airlocks, anterooms, HVAC spaces, and kill tank rooms required to be within the containment perimeter sealable for gaseous decontamination?

Request to CAG:

1. Clarity regarding which of these must be within the containment perimeter:
 - Anterooms,
 - Airlocks,
 - HVAC systems/mechanical spaces and
 - Kill tanks/effluent decontamination systems
2. Would the removal of the shower requirement affect the definition of the containment perimeter?

Additional Information:

'Guidelines for the safe production and quality control of poliomyelitis vaccines, Annex 4, TRS No 1016' indicates the following requirement for vaccine production and control:

Section: Decontamination and waste disposal systems

8.4.4 Effluents from equipment, showers and sinks within the containment facility should be decontaminated by autoclaving or by discharge into a liquid effluent decontamination system. Such a system should be fully validated to ensure efficacy and be located in the containment facility. The effluent treatment tanks should be situated in an area with floor dams or other measures capable of containing the full tank volume and allowing for the full inactivation of its contents.

CAG Recommendation:

- Anterooms and personnel airlocks are to be considered within the containment perimeter and must meet the requirements of spaces within the containment perimeter.
- Kill-tank rooms or equivalent must meet all construction, sealing, and HVAC requirements of the primary containment space and are required to have an anteroom/personnel airlock for controlled entry as described above.

Operator IPV Immunization and Poliovirus Antibody Titer Determination Requirements
 Dr Harpal SINGH, Technical Officer, Poliovirus Containment, Department of Polio Eradication, WHO headquarters in Geneva, SWITZERLAND and Secretariat, Containment Advisory Group (CAG)

Relevant Section or Text in GAPIII:

- Requirement: Based on risk, the need for vaccination has been determined and covers groups identified as being potentially exposed to poliovirus.
- Guidance: The organization will ensure the availability of IPV for individuals associated with the facility, consistent with the objectives to:
 - a) restrict access to the containment facility to individuals who have demonstrable immunity to poliovirus (defined as annual verification of serum neutralizing antibody titres of 1:8 or greater against all three poliovirus types), including:
 - personnel assigned to work within the containment perimeter;
 - contractors, auditors and visitors who must enter the containment perimeter;
 - support personnel and contractors working immediately outside the containment perimeter (e.g. maintenance personnel, cleaning staff);
 - b) administer an IPV booster every three years to all personnel mentioned above or in the event of an antibody titre determined to be <1:8 via annual testing;

Issue Raised :

Evidence does not support the need for repeated adult IPV boosters. Annual titer checks represent a significant burden, and the frequency of the requirement is not supported by evidence. Alternatives should be suggested.

Request to CAG:

1. Does this change in requirement be perceived as a conflict with existing vaccination strategies.
2. Does CAG support the change of this requirements from prescriptive guidance to risk-based approaches for each facility according to its local situation?

Evidence:

Vaccination in the context of facility level containment is different from population immunity safeguards

IPV Vaccination:

- Regarding naïve infants, literature suggests immunization of infants with one, two, or more doses of IPV does not prevent shedding of poliovirus in stool following OPV challenge
- There is a lack of evidence suggesting that IPV history (either single or multi-dose) raises EC₅₀ of poliovirus necessary to induce shedding

Conclusions:

- IPV vaccine protects workers against illness caused by poliovirus.
- IPV vaccine does not prevent fecal shedding of poliovirus.
- IPV vaccine does not make infection less likely after an exposure to 1poliovirus.

For this reason, a risk-based approach to determine the necessity of workplace and community vaccination with IPV is warranted to balance:

- The protections afforded to workers and their families
- Complication of early detection of loss of poliovirus containment.

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12. Onorato, I.M., et al., Mucosal immunity induced by enhanced-potency inactivated and oral polio vaccines. *Journal of infectious diseases*, 1991. 163(1): p. 1-6.

CAG Recommendation:

- Individuals associated with the poliovirus-essential facility must demonstrate established immunity to poliovirus through evidence of poliovirus antibodies prior to accessing the facility
- Subsequent need for IPV vaccination and antibody titre testing should be determined by a local risk assessment and should be consistent with national occupational health guidelines.

Issues associated with the GAPIII requirement for
walk-through exit shower from the containment perimeter

Use, effectiveness and risks associated with a walk-through exit shower as poliovirus containment barrier
Dr Karen VAN DER MEULEN, Biosafety and Regulatory Specialist, Perseus BVBA, Belgium

This study commissioned by CAG was to obtain more insight into the need to implement the current GAPIII requirement of a walk-through shower when exiting the containment perimeter. This requirement does not have a clear rational or robust set of criteria, supported by evidence-based risk assessment to justify if showers constitute a significant barrier for a facility-associated release of poliovirus. This study was implemented in two parts: a systematic literature review and survey. The survey aimed to obtain information from operators working in facilities deemed suitable to become PEFs and those working in animal biosafety level 3 (ABSL3) and ABSL4 facilities on the use of showering-out as a containment measure, use of alternative measures, and experiences with showering-out.

The following are the observations and recommendations from this study:

1. Among veterinary facilities:
 - a. showering-out is an effective containment measure for the physical removal of pathogen contamination, if present;
 - b. the procedure of showering-out functions as a strong containment barrier and helps create awareness, obliging operators to leave potentially contaminated items in the containment area.
2. Showering-out is considered one of the measures when exiting the containment perimeter, and its usefulness should be evaluated in the case of potential exposure, which can be reduced by the use of closed primary containment and closed process systems, appropriately selected personal protective equipment (PPE) and strict de-gowning procedures;
3. When correctly implemented, PPE and handwashing can reduce the risk for exposure, thereby reducing the need for stringent exiting requirements such as showering-out;
4. Well-defined and validated 'closed' systems can prevent exposure to polioviruses, thereby eliminating the need for stringent exit requirements such as showering-out. However, as a prerequisite the minimal features and validation methods of a 'closed system' should be defined;
5. Guidance on risk assessment methodologies that could be used by PEFs and indications of circumstances requiring the implementation of showering-out would be useful.

Distinguishing the Risk Reduction Potential of Exit Showers Versus Enhanced Personal Protective
Equipment in Poliovirus-essential Facilities.

Dr Christy OTTENDORFER, Microbiologist and Auditor, U.S. National Authority for Containment of
Poliovirus, Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America

This study commissioned by the US NAC aimed to compare the risk-reduction potential and evidence of a walk-through exit shower versus enhanced PPE in facilities deemed suitable to become PEFs in the US and to better understand how to reduce a facility-associated risk of release of poliovirus following a loss of containment (LOC) event using evidence-based risk controls and management for PEFs. This study involved the development of a quantitative, event-tree-based model to simulate a LOC resulting in the contamination of an operator as only such events could be mitigated by the use of PPE or an exit-showers.

The following are the observations and recommendations from this study:

1. Enhanced PPE and enhanced hand hygiene procedures should be implemented in place of showering-out to mitigate LOC events resulting in operator contamination. Full body PPE may be important when considering the risk mitigation of LOC events should their occurrence be deemed likely.
2. Perform as much work with polioviruses as possible in primary containment including when using equipment such as vortexers and centrifuges. Primary containment reduces risk of exposure to polioviruses better than any other alternative.
3. When transporting polioviruses outside primary containment, a secondary container should be used. Double containment will reduce risk of LOCs in case of falls, drops or spills.
4. Because LOCs resulting in contamination of the hands is likely to occur more frequently, double gloves should be worn, changed and sanitized frequently.
5. If aerosolization of polioviruses could occur outside primary containment e.g., outside a BSC, operators should be provided with respiratory protection.
6. Educate operators about aerosol generation and circumstances of its occurrence, including the possibility of aerosols being generated in the absence of an accident. Educate operators on responding to aerosols e.g., vacating the room should uncontained aerosol be present.
7. Train operators on the identification and reporting of any possible accidents or exposures, as even small amounts of poliovirus can lead to infection. Infections to operators comprise most of the infection risk, far outweighing the risk that member of the community is infected first.
8. Include wastewater workers, and, if relevant, septic systems and water wells operators in emergency response planning to a breach in poliovirus containment. Although of lower risk than other escape routes, polioviruses in wastewater could cause infections.

Risk-based Approach for Walk-through Exit Shower from the Containment Perimeter in line with the Most Recent CAG Recommendation.

Dr Harpal SINGH, Technical Officer, Poliovirus Containment, Department of Polio Eradication, WHO headquarters in Geneva, SWITZERLAND and Secretariat, Containment Advisory Group (CAG)

Relevant Section or Text in GAPIII:

- Controlled exit from the containment perimeter is via a walk-through exit shower. Showering out is mandatory except for facilities employing closed systems demonstrating validated primary containment. Such systems may include contained lines for use in vaccine production and/or facilities employing fully functional Class III BSCs or similar isolators. For such facilities, showering out is required as a precautionary measure, in the event of an uncontrolled breach of the primary containment equipment, during the period when further assessment of the effectiveness of showering is being undertaken.
- The CAG urged the secretariat to commission a study to collect information on the use, effectiveness and risks associated with showering, including in facilities where showering is currently being used. The CAG will undertake further discussion on showers when the secretariat has collected the information necessary to make an evidence-based recommendation or has shown that it is not feasible to collect such information

Issue Raised :

The requirement for showering out should be changed to a risk-based requirement in response to a release only. There is no evidence that showering-out under routine operations reduces exposure or release risk.

Request to CAG:

Does CAG support this shift from the prescriptive to risk-based approach for egress in line with CAG recommendation on this issue?

Evidence:

There is a lack of evidence to support showering out reduces exposure or release risk

CAG Recommendations:

- Exit shower requirement should be replaced with performance-based language which would generally be more applicable to the range of PEFs – this should emphasize the need for facility-specific risk assessment.
- Additional measures should be considered when exiting from the containment perimeter to prevent exposure to contaminated PPE or personnel.

Risk-based Approach for Storage of Poliovirus Materials Outside of GAPIII Containment.
 Dr Harpal SINGH, Technical Officer, Poliovirus Containment, Department of Polio Eradication, WHO headquarters in Geneva, SWITZERLAND and Secretariat, Containment Advisory Group (CAG)

Relevant Section or Text:

- Storage of polioviruses must be performed under appropriate containment conditions, as determined by a risk assessment approved by the competent authority (NAC), in line with the approach detailed in the Containment Certification Scheme to support the WHO Global Action Plan for Poliovirus Containment (GAPIII-CCS) for an interim certificate of containment (ICC) as well as for a certificate of containment (CC) assessment. Any derogations applied for and accepted by the NAC will be reflected on the certificate scope, and associated certificates, and regularly reassessed. (Source: CAG2 report)
- Areas used for the storage of poliovirus seed stock should be fully secured against entry by non-authorized personnel. For secondary (back-up) seed storage locations where stocks are not normally used for production, the NRA may approve storage in leak-proof containment containers within a dedicated freezer that is subject to security and access restrictions appropriate for the storage of poliovirus. Outside the containment facility, polioviruses should be stored under appropriate containment conditions, as determined by a risk assessment approved by the competent authority (for example, the NAC) and in line with the approach detailed in the GAPIII CCS as recommended by CAG. (Source: Guidelines for the safe production and quality control of poliomyelitis vaccines, Annex 4, TRS No 1016).

Issue Raised :

Guidelines for the safe production and quality control of poliomyelitis vaccines, Annex 4, WHO TRS No 1016 and Annex 3, WHO TRS No 1028 (Amendment to Annex 4 of WHO TRS No 1016) and CAG recommendations provide provisions for storing poliovirus material outside the containment perimeter provided it is packaged appropriately and secured via a risk-based approach. This greatly reduces the burden of containment space required specifically for storage and should also be outlined in GAPIII.

Request to CAG:

As outlined in previous CAG rulings, is storage of poliovirus infectious materials inside the PEF, but outside the containment perimeter acceptable provided the above conditions are met?

CAG Recommendation:

- The current version of GAPIII does not address storage of polioviruses outside of the containment perimeter. Therefore, the BRM element associated with 'poliovirus inventory and information' should be expanded to include storage procedures for polioviruses outside of the containment perimeter including conditions to be met e.g., leak-proof containers, dedicated freezers, proper labelling and other biosecurity measures, etc. as determined by a facility-specific risk assessment with the approval from the NAC.

Alternative Measures for Gaseous Decontamination and Guidance for Use.

Dr Harpal SINGH, Technical Officer, Poliovirus Containment, Department of Polio Eradication, WHO headquarters in Geneva, SWITZERLAND and Secretariat, Containment Advisory Group (CAG)

Relevant Section or Text in GAPIII

The containment perimeter is a defined working area sealable for gaseous decontamination

Issue Raised :

Request that alternatives to gaseous decontamination should be provided if gaseous decontamination is not possible or feasible in a facility. These could include manual decontamination, spray decontamination, etc. as determined by risk assessment

Request to CAG:

Should guidance on alternative decontamination methods be presented?

CAG Recommendation:

- The containment perimeter for existing facilities must be an area sealable for gaseous decontamination. For new facilities or facilities undergoing renovation, retrofitting or refurbishing, alternative methods of decontamination e.g. physical decontamination, etc. may be considered provided it is guided by the performance of a comprehensive risk assessment.

HEPA Filtration on Exhaust Side As Requirement Prior to Final Containment of all WPV.

Dr Harpal SINGH, Technical Officer, Poliovirus Containment, Department of Polio Eradication, WHO headquarters in Geneva, SWITZERLAND and Secretariat, Containment Advisory Group (CAG)

Relevant Section or Text in GAPIII

The controlled air system maintains directional airflow via a dedicated ventilation system with ductwork sealable for gaseous decontamination, HEPA filtration on exhaust, backflow protection on supply, and monitors/alarms to ensure directional airflow can be readily validated” for WPV final containment”

Issue Raised :

The requirement for HEPA filtration of exhaust prior to final containment represents an unnecessary burden

Request to CAG:

1. Should the requirement for HEPA filtration of exhaust for WPV final containment be removed?
2. Does the use of supply-side HEPA filters directly on the containment barrier in the absence of interconnections (supply connections to other spaces or return exhaust from other spaces), if correctly maintained and routinely tested, not functionally equivalent being dedicated?

CAG Recommendation:

- The use of supply-side HEPA filters directly on the containment barrier if and when correctly maintained would functionally meet the intent of a dedicated HVAC system.
- This requirement i.e., HEPA filter on exhaust or its functional equivalent, is to be maintained for facilities retaining WPV polioviruses in the containment phase of all WPV serotypes.

Changes made in primary, secondary and tertiary safeguards as described in GAPIII
 Dr Harpal SINGH, Technical Officer, Poliovirus Containment, Department of Polio Eradication, WHO
 headquarters in Geneva, SWITZERLAND and Secretariat, Containment Advisory Group (CAG)

.Replacement of GAPIII Jargon 'Primary, Secondary and Tertiary Safeguards'
 with Technical Language or Definition

Issue Raised :

The terminology of primary, secondary and tertiary safeguards is unique to GAPIII and thus unfamiliar to those outside poliovirus containment.

Request to CAG:

For consensus.

CAG Recommendation:

Replace the term 'primary safeguards' to 'facility safeguards', 'secondary safeguards' to 'immunization coverage safeguards' and 'tertiary safeguards' to 'environmental control safeguards'.

Operationalization of Population Immunity Safeguards Within the
 Context of SAGE Current Recommendations

Relevant Section or Text:

Countries with PEFs and currently using a single dose of IPV are recommended to adjust their IPV schedule, coverage targets and geographical scope as soon as possible and no later than at the time of all OPV cessation, to:

1. Implement a routine immunization schedule with a minimum of 2 IPV doses (full or fractional, standalone or in combination vaccines), with the first dose administered at 4 months and second dose at an interval of at least 4 months after the first dose.
2. Maintain high population immunity with $\geq 90\%$ of IPV2 coverage in infants in the area surrounding the PEF defined as within a 100km commutable distance from the PEF. Maintain the GVAP target coverage (90% national coverage and 80% in every district or equivalent administrative unit with all vaccines in national programmes, unless otherwise recommended) beyond the immediate zone of 100 km from the PEF.
3. Have an outbreak plan specifying response to containment breach and conduct outbreak simulation exercises'

(Source: Meeting of the Strategic Advisory Group of Experts on immunization, April 2018 – conclusions and recommendations, Weekly Epidemiological Record 2018;93:329–44. Available at:

<http://apps.who.int/iris/bitstream/handle/10665/272782/WER9323.pdf?ua=1>)

Issue Raised :

Data stratified by infants and geographical area of 100 km is not available and would entail the need for serosurveys. In some countries the 100 km radius extend to another country. In addition, some countries do not have an IPV2 dose schedule implemented.

Request to CAG:

For consensus

CAG Recommendation:

- Based on the Polio Eradication Strategy 2022 – 2026: Delivering on a Promise, the complete phase out of all oral poliomyelitis vaccine (OPV) is anticipated in 2030+ and this provides sufficient time for countries hosting PEF to achieve these requirements i.e., two-IPV doses and IPV2 coverage.
- In line with the recommendation made by the Strategic Advisory Group of Experts (SAGE) on immunization which permits countries-hosting PEFs to implement this requirement no later than

time of all OPV cessation, the approach to be taken in the revised GAPIII should be adjusted to make it more globally implementable and pragmatic based on data availability and local circumstances. In the interim period (before complete phase out of all OPV), the immunity requirements should consider the current IPV supply, IPV in routine immunization, and availability of IPV coverage data, etc. with the goal of achieving the recommendation made by SAGE by the time of all OPV cessation. Therefore, two options are recommended for the operationalization of these safeguards: (1) pre-OPV cessation period and (2) post-OPV cessation period. The post-OPV cessation period is to be considered the deadline for countries hosting PEFs to meet this requirement, but CAG encourages an early compliance with this requirement.

	OPV/Sabin	WPV/VDPV
Population Immunity Safeguards		
IPV1 or IPV2 coverage during the pre-OPV cessation period	= DTP3 coverage or $\geq 90\%$	= DTP3 coverage or $\geq 90\%$
IPV2 coverage during the post-OPV cessation period	$\geq 90\%$	$\geq 90\%$

Depending on the country context and location of the PEF, coverage data may represent national level or subnational level, whichever appropriate.

Local Risk-based Approach for Environmental Control Safeguards

Relevant Section or Text:

Tertiary safeguards of facility location minimize the consequences of the unintentional release of highly transmissible WPV by placing poliovirus-essential facilities in areas with demonstrated low poliovirus R_0 , i.e. in areas with closed sewage systems with a minimum of secondary treatment of effluents.

Issue Raised :

There are no indicators stated in GAPIII to assess tertiary safeguards. In addition, the parameters indicated in the present definition may not represent actual PEF-location circumstances e.g., population density, etc.

Request to CAG:

For consensus

CAG Recommendation:

- The requirement for PEFs to be located in areas with closed sewage systems with secondary or greater treatment of effluents in the community should be replaced with risk-based language that maximizes the utilization of local environmental parameters that reduces the risk of poliovirus transmission (R_0).
- Consideration should also be provided for the implementation of additional environmental safeguards by the NAC e.g., environmental surveillance for communities living close to the PEF.
- Thus, the definition is to be expanded to include local context in the determination of the R_0 of poliovirus and is risk-based in approach tailored to local situations i.e., 'The environmental, sanitation and hygiene conditions (e.g., good personal, domestic, and environmental hygiene standards; closed sewage systems with secondary or greater effluent treatment; low population density in surrounding areas) that minimize the risk of re-establishing the circulation of highly transmissible wild poliovirus in the event of reintroduction'

Revision Made in the Survey, Inventory and Destruction Activity Section of GAPIII.
 Dr Harpal SINGH, Technical Officer, Poliovirus Containment, Department of Polio Eradication, WHO
 headquarters in Geneva, SWITZERLAND and Secretariat, Containment Advisory Group (CAG)

Issue Raised :

Many of the timelines, and activities in the current version of GAPIII do not represent the actual implementational level in countries. In addition, verification/validation processes are not described in the current version of GAPIII. Since the publication of the current version of GAPIII, several other guidance documents have been published e.g., PIM Guidance, PIM Tool and the development of novel poliovirus strains.

Request to CAG:

For consensus

CAG Recommendation:

- CAG noted that the revision of this section was based on the outputs from the 'Kick-off' meeting held on 15 April 2021 (Table 1) and consented to the following recommendations:
 - Definitions (previously Annex 1) moved to the beginning of the document
 - Revision and update of the introduction
 - Addition of the 'Roles and Activities' section to describe poliovirus containment stakeholders and their terms of reference in the context of this document
 - Addition of 'Containment Requirements for Novel Poliovirus Strains' section based on previous CAG requirements
 - Complete removal of the 'Phases' approach from GAPIII
 - Replaced with 'Inventory and Destruction' and 'Containment' phase.
 - 'Inventory and Destruction' described as ongoing and in-effect for all strains, WPV and Sabin/OPV, globally.
 - Containment' requirements to be implemented in stages by strain as determined by GCC based on eradication progress and involves four parts:
 - 'Establishment' (as needed),
 - 'Verification' (in-transition for all strains),
 - 'mOPV stockpiles' (in-transition for all OPV strains), and
 - 'Final Containment' (in-transition for WPV2 and WPV3)

Containment Requirements for Potentially Infectious Materials, WPV/VDPV.
 Dr Harpal SINGH, Technical Officer, Poliovirus Containment, Department of Polio Eradication, WHO
 headquarters in Geneva, SWITZERLAND and Secretariat, Containment Advisory Group (CAG)

Issue Raised: (see Figure)

- In its current version, GAPIII requires all potentially infectious materials (PIM), polioviruses to be handled according to Annex 2 (WPV/VDPV) or Annex 3 (Sabin/OPV) of GAPIII.
- The current PIM guidance does not subject Sabin/OPV PIM to Annex 3 of GAPIII but rather that a risk determination be conducted based on both the sample type and nature of the work to be performed, and specific risk mitigation measures taken to minimize the risk of handling and storing such material.
- The PIM guidance continues to require WPV/VDPV PIM be subjected to Annex 2 of GAPIII.
- Consideration should be provided for the requirements for WPV/VDPV PIM to be subjected to a risk determination process and the containment requirements for handling and storing WPV/VDPV PIM be in line with the risk mitigation approach by risk stratification as was done for Sabin PIM as per PIM Guidance.
- This is because, in several countries hosting many laboratories, implementation of the PIM surveys have indicated a large number of facilities planning to retain WPV/VDPV PIM only. At present, these facilities will have to implement Annex 2 of GAPIII and enter the CCS placing a burden on the NACs in their performance of audits and associated activities. In the 2004 PIM survey implemented in the US, a total of 56 laboratories were identified as planning to retain WPV/VDPV PIM only.

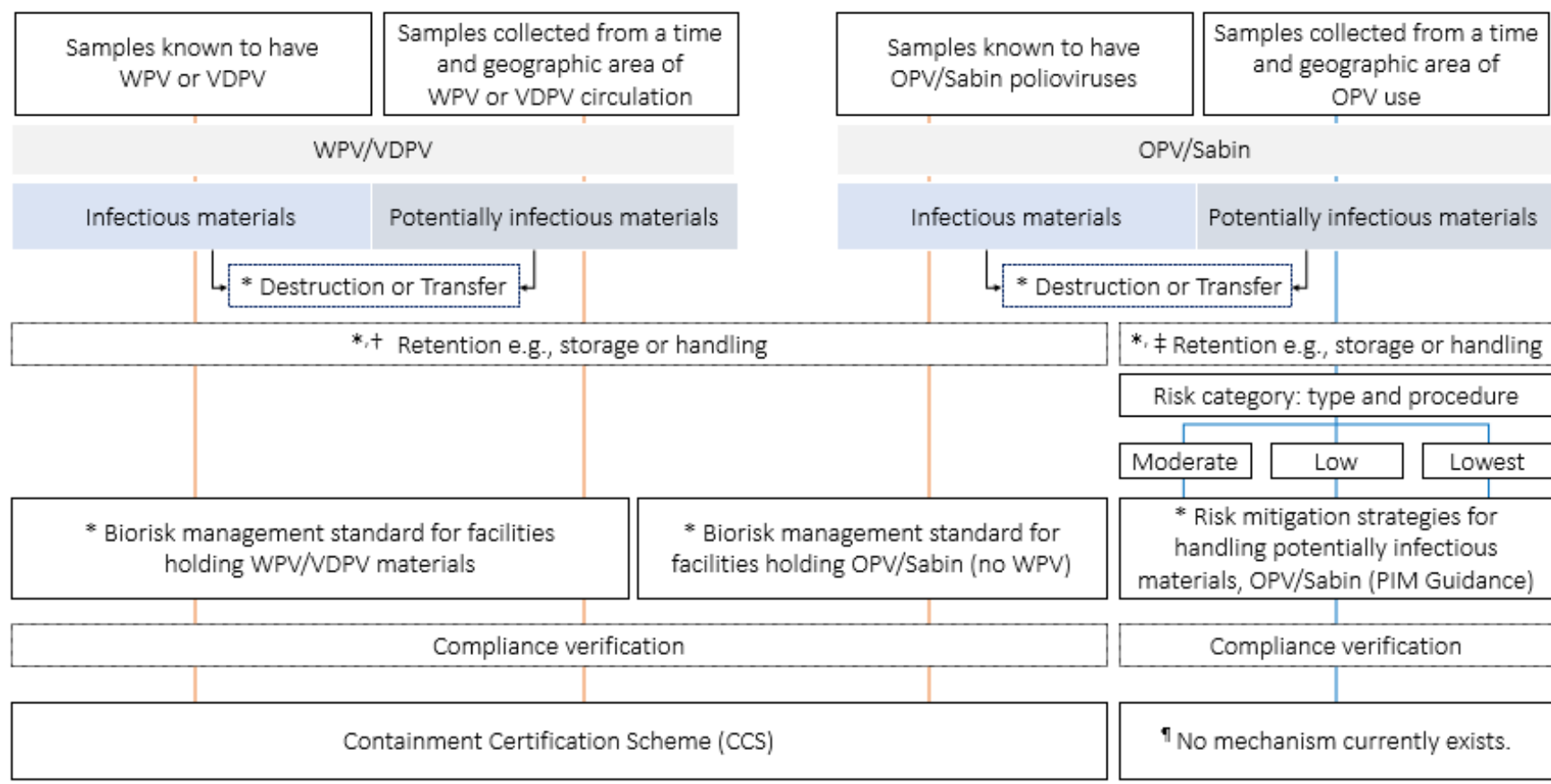
Request to CAG:

CAG is requested to provide input into the containment requirement of WPV/VDPV PIM and if they should remain subject to Annex 2 of GAPIII.

CAG Recommendation:

- CAG noted the concerns raised by the NACs of the need for facilities retaining for potentially infectious materials, WPV/VDPV to implement the containment requirements in GAPIII, undergo compliance verification as per CCS which places an additional burden on the NACs in countries with numerous facilities retaining only such materials.
- CAG recommends the following:
 - In line with the strategy for the implementation of GAPIII i.e., risk elimination, the concerned NACs should encourage these facilities to destroy such materials.
 - The containment requirements for the retention of potentially infectious materials, WPV/VDPV will remain in line with the requirements of GAPIII or its revised version for now. A more in-depth review of the containment requirements of potentially infectious materials, WPV/VDPV in regards to the applicability of GAPIII or its revised version, will be undertaken by the Potentially Infectious Materials, Polioviruses Guidance Development Group (previously established and tasked with the development of the PIM Guidance, 1st edition) in 2022.
- In addition, CAG also highlighted several issues associated with the retention of potentially infectious materials, polioviruses which require resolution and encourages the Secretariat to coordinate with the Potentially Infectious Materials, Polioviruses Guidance Development Group to deliberate on the following:
 - The compliance verification mechanism, currently lacking in the PIM Guidance for facilities retaining potentially infectious materials, Sabin materials with the risk mitigation strategies described in the PIM Guidance.
 - In line with the current goal of eliminating the use the of all type 2 polioviruses (including Sabin serotype 2 poliovirus and OPV2), the longer-term containment requirement for the retention of potentially infectious materials, Sabin specifically in the post-OPV cessation period should be discussed.

Figure: Risk elimination and risk mitigation (biorisk management) strategies to minimize facility-associated release of the different types of poliovirus materials post-eradication and the respective oversight mechanism as per current CAG recommendations and relevant poliovirus containment documents e.g., GAPIII, CCS, PIM Guidance, etc.



Abbreviations: CCS: Containment Certification Scheme; GAPIII: Global Action Plan for Poliovirus Containment, 3rd ed., 2015; MOH: Ministry of Health; OPV: Oral poliomyelitis vaccine; PIM: Potentially infectious materials, poliovirus; VDPV: Vaccine-derived poliovirus and WPV: Wild poliovirus.

*Global strategy to minimize facility-associated release of poliovirus post-eradication consists of risk elimination by destruction or transfer of poliovirus materials to a facility deemed suitable to become a PEF and risk mitigation (or biorisk management) by adherence to required safeguards in GAPIII in facilities retaining polioviruses deemed needed and worth storing to ensure continuation of critical functions e.g., Salk- and Sabin-IPV production and quality control, development/storage of OPV stockpiles, diagnostic reagent production, diagnostic/reference functions, and crucial research, etc.

†Retention is subject to approval of- and designation of the facility by - a national authority e.g., MOH, NAC, etc. as serving critical functions requiring the retention of needed poliovirus materials.

‡ Retention is subject to declaration to a national authority e.g., NPCC, NTFC, NCC, MOH or equivalent, for national survey and inventory activities of polioviruses.

¶Responsibility for compliance lies with the facility and the national authority (e.g., MOH), in coordination with the NPCC,, NCC, or equivalent, and others, as applicable.

Updated Recommendations from the CAG - Expert Support Group (CAG-ESG) on Novel Poliovirus Strains.
Dr Mark PALLANSCH, Member, CAG; Chair, CAG-ESG on Novel Poliovirus Strains and Co-Chair, CMG

Background:

- Poliovirus will be fully eradicated only when all sources of the virus including both WPV and VDPV, are eliminated. This definition takes into consideration the retention of needed polioviruses in facilities post-eradication for the continuation of critical functions and the development and ongoing work with novel poliovirus strains that are considered more attenuated, less pathogenic and safer than OPV/Sabin strains.
- nOPV2 is an attenuated Sabin OPV2 with the following properties: highly attenuated, grows sufficiently for purposes of vaccine production, antigenically indistinguishable from Sabin OPV2, genetically stable, maintains an attenuation phenotype in studies to date both in-vitro and in field use although non-significant mutations and recombination have been observed in its first year of use from AFP and environmental surveillance samples.
- The S19 - poliovirus strains¹³ are attenuated Sabin OPV with capsid sequences of both Salk and Sabin series vaccine strains with the following properties: highly attenuated, grows sufficiently for purposes of vaccine production, antigenically indistinguishable from the corresponding vaccine strains, genetically stable as the construct is observed to remain stable during replication, maintains an attenuation phenotype in mice and is likely non-infectious to humans.

Issues:

Issues concerning the definition of novel poliovirus strains:

- Sabin monovalent oral poliomyelitis vaccine serotype 2 (mOPV2), Sabin trivalent oral poliomyelitis vaccine serotypes 1, 2 and 3 (tOPV), nOPV2, S19 all consist of live, oral attenuated poliovirus serotype 2. At present, mOPV2, tOPV and nOPV2 can only be used for outbreak response¹⁴, with the use of nOPV2 having additional requirements as part of EUL. As the present goal remains consistent i.e., elimination of all live poliovirus serotype 2 globally, and in line with poliovirus serotype 2 being defined only by the sequence of the capsid region, this goal currently extends to these four vaccines and will ultimately be applicable to poliovirus serotype 1 and 3.

Issues concerning the containment requirements of novel poliovirus strains:

- nOPV2 and all S19 strains are live polioviruses and by definition subject to GAPIII
- To date, CAG recommendations have been related to the containment requirements i.e., Annex 2 or 3 of GAPIII for the handling of nOPV2, S19-poliovirus strains and PVSRIPO¹⁵ for specific uses. These recommendations were developed based the 'Criteria for the evaluation of improved safety of novel poliovirus strains to determine the containment requirements for their storage and handling'¹⁶ as developed by CAG, resulting in the following:
 - nOPV2 is temporarily waived* from the requirements of Annex 3 for these specific uses⁵:
 - Vaccine production
 - Vaccine quality control
 - Clinical trials

¹³ S19-poliovirus strains: S19 with the structural (capsid) protein encoding P1-region (of WPV or Sabin polioviruses; serotypes 1, 2 or 3); S19/N18S-poliovirus strains: S19 with the structural (capsid) protein encoding P1-region (of WPV or Sabin polioviruses; serotypes 1, 2 or 3) with mutation (substitution) of asparagine (N) by serine (S) at amino acid 18 of the non-structural protein 2A for better growth in Vero cells

¹⁴ For countries planning on conducting nOPV2 outbreak response campaigns, early discussions and deliberations on evaluating country-use should involve the NACs or another authority (e.g., MOH), in addition to all other relevant institutions or committees [e.g., National Regulatory Authority (NRA)], relevant ministries, and professional bodies of the related disciplines [e.g., biosafety].

¹⁵ Neuro-attenuated recombinant poliovirus consisting of live attenuated Sabin serotype 1 with heterologous internal ribosomal entry site (IRES) of human rhinovirus type 2.

¹⁶ Criteria for the evaluation of improved safety of novel poliovirus strains to determine the containment requirements for their storage and handling . Available at: <http://polioeradication.org/wp-content/uploads/2017/08/criteria-evaluation-novel-pv-june-2019-eng.pdf>

- Outbreak response¹⁴
- S19 strains is temporarily waived* from the requirements Annex 2 and Annex 3 for these specific uses⁵:
 - IPV production
 - Rat neutralization IPV potency assays
 - Human serum neutralization test for poliovirus antibody determination
 - Potency testing for immunoglobulin (human) lot control and release

Issues concerning survey and inventory activities for polioviruses:

- There is no exemption of novel poliovirus strains of any kind from the survey and inventory requirement which includes reporting to the responsible national authority in the countries i.e., NPCC or a similar body who should inform the NCC for inclusion in the annual reports to the RCC. The reported information should include the number of doses/vials used, number of remaining opened/unopened vials, verification/validation of collection, disposal of remaining vials, etc.

Issues concerning nOPV2 vaccine accountability: :

- Vaccine accountability requirements are equivalent for both nOPV2 and mOPV2, which will also be applicable to tOPV with the additional specific requirement for enhanced environmental surveillance for the use of nOPV2. Unless otherwise decided by CAG, the containment requirements for nOPV2 vial management is the same as those for mOPV2¹⁷.

Issues concerning alignment of nOPV2 guidance documents:

- The alignment of the different nOPV2 guidance and technical briefing documents is critical to ensure a harmonized understanding of its production, storage, deployment and management in field use. Such documents include: novel OPV2 (nOPV2) Management: Monitoring, Removal and Disposal (in 50 dose vials with VVM type 2): Interim Technical Guidance for Initial Use Period¹⁷; nOPV2 Readiness Verification and Dose Release Process: Interim guidance for the Initial Use Phase¹⁸; revised GAPIII; CAG recommendations; Guidelines for the safe production and quality control of poliomyelitis vaccines, Annex 4, WHO TRS No 1016 and Annex 3, WHO TRS No 1028 (Amendment to Annex 4 of WHO TRS No 1016), etc.

*The issuance of a temporary waivers for the specified uses indicated above is not to ease oversight but was granted to facilitate the eradication programme's response to the ongoing cVDPV2 outbreaks and failures of outbreak response campaigns, specifically those related to nOPV2. Additionally, the waiver was intended to create equivalency of the field use of nOPV2 and mOPV2 not a different standard. Temporary waivers only cover specific viruses and specific uses and cannot be generalized to other novel poliovirus strains or other uses. The exemption granted will be extended to the containment requirements of the revised GAPIII, upon its publication. The duration of validity of the temporary waivers and the containment requirements for the handling of novel poliovirus strains, after the end-validity of these waivers, is currently being discussed by the CAG – ESG.

[¶]Based on the experience with these two strains, more formal in vitro and in vivo criteria will be finalized.

CAG Recommendation:

In line with the submissions received by CAG on the use of specific novel poliovirus strains for specific uses, CAG recommends the following:

1. CAG – ESG through the CAG Secretariat to request for access to genetic stability data after first year use of nOPV2 at scale from the nOPV2 Working Group.
2. The following specific uses are granted a temporary waiver* to be exempt from the containment requirements of Annex 3 of GAPIII:
 - I. trivalent formulation of nOPV1, nOPV2, and nOPV3.
 - II. nOPV (all four) formulation studies and tOPV clinical trials

¹⁷ Novel OPV2 (nOPV2) Management: Monitoring, Removal and Disposal (in 50 dose vials with VVM type 2) Interim Technical Guidance for Initial Use Period. Available at: <https://polioeradication.org/wp-content/uploads/2021/02/nOPV2-Vaccine-Handling-Technical-Guidance-20201103-ENG.pdf>

¹⁸ nOPV2 Readiness Verification and Dose Release Process: Interim guidance for the Initial Use Phase. Available at: <https://polioeradication.org/wp-content/uploads/2020/12/nOPV2-Readiness-Verification-and-Dose-Release-Process-20201208.pdf>

3. For specific research purposes, the following novel poliovirus strains are granted a temporary waiver* from the containment requirement of Annex 2 or 3 of GAPIII, whichever applicable as follows:

Strains	Specific Uses
<ul style="list-style-type: none"> • nOPV2 candidate 1 (aka nOPV2-c1, or S2/cre5/S15domV/rec1/hifi3/S2P1) • nOPV3 candidate 1 (aka nOPV3-c1, or S2/cre5/S15domV/rec1/hifi3/S3P1) • nOPV1 candidate 2 (aka nOPV1-c2, or S2/cre6/S15domV/CpG30/rec1/hifi3/S1P1) • nOPV2 candidate 2 (aka nOPV2-c2, or S2/S15domV/CpG40) • nOPV3 candidate 2 (aka nOPV3-c2, or S2/cre6/S15domV/CpG30/rec1/hifi3/S3P1) • nOPV2 candidate 3 (aka nOPV2-c3 or S2/cre6/S15domV/CpG40/rec1/hifi3) • S19S1 • S19S2 • S19S3 • S19S1_N18S • S19S2_N18S • S19S3_N18S • S19Mah • S19MEF1 • S19Skt • S19Mah_N18S • S19MEF1_N18S • S19Skt_N18S 	<ul style="list-style-type: none"> • Laboratory activities to support clinical trials and ongoing monitoring of continued use • Viral concentration from environmental samples • Development or refinement of methods for viral concentration and detection from environmental samples • Frozen storage of stool specimens from clinical trials • Determination of D-antigen content • Determination of viral titer • Stability studies, including for alternative nOPV formulations • Characterization of aliquots from stability studies (e.g., pH, aggregation assays, HPLC) • Immunogenicity assays in mice and rats • Detection of nOPV and mucosal antibodies to nOPV in stool samples • Neutralization assays • Isolation of antibodies and virus from stool samples (human, mouse, rat) • Mass spectroscopy • Small-scale propagation • Nucleic acid extraction • Sequencing • Potency testing for immunoglobulin (human) lot control and release • Testing effectiveness of inactivation and disinfection methods • Sterility studies to confirm inactivation and disinfection methods • Spiking biosolids (sewer sludge) or wastewater to demonstrate effectiveness of treatments

4. Deliberation by the CAG-ESG should be initiated as soon as possible to address outstanding issues associated with the temporary waiver granted for the use of novel poliovirus strains for specific uses including:

- CAG recommendation on the compliance monitoring of relevant facilities with the terms of the temporary waiver as there currently is no mechanism to do so.
- The duration of validity of the temporary waivers as there are implications to the CCS and the containment requirements for the handling of novel poliovirus strains, after the end-validity of these waivers.
- Related to the point mentioned above, the role of CAG in resolving the exemption from the containment requirements of novel poliovirus strains for specified uses in the post-OPV cessation period when all live poliovirus are expected to be fully contained.

*The issuance of a temporary waivers for the specified uses indicated is not to ease oversight but has been granted to facilitate the eradication programme's response to the ongoing cVDPV2 outbreaks and failures of outbreak response campaigns. Temporary waivers only cover specific viruses and specific uses and cannot be generalized to other novel poliovirus strains or other uses. The duration of validity of the temporary waivers and the containment requirements for the handling of novel poliovirus strains, after the end-validity of these waivers, is currently being discussed by the CAG – ESG. The exemption granted will be extended to the containment requirements of the revised GAPIII, upon its publication.

Session 3: Other Issues Associated with the Revision of GAPIII

Timelines and Remaining Steps in GAPIII Revision

Dr Harpal SINGH, Technical Officer, Poliovirus Containment, Department of Polio Eradication, WHO headquarters in Geneva, SWITZERLAND and Secretariat, Containment Advisory Group (CAG)

Issue Information :

The timelines proposed as described below aims to have the revised version of GAPIII endorsed by CAG by end of Q2/2022 and published in July 2022.

Proposed Timelines for the Remaining Steps in the Revision Process:

Date(s) [2022]	Days	Activity or Steps
*2, 4 and 9 Mar	3	CAG5 meeting: follows critical review of draft revised GAPIII by CAG. Main agenda items are presentations and discussions on the revision of GAPIII for consensus and recommendations by CAG and discussions on associated issues.
		↓
10 – 20 Mar	7	Feedback from CAG incorporated into the working GAPIII draft.
		↓
21 – 27 Mar	5	Updated revised GAPIII is shared with CAG as background reading materials ahead of TC (28 Mar). At the same time, the draft document will be prepared for public consultation e.g., formatting, comment template, instructions, outreach strategy, etc.
		↓
†28 Mar	1	CAG TC on the changes made to GAPIII draft post-CAG5 and to obtain approval from CAG to pursue public consultation.
		↓
29 Mar – 1 May	24	Public consultation period..
		↓
2 – 15 May	10	Analysis of submissions received from public consultation including categorization of comments, frequency of issue raised, originator of submission, prioritization of comments, justification/evidence and other relevant information, etc.
		↓
16 – 22 May	5	Analysis of comments from public consultation with log-sheet of all submissions is shared with CAG ahead of TC (23 May).
		↓
†23 May	1	CAG TC to discuss comments from public consultation and to seek recommendations from CAG for further revisions to be made in the draft document based on the comments received.
		↓
24 May – 5 Jun	9	Comments or suggestions from public consultation are incorporated into the working GAPIII draft based on recommendations made by CAG at previous TC (23 May) and preparation of draft document for final review and endorsement by CAG.
		↓

Date(s) [2022]	Days	Activity or Steps
†6 Jun	1	CAG TC .on changes made based on comments from public consultation as per CAG recommendation and TC to mark the 'kick-off' for final review and endorsement by CAG of the revised GAPIII draft.
		↓
7 – 29 Jun	17	Final review of by CAG and for purposed of endorsement of the revised GAPIII draft.
		↓
†30 Jun	1	TC for endorsement of the revised GAPIII draft by CAG.
		↓
1 July	1	Publication of CAG-endorsed 'advanced unedited version' of the revised GAPIII
		↓
	TBD	Translations into official UN languages, document graphic-design and layout followed by web publication of the document.
	1	Potential launch event of revised GAPIII with Chair and potentially Members of CAG, Director, Polio Eradication, WHO headquarters in Geneva, SWIITZERLAND and other relevant stakeholders.
4 July onwards	TBD	Preparations to inform the Governing Bodies of WHO i.e., EB (2022) and WHA (2023) of the following: <ul style="list-style-type: none"> • Completion of the GAPIII revision process resulting in a revised document which has been endorsed by CAG. • Revised version supersedes the previous version with effect from 1 July 2022 - due to the changes required, relevant stakeholders have a three year transition period to meet the requirements of the revised GAPIII[‡]. • In line with its mandate, CAG has been involved through the revision process including the endorsement of the revised GAPIII. The endorsement by CAG[¶] was due to the transfer of the oversight function of containment documents, previously held by SAGE, to CAG in late-2018.

List of Abbreviations: CCS: Containment Certification Scheme; EB: Executive Board; GAPIII: WHO Global Action Plan for Poliovirus Containment (2015); IM: Infectious Materials, Poliovirus; PIM: Potentially Infectious Materials, Poliovirus; SAGE: Strategic Advisory Group of Experts of immunization; TC: Teleconference and WHA: World Health Assembly.

*Ongoing

†Planned teleconferences with CAG as part of the revision process of GAPIII for agreement from CAG.

‡The intent of the transition period is to allow a reasonable amount of time for the development of resources, procedures, methods and where appropriate their validation, and documentation time to meet the new requirements in the revised GAPIII..

¶ GAPIII, 2015 was endorsed by SAGE In October 2014 (Available at: <http://www.who.int/wer/2014/wer8950.pdf?ua=1>) and WHA 68.3 in 2015 (Available at: http://apps.who.int/gb/ebwha/pdf_files/WHA68-REC1/A68_R1_REC1-en.pdf#page=27). CCS was endorsed by SAGE in 2016 (Available at: <http://apps.who.int/iris/bitstream/10665/251810/1/WER9148.pdf?ua=1>) to supersede Annex 4 of GAPIII (WHO verification that certified poliovirus-essential facilities comply with GAPIII) - EB140 was informed of this change in January 2017 (Available at: http://apps.who.int/gb/ebwha/pdf_files/EB140/B140_13-en.pdf).

CAG Recommendations:

- CAG agreed to the proposed processes and timelines, including dates for the teleconferences in order to complete the revision of GAPIII by end of Q2/2022, should they remain appropriate.

Naming of the Revised GAPIII

Dr Harpal SINGH, Technical Officer, Poliovirus Containment, Department of Polio Eradication, WHO headquarters in Geneva, SWITZERLAND and Secretariat, Containment Advisory Group (CAG)

Relevant Section or Text:

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 (full title), WHO Global Action Plan for Poliovirus Containment (short title) and GAPIII (abbreviation).

Issue Raised :

- This revision is to be considered a major revision in the current GAPIII, as the changes proposed have involved a substantive change in the structure, requirements and approach in the revised document.

Background information:

Year Published	Full Title	Short Title, if any	Abbreviation
1999	WHO Global Action Plan for laboratory containment of wild polioviruses	Global Action Plan, 1st edition	GAPI
2004	WHO Global Action Plan for laboratory containment of wild polioviruses	Global Action Plan, 2nd edition	GAPII
2009	WHO global action plan to minimize poliovirus facility-associated risk after eradication of wild polioviruses and cessation of routine OPV use	Global Action Plan, 3rd edition	GAPIII*
2015	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*	WHO Global Action Plan for Poliovirus Containment*	

*version undergoing revision

Proposed Options:			
Year Published	Full Title (options)*	Short Title (options)*	Abbreviation (options)*
2022	<ul style="list-style-type: none"> • 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 • Global Action Plan for Poliovirus Containment: Survey and inventories-, destruction-, preparation for- and the containment of- serotype specific wild poliovirus following eradication and time-appropriate cessation of oral polio vaccines • WHO Global Action Plan for Poliovirus Containment • WHO Global Action Plan for the Containment of Polioviruses • Safe and Secure Poliovirus Containment Action Plan • Poliovirus Risk Elimination and Post-eradication Biorisk Management Action Plan 	<ul style="list-style-type: none"> • WHO Global Action Plan for Poliovirus Containment • WHO Global Action Plan for Poliovirus Risk Elimination and Biorisk Management Post-eradication 	<ul style="list-style-type: none"> • GAPIII • GAPIII, 2022 • GAPIV • GAP2022

*proposed but not limited to the options indicated.

CAG Recommendations:

CAG recommends the following: WHO Global Action Plan for Poliovirus Containment (full- and short-titles) and GAPIV (abbreviation).

Discussion and Next Steps

As with the current version of GAPII, there is no hierarchy of importance between the different safeguard requirements in the revised GAPIII. For facility-based safeguards: the polio-prescriptive requirements in the current version of GAPIII generally lacked evidence to support its inclusion in the revised GAPIII and where appropriate were shifted to a local risk-based approach requiring the approvals from NACs, some were not in line with other containment standards, studies performed on certain requirements concluded that a combination of alternative measures were more effective than the implementation of a specific polio-prescriptive requirements e.g., enhanced PPE and enhanced hand-washing was shown to be more effective than the walk-through exit shower requirement, etc., the inclusion of new requirements in the revised GAPIII were evidence-based measures e.g., hand-washing, etc.

Several crucial issues associated with medium- and longer-term poliovirus containment implementation were raised by CAG that will require resolution through the implementation of research studies e.g., data-driven modelling studies. Among the issues raised by CAG were:

Countries-hosting PEFs
<ul style="list-style-type: none"> • effectiveness of immunization coverage and environmental safeguard parameters, as it is currently described in minimizing the consequences of a facility-associated release of poliovirus or reestablishment of circulation of WPV; • combination and coverage and dose requirements of immunization coverage safeguards that must be met to effectively reduce the consequence of a facility-associated release of poliovirus and to interrupt transmission of poliovirus following a release (the same would apply to environmental safeguards or when in combination of these safeguards); • role of routine environmental surveillance and its impacts on confidence of no detection of polioviruses in areas surrounding the PEFs to determine if such a measure should be made a requirement especially in the post-eradication and post-cessation periods; • hierarchy, if any of effectiveness or importance of the different safeguards in minimizing the risk- or mitigating the consequences- of a facility-associated release of poliovirus
Countries-hosting only facilities retaining potentially infectious materials, Sabin
<ul style="list-style-type: none"> • Studies have shown the existence of risk, although low, for Sabin poliovirus detection in potentially infectious materials, polioviruses. In line with that: <ul style="list-style-type: none"> ○ risk of detection and risk- and consequence- of a release of poliovirus from a facility retaining Sabin PIM in the post-OPV cessation period and the role of IPV use in routine immunization in countries hosting such facilities (current recommendation for routine immunization IPV use in the post-OPV cessation period: countries hosting PEFs should continue the use of IPV as long as they continue to host PEFs, and all other countries without PEFs for up to 10 years after cessation of all OPV) ○ In line with the current goal of eliminating the use the of all type 2 polioviruses (including Sabin serotype 2 poliovirus and OPV2) and other serotypes in the future, the longer-term containment requirement for the retention of potentially infectious materials, Sabin specifically in the post-OPV cessation should be explored.
Other issues
<ul style="list-style-type: none"> • Relevance and confidence in the current containment criteria for the certification of WPV eradication.

CAG recommendation:

In line with these issues raised, CAG has requested the Secretariat to present at the next CAG TC a summary document with the supporting evidence for safeguards in the revised GAPIII as well as a brief study proposal utilizing the most these issue medium- and longer-term issues raised by CAG and proposed methodology for its resolution. In addressing some of these broader issues, the Secretariat should collaborate with Secretariats of other containment supporting groups, as needed e.g., GCC, GCC – CWG, SAGE, etc.

Next steps:

1. Secretariat to incorporate the comments, feedback and recommendations from CAG members obtained at this meeting into the working draft of GAPIII clearly identifying subsequent changes made. This draft should be shared with CAG members a week prior to the planned TC on 28 Mar.
2. Secretariat to develop and present a summary document with the supporting evidence for safeguards in the revised GAPIII. In addition, the Secretariat should develop in collaboration with the Secretariats of other containment supporting groups e.g., GCC, GCC – CWG, SAGE, etc. a brief document on the medium- and longer-term containment implementation issues raised by CAG including potentially a brief study proposal utilizing the most appropriate methodology to address them. The Secretariat is requested to present the contents of this document during the same TC planned for 28 March 2022.

The next meeting of the CAG will be a teleconference associated with the revision process of GAPIII scheduled for 28 March 2022.

List of Annexes:

- | | |
|---------|--|
| Annex 1 | Agenda |
| Annex 2 | List of Participants |
| Annex 3 | Summary of Proposed Changes Made in the Revised GAPIII for Deliberation by CAG |



Fifth Meeting of the Containment Advisory Group

2, 4 and 9 March 2022

Time: 1400 – 1700 (CET/ Geneva time)

Virtual Meeting (Zoom)

Agenda

Objectives:

3. Provide an update on the Polio Eradication Strategy 2022 – 2026: Delivering on a Promise and develop a shared understanding of the epidemiology, the status of the programme towards eradication and stopping outbreaks, etc.
4. Provide an update on the implementation of the poliovirus containment programme (survey, inventory destruction activities and containment certification) including ongoing work and future direction.
5. Provide an update on the progress with the revision of GAPIII including process, basis for changes made and proposed revision, discuss to generate CAG consensus on the revisions made in the requirements of GAPIII or to provide recommendations on outstanding issues associated with the revised GAPIII.
6. Discuss administrative matters related to the work of the Containment Advisory Group (CAG) e.g., membership, frequency of meetings, etc.

2 March 2022 (Day 1)

Time	Agenda Topic	Reference Doc No	Purpose and Expected Outcome(s) of Item, And Questions for CAG	Duration
Session: Introduction		Session Chair: Professor David HEYMANN, Chair of CAG		
1400 - 1410	Opening and welcome Opening: Professor David L HEYMANN, Chair of CAG. 10 min.	Verbal	Opening of the Plenary Meeting.	10 min.
Session 1: Update on Polio Eradication and Poliovirus Containment Programme		Session Chair: Professor David HEYMANN, Chair of CAG		
1410 - 1440	Welcome Update on Global Polio Eradication Strategy, Poliovirus Epidemiology, and Progress Towards Polio Eradication and Stopping Outbreaks. 20 min. Mr Aidan O'LEARY, Director, Polio Eradication, WHO	DOC. 4	<u>For information:</u> Develop a shared understanding of the Polio Eradication Strategy 2022 – 2026: Delivering on a Promise and progress towards the polio eradication programme.	30 min.
1440 – 1500	WHO Containment Programme Update <ul style="list-style-type: none"> • Update on Survey and Inventory Activities • Containment Certification Update • Containment Country Support Activities 	Verbal	<u>For information:</u> Update on the implementation of the poliovirus containment programme (survey, inventory destruction activities and containment certification) including ongoing work, activities implemented to	20 min.

Time	Agenda Topic	Reference Doc No	Purpose and Expected Outcome(s) of Item, And Questions for CAG	Duration
	Presented by Ms Liliane BOULAM, Technical Officer, Containment, Polio Eradication, WHO on behalf of the Poliovirus Containment Team: Mr Aidan O'LEARY, Acting Team Lead, Containment; Dr Nicoletta PREVISANI, Technical Officer; Dr Harpal SINGH, Technical Officer; Mr Joseph SWAN, Communications Officer and Ms Caroline NAKANDI, Assistant to the Team, Poliovirus Containment, Department of Polio Eradication, WHO.		support containment in countries, WPV3 containment, GPEI Containment Strategic Plan, etc.	
1500 - 1520	GCC – Containment Working Group Update on Containment Certification Processes, Challenges, and Progress. Dr Arlene KING, Chair, GCC - Containment Working Group	Verbal	<u>For information:</u> Updates on the work performed by the GCC - Containment Working Group in containment certification as well as global progress in containment certification.	20 min.
1520 - 1540	Discussion Professor David L HEYMANN, Chair of CAG.			20 min.
Session 2: Update on the Progress with the Revision of GAPIII			Session Chair: Professor David HEYMANN, Chair of CAG	
1540 – 1620	Overview of the Process Undertaken for the Revision of GAPIII and Outline of Issues/Changes Made to GAPIII for Consensus or Recommendation by CAG and Structure of the Revised GAPIII. 20 min. Dr Harpal SINGH, Technical Officer, Containment, Polio Eradication, WHO. Discussion. 20 min. Professor David L HEYMANN, Chair of CAG.	DOC. 5.1 or Doc. 5.2, , DOC. 6 and DOC. 7	<u>For discussion and consensus:</u> Brief overview of the process undertaken for the revision of GAPIII till and list of changes made in the revised draft for consensus by CAG, pending issues for CAG recommendation, etc. An overview of the structural changes made in the revised GAPIII for discussion and consensus by CAG will be shared. Examples include merging of the Annex 2 and 3 of GAPIII, removal of Annex 6 of GAPIII, merging of similar- and reorganization of- the biorisk management elements of GAPIII to reduce redundancy, improve flow and clarity, etc.	40 min.
1620 - 1700	Containment Perimeter. 20 min Dr Harpal SINGH, Technical Officer, Containment, Polio Eradication, WHO Discussion. 20 min. Professor David L HEYMANN, Chair of CAG.	DOC. 5.1 or Doc. 5.2, and DOC. 8	<u>For discussion and recommendation:</u> Clarity regarding what must be within the 'containment perimeter' with respect to: anterooms, airlocks, HVAC systems/mechanical spaces and kill tanks/effluent decontamination systems.	40 min.

4 March 2022 (Day 2)

Time	Agenda Topic	Reference Doc No	Purpose and Expected Outcome(s) of Item, And Questions for CAG	Duration
Session 2: Update on the Progress with the Revision of GAPIII			Session Chair: Professor David HEYMANN, Chair of CAG	
1400 – 1405	Administrative Announcements, if any.	Verbal		10 min.
1405 - 1430	<p>Operator IPV Immunization and Poliovirus Antibody Titer Determination Requirements . 10 min. Dr Harpal SINGH, Technical Officer, Containment, Polio Eradication, WHO</p> <p>Discussion. 15 min. Professor David L HEYMANN, Chair of CAG.</p>	DOC. 5.1 or Doc. 5.2, and DOC. 9	<p><u>For discussion and recommendation:</u> Vaccination and titer requirements were revised to be risk-based in approach. Additional guidance from CAG is needed as vaccination in the context of facility level containment is different from community concerns.</p>	
1430 - 1530	<p>Study commissioned by CAG: Use, effectiveness and risks associated with a walk-through exit shower as poliovirus containment barrier. 15 min. Dr Karen VAN DER MEULEN, Biosafety and Regulatory Specialist, Perseus BVBA, Belgium</p> <p>Study commissioned by the US NAC: Distinguishing the Risk Reduction Potential of Exit Showers Versus Enhanced PPE in Poliovirus Essential Facilities. 15 min. Dr Christy OTTENDORFER, Microbiologist/Auditor, U.S. National Authority for Containment of Poliovirus</p> <p>Risk-based Approach for Walk-through Exit Shower from the Containment Perimeter in line with the Most Recent CAG Recommendation. 10 min. Dr Harpal SINGH, Technical Officer, Containment, Polio Eradication, WHO.</p> <p>Discussion. 20 min. Professor David L HEYMANN, Chair of CAG.</p>	DOC. 5.1 or Doc. 5.2, DOC. 10, DOC. 11 and DOC. 12	<p><u>For discussion and consensus:</u> Findings from two independent studies on the GAPIII requirements for walk-through exit-shower will be presented to CAG. This will be followed by presentation of issue associated with this requirement in the context of GAPIII revision i.e., shower-out requirement was revised to be risk-based in approach? Does CAG support this shift from the prescriptive to risk-based approach?</p>	60 min.

Time	Agenda Topic	Reference Doc No	Purpose and Expected Outcome(s) of Item, And Questions for CAG	Duration
1530 - 1600	<p>Risk-based Approach for Storage of Poliovirus Materials Outside of GAPIII Containment. 10 min.</p> <p>Dr Harpal SINGH, Technical Officer, Containment, Polio Eradication, WHO.</p> <p>Discussion. 20 min.</p> <p>Professor David L HEYMANN, Chair of CAG.</p>	DOC. 5.1 or Doc. 5.2 and DOC. 13	<p><u>For discussion and consensus:</u> Storage conditions outside of GAPIII have been revised to be risk-based in approach with approval from NACs. Does CAG agree that storage of poliovirus infectious materials outside the containment perimeter is acceptable provided these conditions are met?</p>	30 min.
1600 – 1620	<p>Alternative Measures for Gaseous Decontamination and Guidance for Use. 5 min.</p> <p>HEPA Filtration on Exhaust Side As Requirement Prior to Final Containment of all WPV. 5 min</p> <p>Dr Harpal SINGH, Technical Officer, Containment, Polio Eradication, WHO.</p> <p>Discussion. 10 min.</p> <p>Professor David L HEYMANN, Chair of CAG.</p>	DOC. 5.1 or Doc. 5.2, DOC. 14.1 and DOC 14.2	<p><u>For discussion and consensus:</u> CAG recommendation is needed for alternative method of gaseous decontamination and HEPA filtration on exhaust.</p>	20 min.
1620 - 1640	<p>Changes made in primary, secondary and tertiary safeguards as described in GAPIII: 10 min.</p> <ul style="list-style-type: none"> • Replacement of GAPIII Jargon ‘Primary, Secondary and Tertiary Safeguards’ with Technical Language or Definition • Operationalization of Population Immunity Safeguards Within the Context of SAGE Current Recommendations • Local Risk-based Approach for Environmental Control Safeguards <p>Dr Harpal SINGH, Technical Officer, Containment, Polio Eradication, WHO.</p> <p>Discussion. 10 min.</p> <p>Professor David L HEYMANN, Chair of CAG.</p>	DOC. 5.1 or Doc. 5.2, DOC. 15.1, DOC. 15.2 and DOC. 15.3	<p><u>For discussion and consensus:</u> Consensus from CAG in regards to the definition of the safeguards which were revised to be more pragmatic and feasible taking into consideration SAGE recommendation. In addition, a risk-based approach is used for tertiary (facility location and associated environmental controls) safeguards.</p>	20 min.
1640 – 1700	Discussion		Time is allocated for catch-up discussions and additional areas for CAG recommendation, if any.	20 min.

9 March 2022 (Day 3)

Time	Agenda Topic	Reference Doc No	Purpose and Expected Outcome(s) of Item, And Questions for CAG	Duration
Session 2: Update on the Progress with the Revision of GAPIII			Session Chair: Professor David HEYMANN, Chair of CAG	
1400 – 1405	Administrative Announcements, if any.	Verbal		10 min.
1405 - 1435	Revision Made in the Survey, Inventory and Destruction Activity Section of GAPIII. 10 min. Dr Harpal SINGH, Technical Officer, Containment, Polio Eradication, WHO. Containment Requirements for Potentially Infectious Materials, WPV/VDPV. 10 min. Dr Mark Pallansch, CAG Member Discussion. 10 min. Professor David L HEYMANN, Chair of CAG.	DOC. 5.1 or Doc. 5.2, DOC. 16 and DOC. 17	<u>For discussion and consensus:</u> Consensus from CAG in regards to this section which was revised as follows: <ul style="list-style-type: none"> • Includes definitions (previously Annex 1) • Addition of 'Roles and Activities' of containment stakeholders • Addition of 'Containment Requirements for Novel Poliovirus Strains' 	30 min.
1435 - 1500	Updated Recommendations from the CAG - Expert Support Group (CAG-ESG) on Novel Poliovirus Strains. 15 min. Dr Mark PALLANSCH, CAG and CAG-ESG Member. Discussion. 10 min. Professor David L HEYMANN, Chair of CAG.	DOC. 5.1 or DOC. 5.2 and DOC 18	<u>For discussion and consensus:</u> An update to CAG recommendation on the containment requirements of novel poliovirus strain for CAG consensus.	25 min.
Con't Session 1: Update on Polio Eradication and Poliovirus Containment Programme			Session Chair: Professor David HEYMANN, Chair of CAG	
1500 - 1515	Process and Outputs from the Reference Group on the Determination of the Criteria for the Validation of the Absence of VDPV Dr Graham Tallis, GCC Secretariat	Verbal	<u>For information</u>	15 min
Session 3: Other Issues Associated with the Revision of GAPIII			Session Chair: Professor David HEYMANN, Chair of CAG	
1515 - 1535	Timelines and Remaining Steps in GAPIII Revision and Naming of the Revised GAPIII. 10 min. Dr Harpal SINGH, Technical Officer, Containment, Polio Eradication, WHO.	Verbal and DOC. 19	<u>For discussion and recommendation:</u> This session aims to discuss and agree on the next steps in the revision process, time needed and proposed dates for these activities e.g., public consultation, feedback to CAG on outcomes from public consultation for further decision	20 min.

Time	Agenda Topic	Reference Doc No	Purpose and Expected Outcome(s) of Item, And Questions for CAG	Duration
	Discussion. 10 min. Professor David L HEYMANN, Chair of CAG.		making, endorsement of the document, etc. Recommendation from CAG is also being sought on the title of the revised document e.g., GAPIV, GAP2022, GAPIII.2, etc.	
Session 3: Administrative Issues for CAG Discussion			Session Chair: Professor David HEYMANN, Chair of CAG	
1535 – 1605	Composition, Membership, Rotational and Reappointment of CAG Members, Frequency of Meetings, etc. 15 min. Discussion. 15 min. Professor David L HEYMANN, Chair of CAG.	Verbal and DOC. 3	<u>For discussion and recommendation:</u> Discuss staggered membership proposal of CAG ('rotation-off' policy) to ensure continuity or reappointment, etc. To decide on the frequency of CAG meetings and other relevant issues.	30 min.
1605 - 1635	'Reengagement Plan of the Containment Advisory Group' for Effective Delivery of Its Mandate as the Advisory Body to DG/WHO on Issues Associated with Poliovirus Containment. 15 min. Dr Harpal SINGH, Technical Officer, Containment, Polio Eradication, WHO. Discussion. 15 min. Professor David L HEYMANN, Chair of CAG.	Verbal and DOC. 20	<u>For discussion and feedback:</u> CAG members are requested to comment, provide additional suggestions on proposed activities and to decide on dates for relevant activities for the next one year. Details of this plan is described in DOC. 19 and will be elaborated during the presentation.	30 min
1635 – 1650	Operationalization of CAG Terms of Reference No 4. 5 min. Dr Harpal SINGH, Technical Officer, Containment, Polio Eradication, WHO. Discussion. 10 min. Professor David L HEYMANN, Chair of CAG.	DOC. 2 and DOC. 21	CAG TOR No 4: To provide guidance on the identification of acceptable alternative containment solutions in the interim period, before full eradication.	15 min
Session 4: Conclusions and Next Steps			Session Chair: Professor David HEYMANN, Chair of CAG	
1645 - 1650	Conclusions and Follow-Up Points. 5 min. Dr Harpal SINGH, Technical Officer, Containment, Polio Eradication, WHO.	Verbal		5 min.
1650– 1700	Closing Mr Aidan O'LEARY, Director, Department of Polio Eradication, WHO headquarters. 5 min Professor David L HEYMANN, Chair of CAG. 5 min	Verbal		10 min.

Annex 2 List of Participants

Fifth Meeting of the Containment Advisory Group
2, 4 and 9 March 2022
1400 – 1700 (CET)
Virtual Meeting

Containment Advisory Group

1. Professor David HEYMANN
Chair of the Containment Advisory Group and
Professor of Infectious Disease Epidemiology,
London School of Hygiene and Tropical Medicine,
London, UNITED KINGDOM OF GREAT BRITAIN AND NORTHERN IRELAND.
2. Dr Jagadish DESHPANDE
Scientific Consultant, Indian Council of Medical Research (ICMR) and Technical Consultant,
National Task Force on Laboratory Containment of Polioviruses,
Mumbai, REPUBLIC OF INDIA
3. Dr Atef M ELGENDY
Former Head, Bacteriology Section and Biological Safety Coordinator,
United States Naval Medical Research Unit (NAMRU-3),
Cairo, ARAB REPUBLIC OF EGYPT
4. Professor George E GRIFFIN
Member, CAG-Expert Support Group for Novel Poliovirus Strains (CAG - ESG) and
Emeritus Professor of Infectious Diseases and Medicine,
St George's University of London,
London, UNITED KINGDOM OF GREAT BRITAIN AND NORTHERN IRELAND.
5. Dr Vibeke HALKJÆR-KNUDSEN
Principal Member of Technical Staff,
Engineering Program/Project Lead,
International Biological and Chemical Threat Reduction Program (SNL/IBCTR),
Sandia National Laboratories,
Albuquerque, New Mexico, UNITED STATES OF AMERICA
6. Dr Janice LO
Consultant Medical Microbiologist (Antimicrobial Resistance),
Infection Control Branch, Health Protection, Department of Health
HONG KONG SPECIAL ADMINISTRATIVE REGION OF THE PEOPLE'S REPUBLIC OF CHINA.
7. Dr Stephen McADAM
Member, CAG-Expert Support Group for Novel Poliovirus Strains (CAG - ESG) and
Global Healthcare Director, DNV GL Business Assurance,
Oslo, KINGDOM OF NORWAY

8. Dr Mark PALLANSCH
Chair, CAG-Expert Support Group for Novel Poliovirus Strains (CAG - ESG), Co-Chair Containment Management Group (CMG), Expert Poliovirus Virologist and former Director, Division of Viral Diseases, National Centre for Immunization and Respiratory Diseases, Centres for Disease Control and Prevention, Atlanta, Georgia, UNITED STATES OF AMERICA
9. Dr Åsa Szekely BJORN DAL
Chair, National Authority for Containment of Sweden and Senior Advisor, Institutional Biosafety Officer and Microbiologist, Department of Microbiology, Public Health Agency of Sweden (PHAS), Solna, KINGDOM OF SWEDEN
10. Professor Shahina TABASSUM
Professor and Chairman, Department of Virology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, PEOPLE'S REPUBLIC OF BANGLADESH
11. Mr Kenneth UGWU
Senior Biocontainment Advisor, Global Affairs Canada, Ottawa, Ontario, CANADA
12. Mr Neil GODDEN (Unable to attend)
Former High Containment Specialist, Science Strategy and Laboratory Engineering, Commercial, Estates and Knowledge Directorate, Department for Environment, Food and Rural Affairs (DEFRA), Herefordshire, UNITED KINGDOM OF GREAT BRITAIN AND NORTHERN IRELAND.

Representatives of Other Containment Supporting Groups

1. Dr Arlene KING
Liaison Member of the Containment Working Group of the Global Commission for the Certification of the Eradication of Poliomyelitis (GCC-CWG) to CAG and Chair, GCC – CWG, Toronto, Ontario, CANADA

Invited Participants

2, 4 and 9 March 2022: Contractual Partners (Observers)

1. Dr Rocco CASAGRANDE
Chair of the Board, Gryphon Scientific LLC, Takoma Park, MD, UNITED STATES OF AMERICA.
2. Dr Ryan RITTERSON,
Executive Vice President, Research, Gryphon Scientific LLC, Takoma Park, MD, UNITED STATES OF AMERICA
3. Ms Erin LAUER
Senior Analyst, Gryphon Scientific LLC, Takoma Park, MD, UNITED STATES OF AMERICA
4. Dr Adam FLEMING
Senior Analyst, Gryphon Scientific LLC, Takoma Park, MD, UNITED STATES OF AMERICA

5. Ms Kelly KIM
Analyst, Gryphon Scientific LLC,
Takoma Park, MD, UNITED STATES OF AMERICA
6. Mr Rob DETTMANN
Analyst, Gryphon Scientific LLC,
Takoma Park, MD, UNITED STATES OF AMERICA

4 March 2022: Presenters (Observers) of Studies Performed on the Walk-Through Exit-Shower Requirement in GAPIII.

1. Dr Karen VAN DER MEULEN,
Biosafety and Regulatory Specialist,
Perseus BVBA (Partnership of Biosafety and Regulatory Experts),
KINGDOM OF BELGIUM
2. Dr Patrick RÜDELSHEIM
Partner, General Manager,
Perseus BVBA (Partnership of Biosafety and Regulatory Experts),
KINGDOM OF BELGIUM
3. Mr Toon DE KESEL
Associate Partner,
Perseus BVBA (Partnership of Biosafety and Regulatory Experts), and
General Manager, Febris Biorisk Consult BVBA,
KINGDOM OF BELGIUM
4. Dr Christy OTTENDORFER,
Microbiologist and Auditor, for Dr Lia HAYNES, Director,
U.S. National Authority for Containment of Poliovirus, Center for Preparedness and Response
Centers for Disease Control and Prevention,
Atlanta, Georgia, UNITED STATES OF AMERICA

WHO Secretariat

1. Mr Aidan O'LEARY
Director, Department of Polio Eradication and Team Lead *a.i.*, Poliovirus Containment,
Department of Polio Eradication, WHO headquarters in Geneva, SWITZERLAND`
2. Dr Nicoletta PREVISANI
Technical Officer, Poliovirus Containment, Department of Polio Eradication,
WHO headquarters in Geneva, SWITZERLAND
3. Ms Liliane BOUALAM
Technical Officer, Poliovirus Containment, Department of Polio Eradication, and
Secretariat, GCC – CWG, WHO headquarters in Geneva, SWITZERLAND
4. Dr Harpal SINGH
Technical Officer, Poliovirus Containment, Department of Polio Eradication, and
Secretariat, CAG, WHO headquarters in Geneva, SWITZERLAND
5. Mr Joseph SWAN
Communications Officer, Poliovirus Containment, Department of Polio Eradication,
WHO headquarters in Geneva, SWITZERLAND

6. Ms Caroline NAKANDI
Assistant to the Team, Poliovirus Containment, Department of Polio Eradication,
WHO headquarters in Geneva, SWITZERLAND
7. Dr Graham TALLIS
Senior Scientific Adviser, Detection and Interruption Unit, Department of Polio Eradication, and
Secretariat, GCC, WHO headquarters in Geneva, SWITZERLAND
8. Dr Jacob Samson BARNOR
Regional Containment Coordinator for the WHO African Region,
WHO - Regional Office for Africa, Brazzaville,
REPUBLIC OF CONGO
9. Ms Gloria REY
Regional Containment Coordinator for the WHO Region of the Americas, WHO - Regional Office
for the Americas/Pan American Health Organization,
Washington DC, UNITED STATES OF AMERICA
10. Dr Humayun ASGHAR
Regional Containment Coordinator for the WHO Eastern Mediterranean Region,
WHO - Eastern Mediterranean Regional Office,
Amman, HASHEMITE KINGDOM OF JORDAN
11. Dr Salmaan SHARIF
Regional Containment Focal Point for the WHO Eastern Mediterranean Region,
WHO - Eastern Mediterranean Regional Office,
Amman, HASHEMITE KINGDOM OF JORDAN
12. Dr Eugene Victor SAXENTOFF
Regional Containment Coordinator for the WHO European Region,
WHO – European Regional Office,
Copenhagen, DENMARK
13. Dr Maria IAKOVENKO
Technical Officer, Poliovirus Containment, WHO – European Regional Office,
Copenhagen, DENMARK
14. Dr Sigrun ROESEL (Unable to attend)
Regional Containment Coordinator for the WHO South East Asia Region,
WHO – South-East Asia Regional Office,
New Delhi, REPUBLIC OF INDIA.
15. Dr Varja GRABOVAC
Regional Containment Coordinator for the WHO Western Pacific Region,
WHO – Western Pacific Regional Office,
Manila, REPUBLIC OF THE PHILIPPINES

Annex 3 Summary of Proposed Changes Made in the Revised GAPIII for Deliberation by the Containment Advisory Group (CAG)

The proposed changes indicated in the table below should not be construed as final requirements or endorsed by CAG.

Section: Strategy for the Implementation of Preparatory Activities for Poliovirus Containment	
1.	Removal of phased implementation of GAPIII i.e., Phase I, II (IIa and IIb) and III (IIIa and IIIb) <ul style="list-style-type: none"> Revised approach separates 'inventory and destruction' from 'containment' Implementation is trigger-based and has also GCC set the global containment status for the different poliovirus strains and serotypes
2.	Containment stakeholders' roles and activities added and covers 'inventory and destruction' and 'containment' activities including containment activities for non-polio laboratories.
3.	New section added to address novel poliovirus strains and criteria to determine the containment requirements for their handling.
4.	Changes in safeguards: <ul style="list-style-type: none"> Renamed primary safeguards to 'facility safeguards' Renamed secondary safeguards to 'population immunity safeguards'. Definition has been adjusted based on SAGE recommendation making it more globally implementable and pragmatic based on data availability and local situations. In the interim period, the immunity requirements takes into consideration current IPV supply, IPV in EPI, and availability of IPV coverage data, etc., with the goal of achieving SAGE recommendation by the time of all OPV cessation. Renamed tertiary safeguards to 'environmental control safeguards'. Definition has been expanded to include local context in the determination of the R_0 of poliovirus and is risk-based in approach tailored to local situations. The requirement that PEFs must be located in areas with closed sewage systems with secondary or greater treatment of effluents has been removed, but facility locations must maximize the use of environmental features that reduce risk of onward transmission with approval by their national authorities for containment.
5.	Annex 1: Definitions of the current version of GAPIII moved to the beginning of the revised document.
Section: Biorisk Management Standard for Facilities Retaining Polioviruses Post-Eradication (Annex 2 and 3* of the current version of GAPIII)	
1.	Language in-line with the most updated version of the WHO Laboratory Biosafety Manual and Associated Monographs, 4th ed., 2020 (LBM4) and reflects CAG recommendations
2.	The entire standard has been amended in accordance with all decisions and recommendations made by the CAG, including guidance for the containment requirements for novel poliovirus strains.
3.	Editorial changes made to reduce redundancy, enhance clarity and flow, emphasized requirements and demarcated guidance. For guidance referencing CEN Workshop Agreement CWA15793 – Laboratory biorisk management (2011), these have been aligned and harmonized with the requirements outlined in other international risk management documents e.g., ISO 35001: Biorisk management for laboratories and other related organisations (2019), etc.
4.	Biorisk Management elements of Annexes 2 and 3* of the current version of GAPIII were reordered for ease of use and clarity. Elements 4 and 8 were incorporated into existing elements that match their content, reducing the total number of Biorisk Management elements from 16 to 14.
5.	Annexes 2 and 3 were combined to reduce redundancy - requirements that apply only to WPV final containment were separated and highlighted.

Annex 3 Summary of Proposed Changes Made in the Revised GAPIII for Deliberation by the Containment Advisory Group (CAG)

The proposed changes indicated in the table below should not be construed as final requirements or endorsed by CAG.

6.	References to CEN Workshop Agreement CWA15793 – Laboratory biorisk management (2011) which is no longer in existence as it has reached its maximum validity of 6 years were removed. References to currently valid biosafety guidance were added throughout e.g., LBM4, ISO 35001: Biorisk management for laboratories and other related organisations (2019), etc.
7.	The introduction to the biorisk management standard for facilities retaining polioviruses post-eradication (Annex 2 and 3 of the current version of GAPIII or Annex 1 of the revised version of GAPIII) was updated. An additional section titled ‘Organization of Management System Elements’ has been added which describes the structure, organization, and intended use of the document.
8.	The annex format has been changed from a tabular presentation to a prose format, in-line with other existing relevant documents. To delineate requirements from guidance, guidance was placed aside from the main text i.e., requirements in boxes with italicized font.
9.	Language was enhanced for some requirements e.g., requiring PEFs to report to the NAC any change in the poliovirus programme of work, scope, processes, procedures or any other factor that may affect facility biorisk management.
10.	Emphasizes the performance of local risk assessment in all biorisk management elements. Biorisk Management Element 2: Risk Assessment has been expanded with reference to the Risk Assessment Monograph of LBM4.
11.	Text referring to WHO inspections and audits of PEFs were removed and replaced with reference to the CCS with national level responsibility given to the NACs.
12.	Document retention requirement reduced from 10 years to 5 years in line with the timeframe for the retention of certification associated documents.
13.	Specific IPV vaccination and poliovirus antibody titer requirements for operators were removed due to a lack of data on protective efficacy. In accordance with the shift to a risk-based approach, these requirements have been replaced with risk-based language.
14.	Risk-based approach for walk-through exit shower from the containment perimeter in line with the most recent CAG recommendation which more generally applies to the range of PEFs.
15.	Risk-based approach for storage of poliovirus materials outside of the containment perimeter.
16.	Language on gaseous decontamination, backflow prevention, and HEPA filtration of exhaust has been modified.
17.	Addition of language to specify that airlocks and anterooms must be within the containment perimeter. HVAC spaces with sealed ductwork and kill tank rooms with sealed plumbing can be housed within or outside the containment perimeter.
18.	Guidance on inactivation and validation techniques as well as equipment decontamination has been enhanced.
19.	Requirements for biosafety cabinet certification and labelling stored poliovirus materials have been added, although volume of poliovirus materials need not be maintained in the inventory documentation.
20.	Facility specific requirements have been expanded to include considerations for retrofitting existing spaces.
21.	Language defining the containment perimeter, organizational responsibilities, animal care, storage conditions, and non-dedicated spaces has been updated.
22.	Emergency planning has been expanded to encourage the involvement of external agencies, implement environmental surveillance following an incident, and reporting in line with the International Health Regulations (2005).

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23.	Additional requirements describing primary containment needs as well as additional specific mitigation measures applicable to all PEFs, such as the requirement of a hands-free hand washing sink and updated BSC certification requirements, have been included.
Other Annexes of GAPIII	
1.	Annex 1: Definitions is moved to the beginning of the document and updated in line with previous recommendations made by CAG e.g., poliovirus nucleic acid, etc.
2.	Annex 4: WHO verification that certified poliovirus-essential facilities comply with GAPIII is dropped. References to the CCS is made throughout the document for activities involving compliance verification.
3.	Annex 5: Risk assessment strategy is dropped. Instead the emphasis on risk assessments is made by referencing the risk assessment monograph of LBM4 throughout all biorisk management elements.
4.	Annex 6*: Biorisk management standard for safe handling of new samples potentially containing poliovirus material in poliovirus-non-essential facilities is dropped and proposed to be merged with the PIM Guidance at such a time that the PIM Guidance undergoes revision. `

* Annex 2 (Biorisk management standard for poliovirus-essential facilities holding wild poliovirus), Annex 3 [Biorisk management standard for poliovirus-essential facilities holding OPV/Sabin (no wild)] and Annex 6 (Biorisk management standard for safe handling of new samples potentially containing poliovirus material in poliovirus-non-essential facilities) of the current version of GAPIII. Available at: https://polioeradication.org/wp-content/uploads/2016/12/GAPIII_2014.pdf

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