Appraisal of options for certification of global poliovirus eradication

The chairs of the committees which advise and support the Global Polio Eradication Initiative (GPEI) met on 16 April 2018 to harmonize and align the various committees' functions in the lead up to certification of WPV eradication[1]. As follow-up to the meeting, the chairs requested the secretariat of the Global Commission for the Certification of Polio Eradication (GCC) to prepare an appraisal of options for certification of global poliovirus eradication, particularly with respect to the relationship between wild poliovirus (WPV) eradication and circulating vaccine-derived poliovirus (cVDPV).

This paper presents options for consideration along with possible advantages/risks of each option, including the relative impact that each will have on the timeline and process of certification. Options 1A and 1B limit the scope of certification only to WPV and differ by whether to consider cVDPV status in the final declaration of WPV eradication. Both options include a separate, future process for validating the absence of VDPVs. Option 2 proposes to expand the concept of certification to a multi-stage process including all polioviruses.

A core assumption underlying the options is a distinction between the concepts of *certification* vs *validation of absence*. As has been the case to date for regional and type 2 global eradication considerations, *certification* implies a high degree of certainty that specific criteria have been met. Although providing an absolute guarantee of eradication would be problematic, modeling can provide some probabilities of undetected transmission which provide confidence in making such a determination. [2] Due to unknowns about transmission and/or substantial challenges to meeting certain criteria, *validation of absence* implies a lower level of certainty. This determination also does not guarantee zero transmission, but, reflective of a lower level of confidence, may be considered to denote elimination of a public health problem (e.g. like MNT). This paper does not attempt to provide all the details of the criteria expected to be met in order to declare either *certification* or *validation of absence*.

All the proposed options could include sub-options to sequentially address certification of first type 3 and then type 1.

General links between certification of eradication and containment are noted below. However, due to complexities of the interaction and the ongoing evolution of containment implementation, this paper does not attempt to provide specific details. Further relevant information on containment is provided as background in Annex 2.

[1] See Meeting Note. *Building consensus for certification of poliovirus eradication: meeting of the chairs of the committees with advice and support the GPEI*. Geneva, 16 April 2018.

[2] Eicher M, Dietz K. Eradication of poliomyelitis: when can one be sure that polio virus transmission has been terminated? Am J Epidemiol. 1996;143(8)816-22.

Proposed Options

1A - Certification of eradication based on the interruption of transmission of WPV alone followed later by separate process to validate the absence of VDPVs

1B - Certification of eradication based on the interruption of WPV transmission, with consideration of the context of ongoing or recent cVDPV outbreaks, followed later by separate process to validate the absence of VDPVs.
Proposed context at GCC meeting in Feb 2018:

- *Consider all types of cVDPV*: No detection of a persistent cVDPV2 outbreak from any population source in the previous 18* months; and no detection of a cVDPV 1 or 3 outbreak from any population source in the previous six* months.

Or (newly proposed for this paper):

- *Consider only types 1/3*: No detection of a cVDPV 1 or 3 outbreak from any population source in the previous six* months
  *time frame could be further discussed

2 – Certification of eradication in two stages: Stage 1 based on interruption of WPV transmission; Stage 2 based on evidence of no new VDPV emergence or circulation following OPV cessation.

Background--prior definitions of certification of eradication

Global

The 1988 World Health Assembly (WHA) resolution[3] calling for the global eradication of poliomyelitis by 2000 referred only to WPV eradication. While the potential impact of VDPVs may not have been appreciated at the time of the initial resolution, later relevant WHA documents in 2012 and 2015 specifically highlighted WPV eradication and directly referred to cVDPV only in the context of heightened surveillance.[4]

Consistent with this perspective, the initial meeting of the GCC in 1995 defined eradication as "eradication of all wild polioviruses".[5] Following the first confirmed outbreak of cVDPV on the island of Hispaniola in 2000, the GCC in 2001 re-affirmed that its objective was "to certify eradication of wild poliovirus, including completion of the containment process" , but also recognized " that the full benefits of polio eradication will only be realized in the absence of VDPV circulation" and called on WHO to " develop a process for verifying the absence of VDPV circulation after certification of wild poliovirus eradication."[6]

[3] http://www.who.int/ihr/polioresolution4128en.pdf
[4] See http://apps.who.int/gb/ebwha/pdf_files/wha65/a65_r5-en.pdf and http://polioeradication.org/wp-content/uploads/2016/07/A68_R3-en.pdf
[5] Report of the 1st meeting of the Global Commission for the Certification of the Eradication of Poliomyelitis. Geneva: World Health Organization; 1995. WHO document WHO/EPI/GEN/95.6.
[6] Report of the 6th meeting of the Global Commission for the Certification of the Eradication of Poliomyelitis. Geneva: World Health Organization; 2001. WHO document WHO/V&B/01.15.

An overview of the global certification process published in the Bull WHO in 2004[7] summarized the main criteria set by the GCC and noted the prerequisites for global polio-free certification included the absence of **wild** poliovirus, isolated from cases of acute flaccid paralysis (AFP) (suspect polio), healthy individuals, or environmental samples, in all WHO regions for a period of at least three years in the presence of high- quality, certification-standard surveillance; and the containment of all **wild** poliovirus stocks in laboratories through completion of the requirements of the WHO global action plan for laboratory containment of wild polioviruses.

The 2015 GCC declaration that WPV2 had been eradicated worldwide did not consider the presence or absence of cVDPV2 (i.e. consistent with option 1A). However, the declaration was a pre-condition to OPV2 withdrawal, which also was dependent on cessation of persistent cVDPV2 (defined as circulation for greater than six months). Implementation of containment under GAPIII was not included as a pre-requisite for the declaration but was initially considered a criterion for tOPV withdrawal.

In February 2018[8], the GCC re-examined its procedures and recommended the following criteria for certification of WPV eradication:

- No WPV transmission detected from any population source for the previous three years,
- Adequate global poliovirus surveillance
- Safe and secure containment of WPV retained in facilities, such as laboratories and vaccine manufacturing facilities

Additionally, the GCC recommended that the announcement of the eradication of WPV should take into consideration the epidemiology of cVDPVs at that time with the following conditions (reflected in Option 1B):

- No detection of a persistent cVDPV2 outbreak from any population source in the previous 18 months; and
- No detection of a cVDPV 1 or 3 outbreak from any population source in the previous six months.

Regional

Certification of four WHO regions as polio free occurred with consideration of WPV eradication only and irrespective of cVDPV transmission. All four have detected cVDPVs post-certification (See **Table 1**).

Table 1: post regional certification cVDPV outbreaks

Region	Year certified	cVDPV outbreaks
Americas (AMR)	1994	Hispaniola, 2000-01
Western Pacific (WPR)	2000	Cambodia 2005-6; China 2004, 2012; Philippines 2001; Lao PDR 2015-16; PNG 2018
European (EUR)	2002	Ukraine 2015
South-East Asia (SEA)	2014	Myanmar 2015

[7] Smith J, Leke R, Adams A, Tangermann RH. Certification of polio eradication: process and lessons learned. Bull WHO. 2004; 82:24-30

[8] Report from the Seventeenth Meeting Global Commission for the Certification of the Eradication of Poliomyelitis, Geneva, 26-27 February 2018. http://polioeradication.org/wp-content/uploads/2018/04/polio-eradication-certification-17th-meeting-global-commission-for-certification-of-poliomyelitis-eradication-20180412.pdf

The options presented in this paper are specifically for global certification and exclude regional certification.

Key considerations

1. Program Strategic and Operational Perspectives

The current program strategies for the GPEI outlined in the *Polio Eradication and Endgame Strategic Plan 2013-18* (PEESP) include:

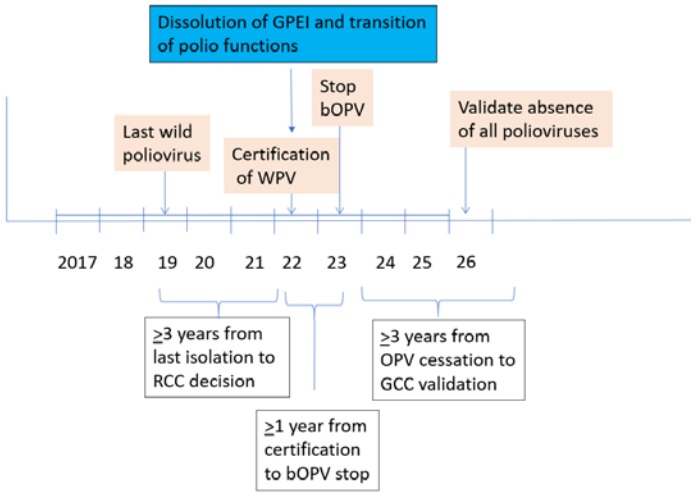
Objective 1: Complete the interruption of WPV transmission globally and more rapidly detect and interrupt any new outbreaks due to cVDPV within 120 days
Objective 2: Strengthen immunization services, introduce IPV, and withdraw OPV2 globally
Objective 3: Certify the eradication and containment of all WPV by end-2018.
Objective 4: Develop a plan to ensure polio investments contribute to future health goals.

As part of Objective 4 ("Transition Planning") the GPEI has drafted a *Polio Post-Certification Strategy (PCS)* which acknowledges the critical importance of stopping all poliovirus transmission but lays out the strategies for transitioning responsibility for polio eradication functions from GPEI to other stakeholders based on achieving certification of WPV eradication. The PCS also lays out the parameters for extending Objective 2 to include withdrawal of all OPV after this certification.

Figure 1 provides the currently anticipated timelines to reach the PEESP and initial PCS objectives. While meeting the projected timeframes remains problematic, the scope of these objectives (including certification of eradication defined as stopping WPV) continue to drive program operations and serve as the basis for determining financial resource requirements.

Options 1A and 1B are therefore clearly within the scope of certification as envisioned in the current strategic plan, although option 1B could delay certification of WPV eradication based on the context of cVDPV. Option 2 however goes beyond the scope of the PEESP and would require a new or renegotiated strategic plan and a process put in place to engage donors and partners in the extended scope. The separate certification of cVDPV could require another four to six years after WPV certification and would most likely exclude consideration of iVDPV (see below).

Figure 1. Anticipated timeline of GPEI, as of July 2018



2. GPEI Partnership

To date, all core global partners of the GPEI have endorsed the concept of certification as applying to WPV eradication and have framed donor communication accordingly. In particular, Rotary International has noted this specific focus as the stated goal of their Polio Plus program since they launched the global effort in 1985 prior to formation of the GPEI.

As an additional component of transition planning, the GPEI has determined that it will dissolve as a management structure at the time of certification of WPV eradication. Any changes to the scope or definitions of certification will required concomitant modifications to these plans and potentially impact engagement of both current and future partners. Future stakeholders who will continue to implement the functions required to sustain WPV-free status and eventually all poliovirus eradication have not yet been officially identified.

3. Epidemiology (as at 26 July 2018)

WPV:

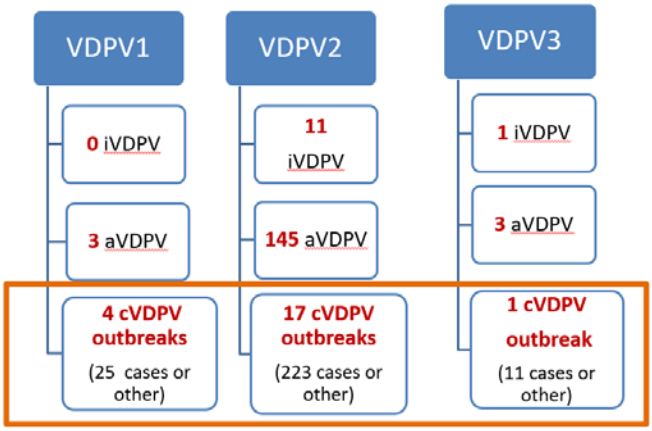
- *type 1*—three countries still considered endemic: Nigeria (onset of last case August 2016), Pakistan (last case- May 2018), Afghanistan (last case-June 2018);
- *type 3*- last case: November 2012 (Nigeria)

VDPV:

The appraisal is based on an analysis of VDPV and cVDPV for the period 2014 – July 2018. This period was chosen as it reflects relevant epidemiology and programmatic responses starting when the GPEI developed standardized classifications and response protocols for VDPVs in the lead-up to the global OPV2 withdrawal in April 2016.

As shown in **Figure 2** the majority of VDPVs detected have been classified as cVDPV (which have the most direct ramifications for future certification of eradication). Detection of aVDPV or iVDPVs (which are overwhelming type 2) will have longer term implications when considering how to eventually deal with VDPVs.

Figure 2. VDPV detections (AFP cases, contacts and environmental) and cVDPV outbreaks, 2014-2018 July 26



cVDPV: serotypes and location

There have been 22 cVDPV outbreaks from 2014-July 2018, affecting 13 countries in five regions (see **table 2**). cVDPV2 was by far the commonest serotype: 17 were type 2, four were type 1, and one was type 3.

Table 2. cVDPV outbreaks by type and region/country, 2014-July 2018

Region	cVDPV1	cVDPV2	cVDPV3
African	Madagascar	Nigeria (6), Kenya, South Sudan, DR Congo (3)	
Eastern Med.		Pakistan (3), Syria, Somalia	Somalia
European	Ukraine		
South East Asian		Myanmar	
Western Pacific	Lao PDR, PNG		

# of outbreaks = 1 unless otherwise indicated (_)

Most of the 17 cVDPV2 outbreaks are thought to have originated from poor coverage with tOPV before the switch or continued inappropriate use afterwards in a few areas. The risk for additional type 2 cVDPVs should decline rapidly over time. However, three cVDPV2 emergences were detected for the first time in 2018 (JIS1 in Jigawa, SOS3 in Sokoto, and DRC Mongala). The date of origin for the DRC Mongala virus remains unclear. Of concern, the new Jigawa and Sokoto detections provide evidence of the first episodes of 'second generation' cVDPV2 (i.e. those seeded after tOPV withdrawal), representing either illicit use/release of tOPV, or the end-result of low-coverage mOPV2 used for response to other VDPV2 events. So far, cVDPV2 outbreaks have all been in known high-risk areas (i.e. poor governance, inadequate health systems, low routine immunization rates, and access issues). Declining mucosal immunity could allow emergence/spread in areas typically considered low-risk.

While cVDPV1 and cVDPV3 outbreaks have been relatively rare to date, their future emergence and thus relevance for certification remains unclear. The recent emergences in Somalia (cVDPV3) and PNG (cVDPV1) underscore that the risk still exists as long as bOPV remains in use. The long-term risk may be highly dependent on population immunity at the time of bOPV cessation. However, based on expected Sabin strain transmissibility and empirical ranking of past cVDPV detections, the risk of cVDPV1 or cVDPV3 outbreaks post-bOPV cessation should be smaller than the risk for type 2 after tOPV withdrawal.

The geographic distribution of all serotype outbreaks demonstrates the continued vulnerability of populations in insecure or inaccessible areas which are susceptible to gaps in both surveillance and population immunity.

cVDPV: temporal analysis

*Please refer to the chart of the timelines for each of the 22 outbreaks in **Annex 1, Figure 3**.*

Globally, cVDPV2s have been found regularly from 2014-July 2018 through AFP and environmental surveillance in multiple countries. Detections of cVDPV1 and cVDPV3 have been fewer, more sporadic, and more widely distributed.

During the period 2014 to June 2018, cVDPV has been consistently detected, and there has been a median of three ongoing cVDPV outbreaks per month globally, with the range from zero (Sept 2016, Jan

2017) to seven outbreaks (Sept 2014, April and May 2017) **(See Annex 1, Figure 4,).** Over these 54 months, there have been only six months (February, April, May, June, and September 2016; and January 2017), when no cVDPVs of any type were detected either in a human case or the environment; and only in two of these months (September 2016 and January 2017) was there no evidence of circulation (i.e. cVDPV neither detected nor presumed).

Due to gaps in surveillance, population movement, and delays or poor-quality vaccination responses, only six [9] of the 17 possibly concluded outbreaks were controlled within 120 days of detection. Ten of 22 outbreaks have continued for longer than six months (i.e. defined as 'persistent')[10]. The three persistent outbreaks, all cVDPV2, detected post-switch have all occurred in areas of insecurity and/or inaccessibility (e.g. DRC, Syria, Somalia).

Nine of the 17 cVDPV2 outbreaks have persisted for longer than 6 months. The longest gap without a persistent cVDPV2 outbreak detected globally has been five months (September 2016 – January 2017), although the designation of persistence could only be determined retrospectively. The longest time between the end of a persistent cVDPV2 outbreak and determination of the next persistent cVDPV2 outbreak has been 20 months (i.e. period between the last detection in Borno, Nigeria in August 2016 and the determination in September 2017 that both the outbreaks in DRC and Syria had passed the persistent threshold.)

Co-circulation of cVDPV and WPV

Low population immunity is a risk factor for both WPV and cVDPV transmission but co-circulation of these polioviruses in the same country has been uncommon during the period under review. Since 2014, nine countries have detected WPV and 13 countries have detected at least one cVDPV. Only two endemic countries, Nigeria and Pakistan, have demonstrated co-circulation of cVDPV and WPV. In non-endemic countries, circulation of VDPV has not preceded an importation of WPV during the analysis period (i.e. cVDPV has not been predictive of WPV risk).

4. Surveillance analysis (2014 – July 2018)

Timeliness of detection

There has been wide variability in timeliness of detection for all types of VDPV outbreaks. For outbreaks initially identified after 1 January 2014, the number of nucleotide (nt) changes from Sabin of the initially detected VDPV ranged from 14-32nt for cVDPV1 (n=4) and from 7 to 38nt (median: 13nt) for cVPDV2 (n=13) (**See Table 3**). Of concern have been the recent outbreaks in Syria and Horn of Africa with extensive nt changes which demonstrate that transmission can persist without detection for prolonged periods, particularly in inaccessible and/or security compromised areas.

[9] Lao PDR, Ukraine, DRC Maniema, South Sudan, Nigeria SOS, Pakistan Quetta. Four outbreaks are still considered ongoing.

[10] *These time intervals are calculated on either the onset date of the index case or collection date of the environmental sample. However, due to inherent steps in the verification process, including transport and lab testing, reporting date can be significantly later, especially in areas where there are security or transport challenges which can result in delay of outbreak determination. For example, the index case in the Syrian outbreak was identified in March 2017 but outbreak notification was not until May 2017.*

Sensitivity of surveillance during outbreaks

Since 2014, after an outbreak has been initially identified, the gap between detections of linked cVDPVs has been less than four months-- with two exceptions which both occurred pre-switch: in security constrained areas of Borno there was a gap of 16 months, and in Guinea there was a gap of 10 months contemporaneous with the Ebola virus outbreak when poliovirus surveillance collapsed.

Sensitivity of surveillance after initial detection appears to have improved since the switch. In the 11 outbreaks first detected post-switch, there has been no surveillance gap of greater than one month between isolates. The overall detection rate (i.e. cumulative monthly detections compared to total number of months of circulation) for these outbreaks is 81% compared to 39% before the switch (**Table 3**). This improvement is likely due to greater focus on VDPV surveillance and response, including increased contact sampling, expanded environmental surveillance (ES), and other intensified surveillance strategies.

Table 3: Indicators of timeliness and sensitivity of global cVDPV surveillance

Country / 'Outbreak name'	**Duration (months) as at July 2018**	**# of months there was at least one detection**	**nt changes of the earliest virus detected**
PRE-SWITCH			
Type 1			
Lao	5	5	32
Madagascar	12	6	20
Ukraine	2	2	20
Type 2			
Nigeria '2005 emergence'	16	4	n/a*
Nigeria 'CHAD emergence'	32	11	n/a
Nigeria 'KDS'	9	4	13
Pakistan 'KAB'	5	4	n/a
Pakistan 'NWZ'	15	3	n/a
South Sudan	1	1	9
Myanmar	6	2	13
Guinea	18	5	12
TOTAL	***121***	***47 (39%)***	
POST SWITCH			
Type 1			
PNG	2 (on going)	2	14
Type 2			
DRC 'Haut Lomami'	16 (ongoing)	13	16
DRC 'Maniema'	3	3	7
DRC 'Mongala'	2 (ongoing)	2	19
Syria	7	7	22
Horn of Africa PV2	8 (ongoing)	1	38

Nigeria 'SOS2'	2	2	12
Nigeria 'JIS'	5 (ongoing)	5	13
Nigeria 'SOS3'	5 (ongoing)	4	8
Pakistan QT	3	3	19
Type 3			
Somalia PV3	4 (ongoing)	4	15
TOTAL	***57***	***46 (81%)***	

*n/a – not applicable as emerged prior to 2014

ES in particular has been key to detection and monitoring duration of circulation of the VDPVs. The recent cVDPV2 and cVDPV3 outbreaks in Somalia were both detected through ES. Nine of the 11 outbreaks detected in locations with pre-existing ES had positive environmental samples at some point during the outbreak, adding confidence to the sensitivity of this surveillance. Conversely, three of the four countries which had detection gaps of >3 months did not have ES at the time of the outbreak. (All three-- Guinea, Madagascar, and Myanmar-- have established ES now.) The current expansion of ES is likely to further increase the sensitivity of global surveillance to detect cVDPV. Of the 27 countries that have had cVDPV since 2000, 23 have already established ES, and in the remaining four (i.e. PNG, Lao PDR, Cambodia and Yemen) plan to do so by 2019.

iVDPV and aVDPV: certification implications

Detection of iVDPV and aVDPV may also have implications for certification under certain circumstances. For example, a single VDPV with a high number of nucleotide (nt) changes may lead to conducting an SIA in a high-risk situation and thus re-introducing OPV vaccine.

iVDPV. Since the GPEI intensified its search for asymptomatic long -term iVDPV excretors in 2006, there has been a marked increase in cases, identified primarily in middle-income countries. Between 1962-2016, WHO registered 101 iVDPV cases; 72% associated with type 2, 17% with type 1, and 16% with type 3.[11] Since the switch in 2016 there have been six iVDPV2s identified in five countries. Evidence of iVDPV among family contacts or into the community is very rare and no poliomyelitis outbreaks have been attributed to iVDPV. However, the risks of transmissibility from asymptomatic long-term iVDPV excretors, especially in the future environment of lowered mucosal immunity, are not fully known. These uncertainties coupled with the limited current surveillance among patients with primary immunodeficiency diseases make long term declarations on the potential for iVDPV emergence problematic, but it is a non-zero risk.

aVDPV. From 2014-2018, WHO documented 42 aVDPV cases: 3 aVDPV1, 35 aVDPV2, and 4 aVDPV3. Since the switch, there have been 44 aVDPV2 events (i.e. from AFP, contact or healthy humans, or ES). A significant number are related to mOPV2 use and clustered in specific countries. The clear majority have $\leq$10 NT changes and have not resulted in further circulation. However, some initially classified aVDPVs with many nt changes (e.g. Somalia 38nt and Syria 22nt) have later been linked to community transmission. While these long chain detections could be expected in high-risk areas, environmental surveillance in Australia picked up a VDPV with 76nt changes. Option 1B specifically refers only to the

[11] Macklin G et al. Prolonged excretion of poliovirus among individuals with primary immunodeficiency disorder: an analysis of the WHO registry. Front. Immunol. 8:1103. Doi:10.3389/fimmu.2017.01103

context of cVDPV but may need to assess how/if to consider long chain aVDPV events in the context of WPV certification.

Key implications of epidemiologic and surveillance analysis for certification options:

- Detection of cVPDVs and even persistent outbreaks have been almost constant since 2014. As the clear majority of detections have been type 2, the overall incidence of cVDPV detections should decline with time since the switch. However, the most recent "second generation" detections possibly linked to mOPV2 use could markedly extend the timeframe in which cVDPV2 may be expected. cVPDV1 and cVPDV3 have been infrequent and historically easier to contain then cVDPV2. Still, recent outbreaks of cVDPV1 and cVDPV3 after a prolonged absence of these types make the future context of all VDPVs highly problematic to predict.
- Outbreaks have occurred predominantly in known high-risk areas and confined to the initial area of detection, allowing future surveillance and context considerations to focus on these areas. However, declining mucosal immunity could allow emergence/spread in areas typically considered low risk.
- Once an outbreak is detected, surveillance gaps of >4 months are rare. ES should increase the overall sensitivity of poliovirus surveillance; however, as recent detections of long-chain VDPVs attest, gaps persist, especially among inaccessible or conflict-affected populations, which can also substantially delay initial discovery of circulation.

5. Communication Considerations

Coordination and alignment of clear, cogent messages defining the scope and program implications of certification will be critical for gaining understanding and support from multiple audiences, including the general public, government officials, donors, public health workers, and the media. All options can present communication challenges. Since paralysis from natural or vaccine poliovirus is indistinguishable, explaining ongoing cVDPV cases in spite of declaring eradication of WPV can be difficult. Even explaining the origins of VDPVs and the necessity to further respond with additional polio vaccine can complicate messaging around eradication strategies and long-term certification issues. And, after multiple claims that eradication is 'this close', any option which further extends the time required to reach certification, especially Option 2, will require careful messaging and advocacy. In all scenarios inadequate or confusing communication can have a negative impact on GPEI credibility and support.

Other components of certification

Containment

The GCC has set safe and secure containment of WPV as a key criterion for certification of WPV eradication. However, for multiple reasons there have been challenges to aligning containment certification timelines (as initially specified in GAPIII) with stopping poliovirus transmission.

Due to delays in implementation of GAPIII, the GCC has recognized that full implementation of the original containment benchmarks by the time poliovirus transmission is stopped may prove difficult. Containment requirements apply to all poliovirus categories (i.e. WPV, VDPV, Sabin) alike but

implementation differentiates by type, starting with type 2. Completing surveys and destroying type 2 viruses that are not kept in poliovirus essential facilities (PEFs) has taken longer than anticipated. The timeframe for eventually completing these tasks for types 1 and 3 as well could be many more years (see **Annex 2, Figure 5**). Ensuring that all PEF's obtain a final certification of containment (CC) has likewise turned out to be a prolonged process (see **Annex 2, Figure 6**) further complicating establishing containment parameters as criteria for certification.

In any case, implementation of containment procedures will need to continue indefinitely. The responsibility for future oversight, including monitoring GAPIII benchmarks for Phase III remains to be determined.

Sequential consideration of type 3 and type 1

All the options propose to concurrently address the certification of eradication of type 3 and type 1. However, all options could be modified to sequentially address type 3 and then type 1. The last WPV3 was detected in 2012. The six years since the last detection of WPV3 provides high confidence that this poliovirus is no longer circulating. From an epidemiologic perspective, it is feasible to consider certifying the global eradication of WPV3 as a 'test run' for certification of all WPV. However, if the parameters for certification conflate both WPV and cVDPV, the expected timeframes to reach certification could be affected by the recent discovery in Somalia which reaffirms that, although rare, the risk for cVDPV3 remains as long as type 3 containing vaccine is in use.

Current plans are to initiate a globally synchronized withdrawal of bOPV within 12 months of the certification of eradication of both WPV1 and WPV3. Sequential certification could potentiate another global switch from bOPV to mOPV1 for routine immunization use to reduce the already small risk for cVPDV3 and VAPP. [12] However, due to supply challenges and other considerations (e.g. logistics, cost, communication) this option is not currently being considered.

Addressing long-term status of VDPVs

Under options 1A and 1B there would still need to be a subsequent process to validate the absence of VDPVs after certification of WPV eradication. The details for this validation process would need to be determined by the time of bOPV cessation, but given their differential risks for emergence, cVDPV and iVDPVs would most likely be considered separately. Option 2 would explicitly require certification of VDPV eradication. Although the process has not yet been defined, this certification could prove problematic, especially for iVDPV, given the uncertainties about the risks for persistent low-level transmission.

[12] While data on incidence is difficult to obtain, VAPP of all types is thought to be a relatively rare occurrence. A 2014 global review found that Sabin 3 was isolated from 42% of recipient VAPP cases and 37% of contact VAPP cases. See L Platt et al. Vaccine-Associated Paralytic Poliomyelitis: A Review of the Epidemiology and Estimation of the Global Burden. JID 2014:210 (Suppl 1), S380-89. https://doi.org/10.1093/infdis/jiu184.

Option Appraisal

Option 1A. Considerations for certification of eradication based on the interruption of transmission of WPV alone, followed later by separate "validation of absence" determination for VDPVs

	Program	Epidemiology and Surveillance	Partnership	Communication
Pro's	• Reflects historical program priorities and measure of program success; consistent with WHA resolutions, GCC 2004 criteria, PEESP, and PCS. • Consistent with declaration of WPV2 global eradication and certifications of regional certification in AMR, WPR, EUR, and SEAR. • Most likely option to meet current GPEI timeline-- thereby keeping within estimated financial resource requirements & program capacity. • Facilitates w/drawal of bOPV as scheduled (& thus potentially lowering risk of future VDPVs) • By limiting criteria, provides the most straightforward eradication process	• Only 12 WPV cases through July 2018 • Sensitive surveillance for WPV and VDPV operational in most countries-- giving confidence to proposed 3-year requirement for certifying polio-free status	• Most aligned with all GPEI partners' initial global commitment • Facilitates implementation of GPEI sunset as planned and transition of functions to other stakeholders	• Widely understood and accepted; simple and straightforward
Risks	• Stopping cVDPV transmission could be seen as a lower priority	• Decline of attention to poliovirus surveillance once WPV certification is attained	• Loss of GPEI credibility if/when cases of cVDPV are detected at or post WPV certification	• Potential confusion and challenges for messaging if/when cases of cVDPV are detected at or post WPV certification

Option 1B. Certification of eradication based on the interruption of WPV transmission, with consideration of the context of ongoing or recent cVDPV outbreaks followed later by separate "validation of absence" determination for VDPVs. Proposed contextual considerations:

- **No detection of a persistent cVDPV2 outbreak from any population source in the previous 18* months; and No detection of a cVDPV1or 3 outbreak from any population source in the previous six* months; OR**
- **No detection of a cVDPV 1or 3 outbreak from any population source in the previous six* months;**

*NOTE: Time parameters could be further discussed

	Program	Epidemiology and Surveillance	Partnership	Communication
Pro's	• Continues attention on achieving PEESP objective to stop all cVDPV outbreaks within 120 days	• See 1A • If limited only to cVDPV1 and 3, recognizes lack of epidemiologic connection among different serotypes and avoids tying WPV1/3 certification to type 2	• May further credibility of GPEI by acknowledging role of VDPV in eradication	• Removes the risk of declaring WPV eradication in the face of a cVDPV outbreak.
Risks	• Depending on the actual cVDPV conditions set and global epidemiology, could lead to delay in WPV certification thereby risk further pushback of the GPEI timeline w/ resulting increased costs, possible diminished program capacity, and postponement of bOPV cessation. • Adds further considerations to certification process—e.g. VDPV detection just before 3-year window could complicate certification process for both global level and remaining regions.	• Multiple post-switch examples of cVDPV2 outbreaks of long duration—may still be circulating when WPV1/3 certification could occur • Recent detections of cVDPV1 and 3 after long absence periods • Insecure or inaccessible areas which are common globally remain at high risk for delayed detection and/or persistent circulation.	• Possible delay could negatively affect donor and partner support; modification of certification concept may be contrary to stated goal of Polio Plus program • Political and media pressure to certify eradication according to historical criteria	• Requires consistent and careful messaging regarding the concept and role of VDPVs. • May require significant shift in communication messaging that certification will occur 3 years after the last WPV case.

Option 2. Considerations for Certification of eradication in two stages: Stage 1 based on interruption of WPV transmission (with or without consideration of context of cVDPVs); Stage 2 based on evidence of no new VDPV emergence and circulation post WPV eradication

	Program	Epidemiology and Surveillance	Partnership	Communication
Pro's	•	• Provides clearest and most explicit framework for the current situation of ongoing emergence and circulation of VDPVs. • Logical progression of WPV to OPV w/drawal to VDPV	• Global commitment to eradicating all poliovirus transmission could increase credibility	• Directly acknowledges risk of paralysis from all polioviruses • Manages the risk of declaring WPV eradication in the face of a cVDPV outbreak.
Risks	• May require a new WHA resolution, revised GPEI strategic plans and PCS • Requires new certification process at global, regional, national levels; including revised mandates for GCC/RCC/NCC • In addition to disadvantages from possible delays noted if Stage 1 uses cVDPV criteria (e.g. Option 1B), could commit GPEI to extended timeframe w/ resulting increased costs and challenges to sustaining program capacity. • Given uncertainty of risks from VDPVs (especially iVDPVs) defining end-point and parameters for VDVP certification could be highly problematic or even unobtainable. • Achieving Stage 2 could be jeopardized by uncertain future availability of nOPV and antivirals which could be required to fully eliminate risk of VDPV emergence and circulation.	• Risks noted in 1B • Capacity for widespread iVDPV surveillance not yet established; potential for long delays or inability to finally classify VDPVs from ES because immune-deficiency can only be determined conclusively from a case. • Infrastructure to maintain "certification standard" surveillance will need to continue globally and raise costs compared with transition to risk-based surveillance envisioned in PCS.	• Disadvantages listed in 1B could be magnified by changing definition & timeframe of certification (especially new funding negotiation) • Requires revision of plans for GPEI sunset and implementing partner commitments • Risks current consensus around certification – some partners may opt out.	• In addition to risks in 1B, further challenge to justify changing 'goalposts'.

	• Adds further considerations to certification process—e.g. VDPV detection just before 3-year window could complicate certification process for both global level and remaining regions. .			

Conclusions

Establishing clear parameters for certification of global poliovirus eradication is critical to setting strategies and priorities for the GPEI and future stakeholders committed to this goal. Although prior definitions of certification have been focused primarily on stopping WPV transmission, the persistence of VDPV circulation has raised questions about whether this scope needs to be expanded. Three primary options (along with possible permutations) for defining certification can be evaluated based on five key considerations: strategic and operational program perspectives, GPEI partnership, epidemiology, surveillance, and communication.

Option 1A limits certification only to consideration of WPV transmission. This option is consistent with prior global and regional certification processes and is the most closely aligned with current GPEI commitments and strategies. Since WPV2 has already been declared eradicated based on this approach, the option deals only with WPV1 and WPV3. While challenges remain to reach the goal of WPV eradication, this option represents the best opportunity to meet proposed GPEI timelines and budget. The primary drawbacks are the communication challenges and potential loss of GPEI credibility associated with any ongoing poliovirus circulation from VDPV at the time of WPV certification. This option acknowledges the importance of eventually stopping all poliovirus transmission and proposes that parameters for validating the absence of VDPVs after certification will be addressed in a future process.

Option 1B also limits certification to WPV but attempts to reduce the risk of declaring eradication in the face of ongoing poliovirus transmission by explicitly taking VDPV circulation into consideration. Although this expanded scope may limit some communication challenges, the uncertainties surrounding persistence of cVDPVs, especially of cVPDV2, may further delay certification--- leading to added costs, challenges to sustaining program quality, and postponement of bOPV withdrawal (which could foster additional cVDPV). The risks for delay could be mitigated by limiting the consideration of cVDPV outbreaks to only cVDPV1 and cVDPV3, thereby delinking any future problems with ongoing type 2 outbreaks from the issue at hand, i.e. certification of WPV1 and WPV3. Option 1B adopts a similar approach as 1A for dealing with VDPVs after certification.

Option 2 widens the scope of certification to include all poliovirus transmission in two sequential stages: WPVs followed by VDPVs. This approach required the most rigorous standards to confirm eradication of all polioviruses regardless of origin. Stage 1 focusing on WPV eradication may or may not include the context of VPDVs with the same advantages/risks of each approach as noted under Options 1A and 1B. Stage 2 would go beyond the validation of absence for VDVPs proposed by these options and require strict parameters (e.g. documentation process by every country, oversight and vetting by regions, and then oversight and vetting globally) which could provide high confidence that VDPV transmission has stopped. Given the uncertainties of future risks from VDPV, this approach could, at a minimum, significantly extend the time frame for achieving overall polio eradication with all the disadvantages inherent to such a delay. Certifying the eradication of iVDPV may not be feasible. Option 2 would also require revising certification strategies, processes, and partner/donor commitments.

While satisfactory implementation of containment phases identified in GAPIII will be a criterion for certification of WPV or WPV + VDPV eradication, certification of containment will need to follow a separate but coordinated time line under all proposed options.

Annex 1.

Figure 3. Monthly global detection of WPV and cVDPV, 2014-2018 July (best viewed in color)

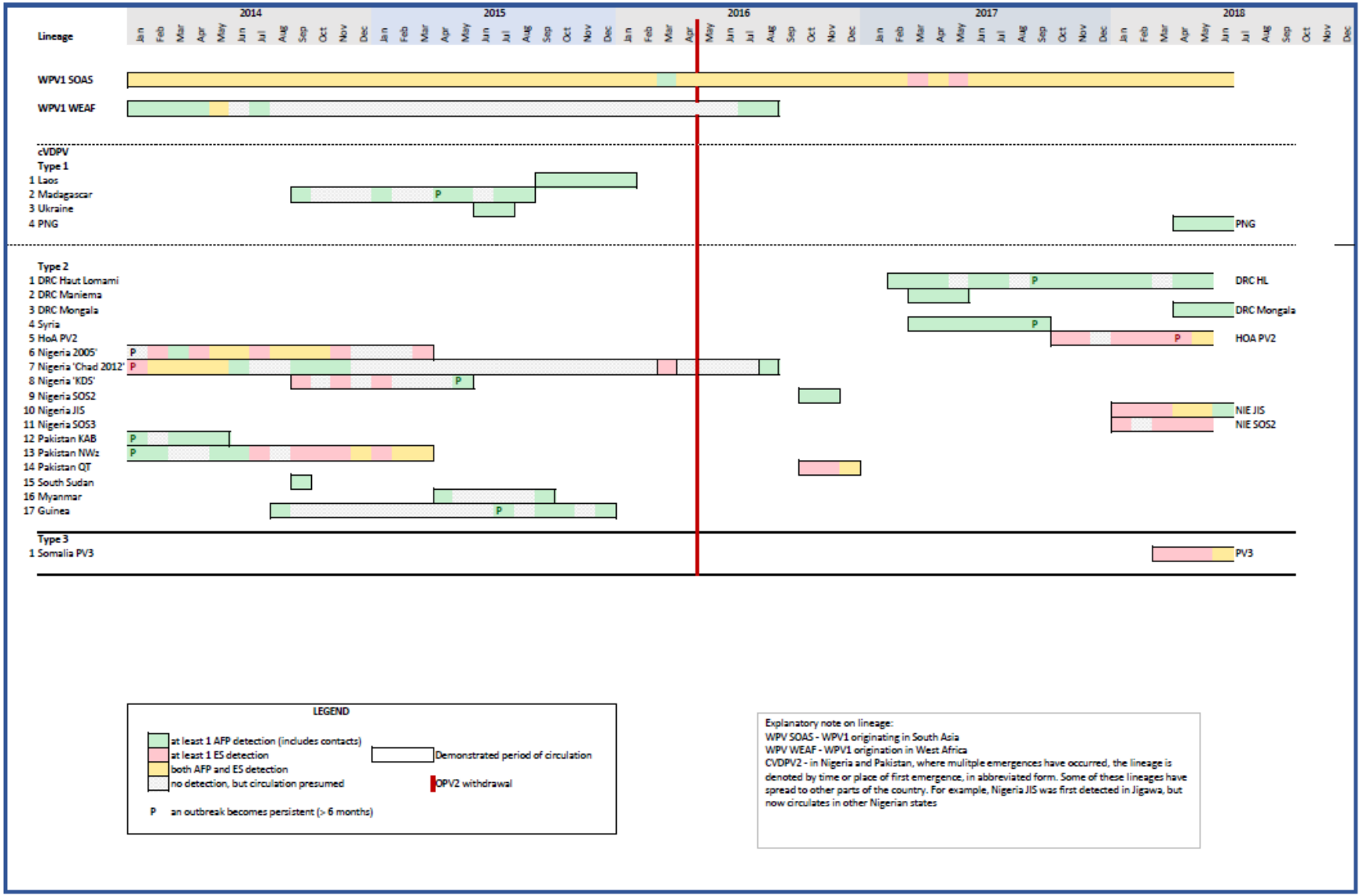
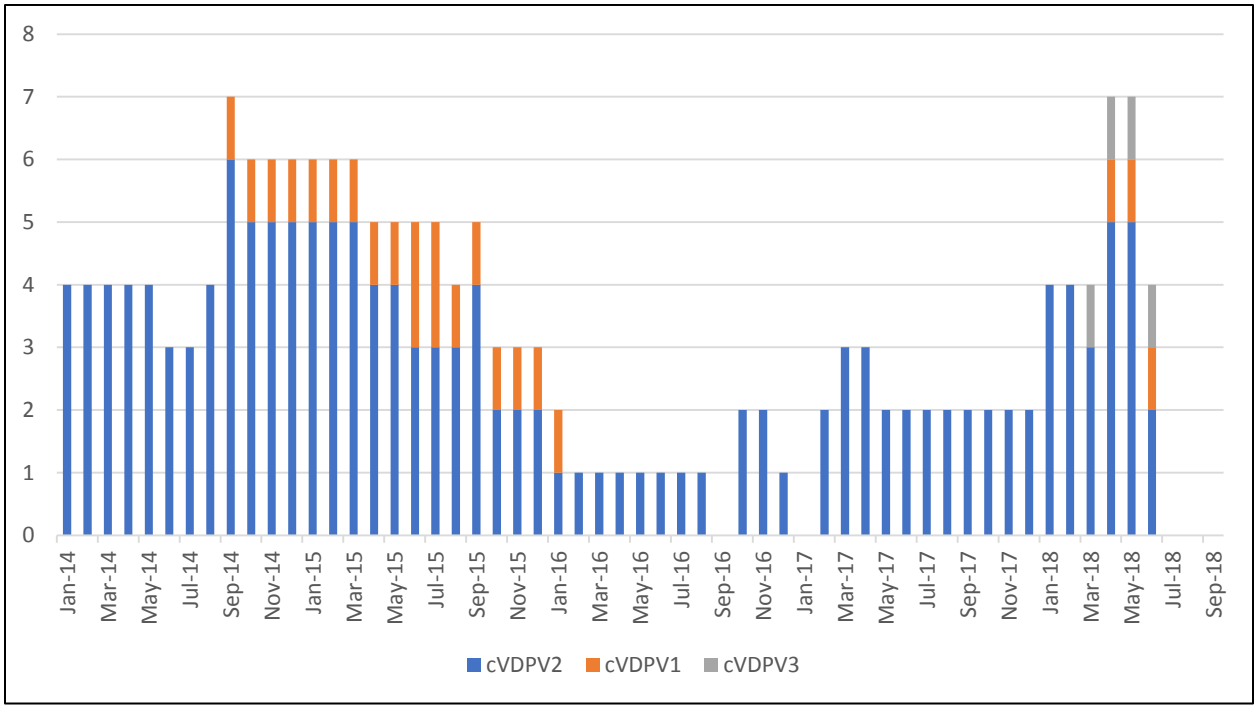


Figure 4. Number of circulating VDPV lineages, by type, 2014-2018 July



Annex 2. Containment

Figure 5. Containment timeline

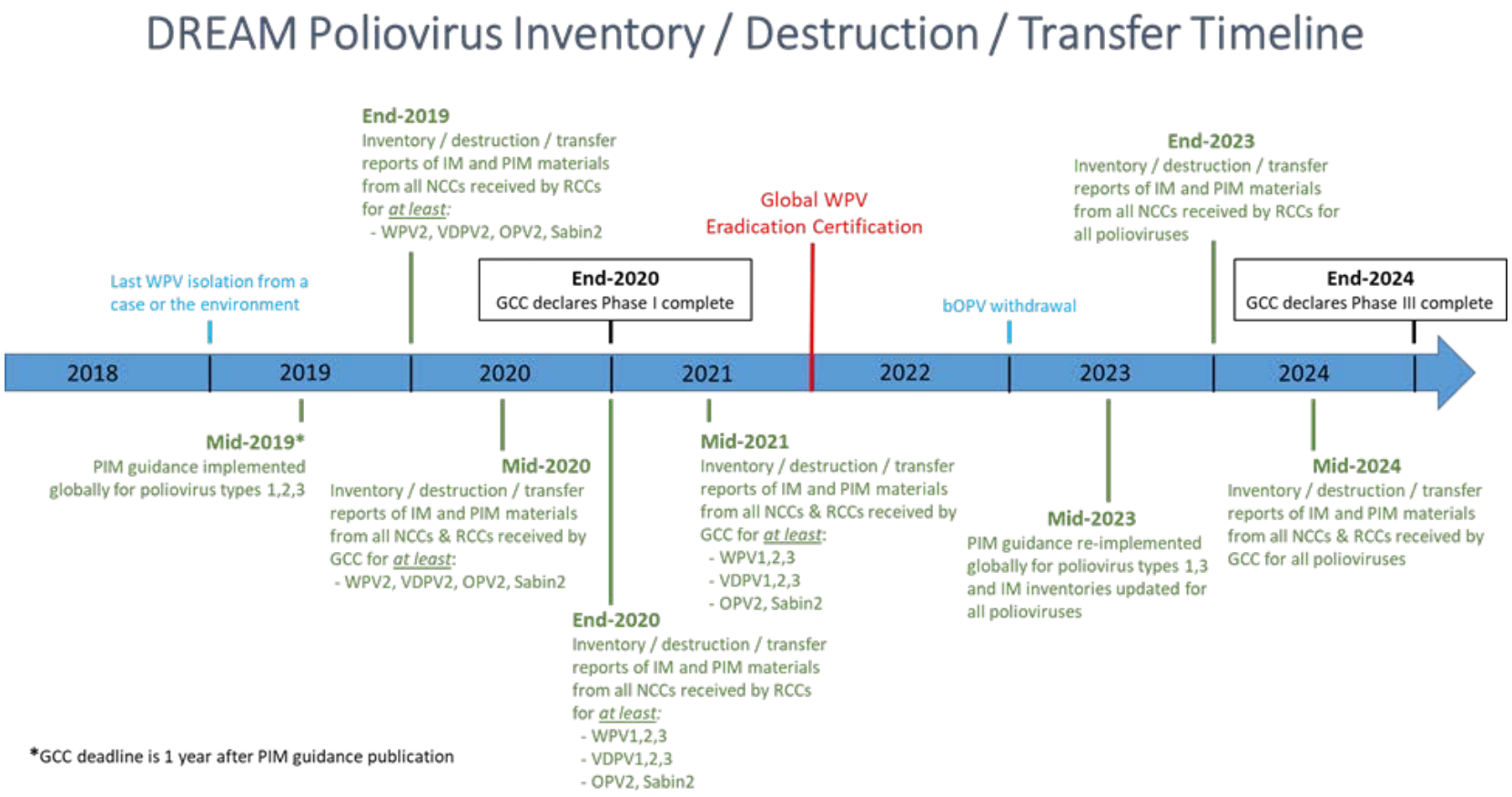
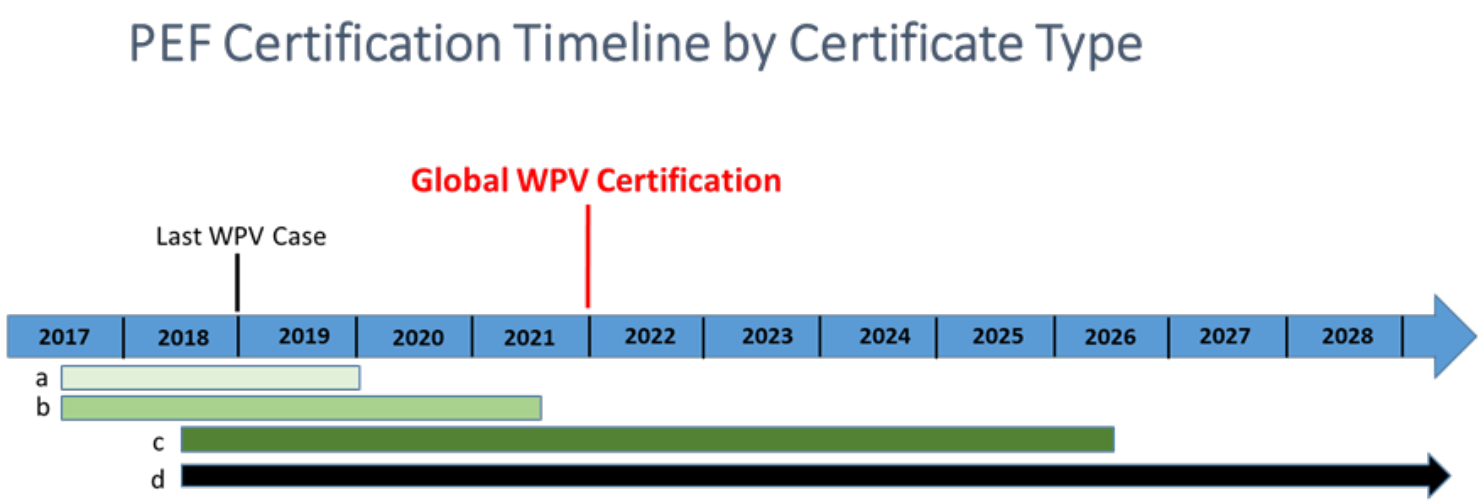


Figure 6. PEF Certification Timeline



a = Certificate of Participation (CP) issuance period*

b = Max CP validity interval**

c = Max Interim Certificate of Containment (ICC) issuance and validity interval***

d = CC issuance interval****

*Latest date possible for CP issuance = 31 December 2019 as per WHA Resolution
**Latest date possible for CP validity is 30 June 2021, i.e. 1.5 years after latest date possible for CP issuance
***Latest date possible for ICC validity is 30 June 2026, i.e. 5 years after latest date possible for CP validity
****Latest date possible for CC issuance is 30 June 2031, i.e. 5 year after latest date possible for ICC validity