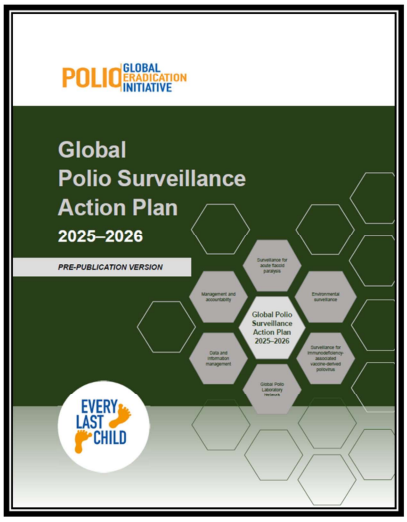
GPSAP Companion Toolkit

Timeliness of Detection for WPV and VDPV



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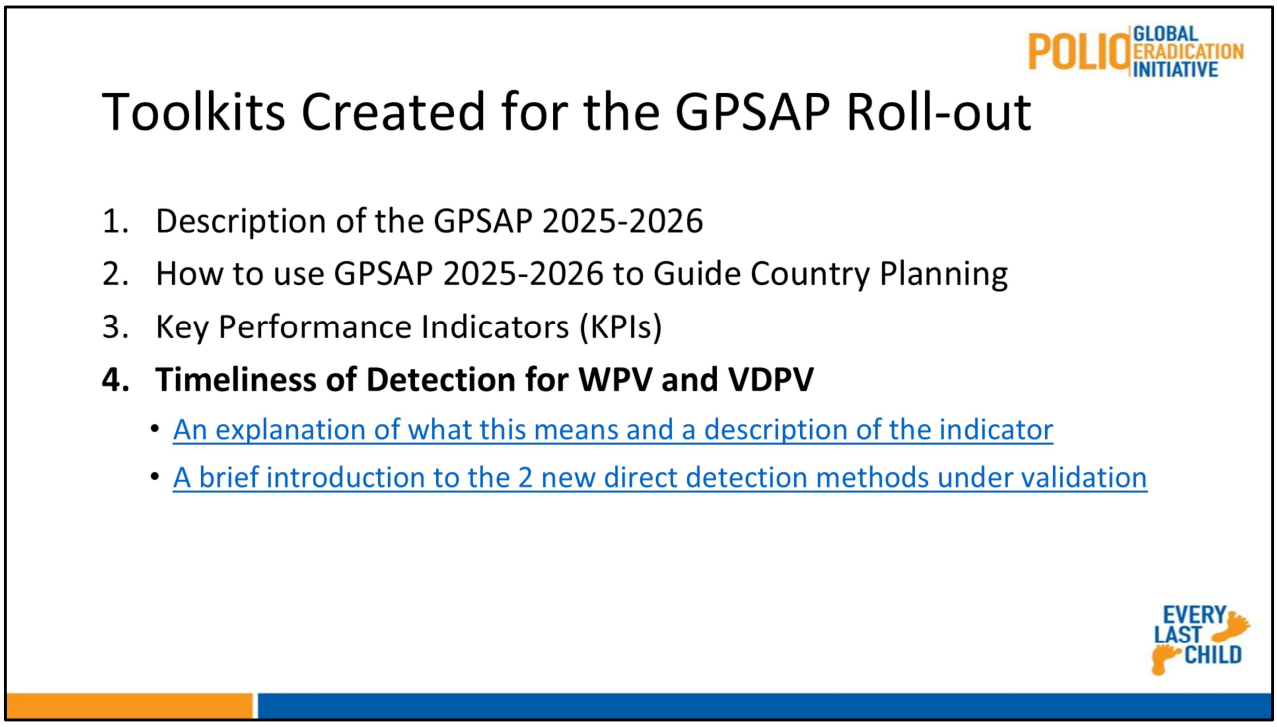

- This technical tool is the 4th in a series of 4 tools pertaining to the GPSAP roll-out toolkit.
- This document is divided up into 2 parts:

- First, an explanation of what Timeliness of detection for WPV and VDPV means, with a detailed description of the indicator and the various intervals that make it up.
- Second, you will have a brief introduction to the 2 new direct detection methods currently under validation.

Overview – 1/4

1) Background

- The 'timeliness of detection' was introduced in the Polio Eradication Strategy 2022-2026 to emphasize the critical need to expedite poliovirus detection, thus enabling rapid response efforts and ensuring the swift interruption of transmission.
- It is measured from the onset of paralysis (for acute flaccid paralysis [AFP] cases) or from the collection of samples (for environmental surveillance [ES]) to final **positive** result.
- The Polio Eradication Strategy 2022-2026 set the target for all polioviruses to be reported **within 35 days** of paralysis onset or ES sample collection.

Overview – 2/4

- **However**, it has become clear that the same target for countries that have WHO-accredited polio laboratories with "full laboratory capacity*" can not be used for countries without "full laboratory capacity*". Indeed, countries lacking full laboratory capacity face challenges in meeting the 'within 35-day' target due to the necessity of one or even two international sample shipments.

  * Full laboratory capacity: virus isolation, intratypic differentiation and sequencing.

- The GPSAP 2025-2026 therefore sets a **second operational target** for countries without full laboratory capacity: all polioviruses to be reported **within 46 days** of paralysis onset or ES sample collection.

Countries with full laboratory capacity	Countries without full laboratory capacity
WPV/VDPV laboratory results available **within 35 days** of paralysis onset or ES sample collection	WPV/VDPV laboratory results available **within 46 days** of paralysis onset or ES sample collection

Overview – 3/4

2) Description

- As an indicator (key performance indicator [**KPI**]), 'timeliness' was further elaborated in the previous GPSAP 2022-2024 and in the Global AFP Surveillance Guidelines.
- The timeline between onset of paralysis or the collection of ES samples and sequencing results is made up of many activities. The speed at which each of these activities is conducted is assessed through **timeliness indicators** (KPIs).
- Each indicator is measured against its own, specific target. See the *GPSAP Companion Toolkit on 'Key Performance Indicators'* for information on timeliness-related indicators (KPIs) and their targets.
- Timeliness targets are only recommended timeframes. Every **effort should be made to expedite each step** to reduce the number of days within the targets.

Overview – 4/4

3) Location in the GPSAP

- The ‘timeliness of detection for WPV and VDPV’ is described in detail in **Annex D** of the current GPSAP.
- This annex is divided into **3 sections**:
  - Certification-standard indicators differ from timeliness-of-detection indicators
  - An overview of timeliness-of-detection intervals and targets
    - For **AFP** cases that turn out to be positive
    - For **ES** samples that turn out to be positive
  - The impact of Direct Detection (DD) on timeliness of detection

Global Polio Surveillance Action Plan 2025–2026

Annex D. Timeliness of detection for WPV and VDPV

This annex provides a brief explanation of the difference between certification indicators and timeliness indicators, an overview of timeliness-of-detection targets, and a review of how direct detection (DD) techniques could impact the timeliness of detection.

Certification-standard indicators differ from timeliness-of-detection indicators

The indicator *stool adequacy* is an acute flaccid paralysis (AFP) surveillance **quality** indicator that is regularly reviewed by national, regional and global certification commissions.[34] It sets a target of 14 days between paralysis onset and the collection of two stool specimens based on findings that this period was the optimal time period in which poliovirus could be detected from stool specimens.[35]

The Global Polio Eradication Initiative (GPEI) Strategy 2022–2026 made clear the imperative to detect wild poliovirus (WPV) and circulating vaccine-derived poliovirus (cVDPV) as early as possible.[36] The Global Polio Surveillance Action Plan (GPSAP) 2022–2024 introduced a new set of indicators (referred to as timeliness-of-detection indicators) and targets to specifically monitor and improve the **speed** of WPV/VDPV detection.[37] One of those indicators is the timeliness of field activities that sets an 11-day target to complete field-level steps from paralysis onset to second stool collection. It is important to remember that this indicator serves a different purpose than the *stool adequacy* indicator and that all timeliness-of-detection indicators should only be used when assessing the speed in which activities are completed. Details for timeliness-of-detection indicators are available in **Annex C**.

Overview of timeliness-of-detection intervals and targets

Timeliness of detection is essential for a quick response to any poliovirus. Measured from the onset of paralysis (for cases of acute flaccid paralysis [AFP]) or from the collection of samples (for environmental surveillance [ES]) to final positive result, the timeliness-of-detection target is ≤35 days.[38] However, differences in domestic laboratory capacity affect timeliness. Countries with full laboratory capacity (i.e. capable of performing virus isolation [VI], intratypic differentiation [ITD], and sequencing) are able to achieve this target, whereas countries without full laboratory capacity face challenges, including delays due to multiple international shipments.

Strategies for improving timeliness

To diagnose and address delays in virus detection, programmes should:
(1) routinely monitor intervals to identify delays;
(2) identify the root causes of delays;
(3) implement mitigation measures; and
(4) continue to monitor and evaluate implementation.

Detailed guidance for improving timeliness of field activities can be found in the *Global AFP Surveillance Guidelines*. For laboratory challenges, refer to *Global Polio Laboratory Network (GPLN) Guidance Papers* (**Annex I**).

[34] Stool adequacy is defined as the proportion of AFP cases with two (2) stool specimens collected ≥**24 hours** apart, both within **14 days** of paralysis onset, AND received in good condition in a WHO-accredited laboratory.
[35] Sutter RW, Kew OM, Cochi SL, Aylward RB. Poliovirus Vaccine–Live. In: Plotkin's Vaccines: Implications for Acute Flaccid Paralysis Surveillance: A Review of Literature. J Infect Dis 179(1): S176–92.1997. https://doi.org/10.1093/infdis/179.Supplement_1.S176, accessed 22 December 2024).
[36] Global Polio Eradication Initiative (GPEI). Polio Eradication Strategy 2022–2026: Delivering on a promise. Geneva: World Health Organization; 2021 (https://iris.who.int/handle/10665/345687, accessed 22 December 2024).
[37] Global Polio Eradication Initiative (GPEI). Global Polio Surveillance Action Plan 2022–2024. Geneva: World Health Organization; 2022 (https://polioeradication.org/wp-content/uploads/2022/05/GPSAP-13Jul2022-EN.pdf, accessed 22 December 2024).
[38] The ≤35-day target is for both AFP surveillance and environmental surveillance.

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Strategies to improve timeliness

To diagnose and address **delays** in virus detection, programmes should:

1) monitor intervals routinely to identify delays
2) identify the root causes of delays
3) implement corrective and mitigation measures
4) evaluate the implementation of those measures

Resources:

- Detailed guidance for improving timeliness of field activities can be found in the Global AFP Surveillance Guidelines.
- For laboratory challenges, refer to Global Polio Laboratory Network (GPLN) Guidance Papers (Annex I of the GPSAP).

- Very briefly, this slide list the 4 main activities to diagnose and address delays in virus detection.
- It also gives you 2 references to resources for further information on how to improve timeliness.

Certification-standard indicators differ from **timeliness-of-detection** indicators

- Before we go into what makes up timeliness of detection, it is important to address a source of potential confusion, that is, to understand the difference between certification-standard indicators and timeliness of detection indicators.

Quality vs. Speed

- ***Stool adequacy*** serves as a quality indicator for AFP surveillance and is regularly assessed by national, regional, and global certification commissions. It targets a 14-day period between the onset of paralysis and the collection of two stool specimens, which is considered the optimal timeframe for detecting poliovirus in stool samples.
- ***Timeliness of field activities*** sets an 11-day target to complete field-level steps from paralysis onset to second stool collection. It is one of a set of timeliness-of-detection indicators introduced by the GPSAP 2022-2024 to specifically monitor and improve the speed of WPV/cVDPV detection.
  - → This indicator thus serves a different purpose than the stool adequacy indicator.
  - → All timeliness-of-detection indicators should only be used when assessing the **speed** in which activities are completed.
  - → Details for timeliness-of-detection indicators are available in Annex C of the GPSAP and in the GPSAP Companion tool 'Indicators'.

- The main source of confusion lies in the difference between quality and speed.
- And this comes up when working with the indicators Stool adequacy and Timeliness of field activities.

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An overview of

Timeliness of Detection Intervals and Targets

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Breakdown of Timeliness of Detection Intervals and Targets

- **Intervals** that make up the timeline for the detection of positive samples fall under 3 main activities:
  1) Field activities (for AFP surveillance only)
  2) Sample shipment (for AFP surveillance and Environmental surveillance)
  3) Lab processing (for AFP surveillance and Environmental surveillance)

  and each main component is further sub-divided.

- **Targets** for the timeliness of detection KPI are as follows, depending on the country's circumstances and whether it has full laboratory capacity* or not:

Country	AFP surveillance	Environmental surveillance
With full laboratory capacity*	**≤ 35 days**	**≤ 35 days**
Without full laboratory capacity*	**≤ 46 days**	**≤ 46 days**

* Full laboratory capacity: i.e. capable of performing virus isolation (VI), intratypic differentiation (ITD), and sequencing.

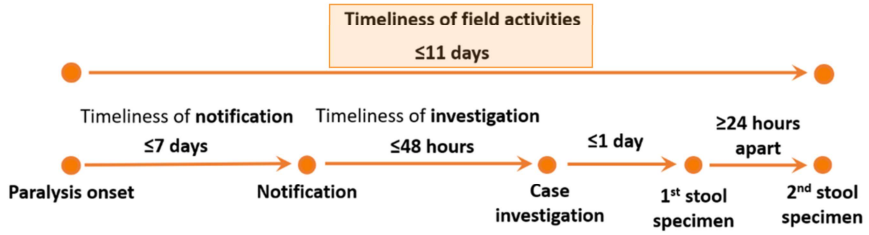
AFP surveillance

‘Optimized field and shipment’ – 1/2

a breakdown of activities from ‘Onset of paralysis’ to ‘Arrival at the Lab’

1) ‘Timeliness of field activities’: ≤11 days

= Notification (≤7 days) + Investigation (≤48 hours) + Stool collection (≤2 days) = ≤11 days



- **This slide and the next one** show the various intervals (activities) between the **Onset** of paralysis and the **Arrival of the stool specimens at the Lab.**
- Added together, these intervals make up a timeline that is measured by the **new KPI ‘Timeliness of optimized field and shipment’**.
- **This slide** shows activities that are conducted in the **field**: Notification, Investigation, Stool collection, and describes the KPI ‘**Timeliness of field activities**’
- The timeliness **targets** for each activity is:
  - Notification of a suspected case: within **7 days** of paralysis onset
  - Case investigation: within **48 hours** of notification
  - The first stool specimen: collected within **1 day** of the investigation
  - The second stool specimen: collected at least **24 hours apart** from the first
- Thus together, these **field activities** should be completed within **11 days** of onset.

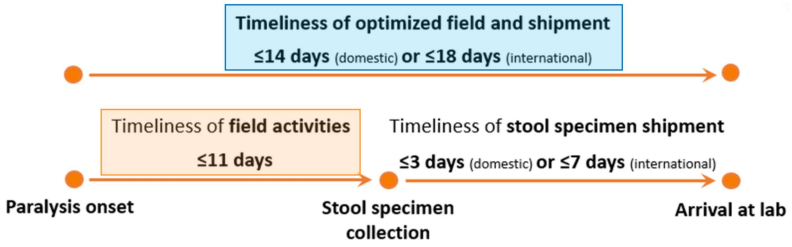
‘Optimized field and shipment’ – 2/2

a breakdown of activities from ‘Onset of paralysis’ to ‘Arrival at the Lab’

2) ‘Timeliness of optimized field and shipment’: ≤14 days or ≤18 days

= ‘Field’ activities (≤11 days) + Domestic shipment (≤3 days) = ≤14 days, or

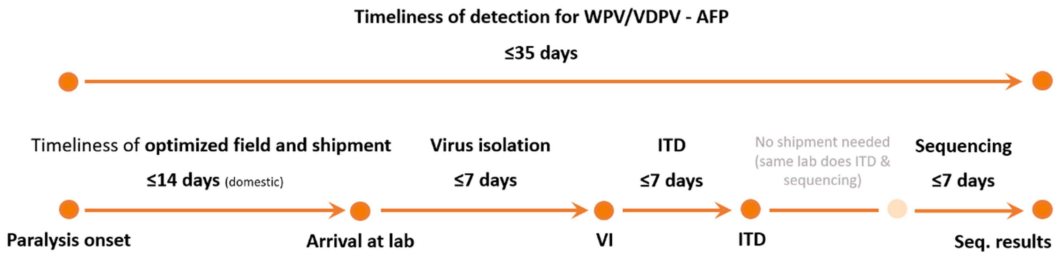
= ‘Field’ activities (≤11 days) + International shipment (≤7 days) = ≤18 days



- **<u>This slide</u>** shows **field activities** and stool specimen **shipment** to the laboratory. Together, their timeliness targets make up the **new KPI ‘Timeliness of optimized field and shipment’**.
- The timeliness **targets** for each activity is:
  - Field activities: completed within **11 days** of onset
  - Stool specimen shipment: completed within **3 days** (for countries with full lab capacity, requiring only domestic shipment), or within **7 days** (for countries without full lab capacity, requiring international shipment(s))
- Therefore, together these activities should be completed within **14 days** (domestic shipment only) or within **18 days** (international shipment) of onset.
- These targets ensure efficient detection and timely processing to support polio surveillance efforts. Hence the word ‘**optimized**’.

Countries with full laboratory capacity (target: ≤ 35 days)

The process timeline for the detection of positive samples for countries **with full laboratory capacity** is the fastest as it requires no international shipment. The target is: ≤**35 days**.



VI = Virus isolation, ITD = Intratypic differentiation

- This slide illustrates how **countries with full lab capacity** can reach the timeliness of detection target of **35 days** for samples positive for WPV/VDPV.
- Note that confirming samples as **negative for poliovirus** in the virus isolation (VI) step can take up to **14 days** (and samples will therefore not proceed onto further steps). However, the VI step will often see results **positive for poliovirus** within **7 days** (samples will then, therefore, proceed onto further steps). Hence, the target for VI is "≤7 days" in this visual.
- The intervals are as follows:
    - With full lab capacity, field and domestic shipment activities (i.e. 'optimized field and shipment') are completed within **14 days** of onset
    - After the specimens arrive at the lab, virus isolation **(VI)** is performed within **7 days**
    - This is followed by intratypic differentiation (**ITD**) within another **7 days**

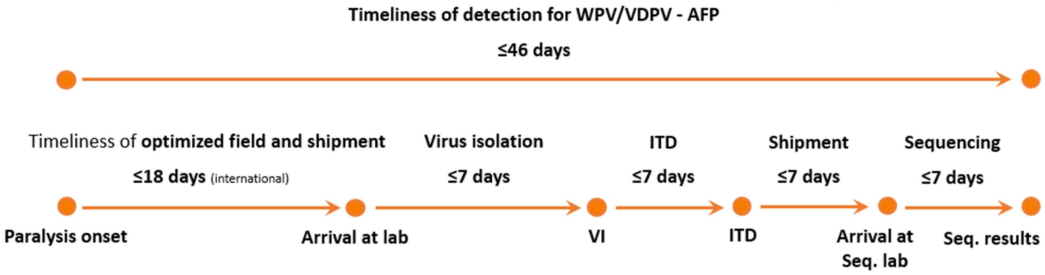
- When the same lab handles both ITD and sequencing, no additional shipment is needed, and sequencing results are obtained within **7 days**

→ **Timeliness of detection** for positive AFP samples is thus achievable **within 35 days of onset**. [14+(3*7)=35]

- This optimized process for countries with full lab capacity ensures timely detection and reporting of poliovirus cases to enable swift outbreak response.

Countries without full laboratory capacity (target: ≤ 46 days)

The process timeline for the detection of positive samples for countries **without full laboratory capacity** takes longer due to the need for multiple international shipments. A target of ≤**46 days** is however achievable by expediting field activities.



VI = Virus isolation, ITD = Intratypic differentiation

- This slide illustrates how **countries without full lab capacity** can achieve a timeliness of detection target of **46 days** for samples positive for WPV/VDPV.
- Note that while confirming samples as **negative** for poliovirus in the virus isolation (VI) step can take up to **14 days** (samples therefore do not proceed onto further steps), the VI step will often see results **positive** for poliovirus within **7 days** (samples will proceed onto further steps). Hence the VI target of ≤7 days in this visual.

- The intervals are as follows:

  - Without full lab capacity, field and international shipment (i.e. 'optimized field and shipment') can be completed within **18 days** of onset

  - After the specimens arrive at the lab, virus isolation **(VI)** is performed within **7 days**

  - This is followed by intratypic differentiation (**ITD**) within another **7 days**

  - Another international shipment may then be needed to reach the sequencing lab: another **7 days**

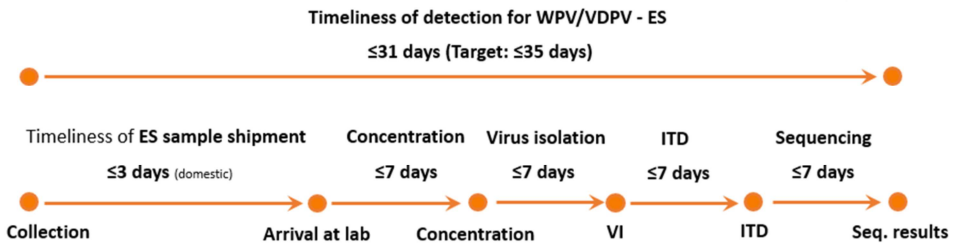
- Sequencing results are then obtained within **7 days**

→ **Timeliness of detection** for positive AFP samples is thus achievable **within 46 days of onset**. [18+(4*7)=46]

Environmental surveillance

Countries with full laboratory capacity (target: ≤ 35 days)

The "faster" process timeline for the detection of positive ES samples is where the domestic lab can reduce VI to ≤7 days and perform sequencing in ≤7 days leading to final results in 31 days (no international shipment of specimens). The target is set at ≤**35 days** from collection.



VI = Virus isolation, ITD = Intratypic differentiation

- ES samples do not have a field investigation component therefore the shipment interval is defined as the time between the collection of samples and their arrival at the laboratory.
- ES samples do have a separate concentration step (7 days), however. While the targets for VI (14 days*) and ITD (7 days) are the same as specimens from AFP cases, ES samples may be more complicated to sequence and require a longer timeframe (14 days) due to the presence of poliovirus mixtures. Sequencing however can be expedited to ≤7 days. [*However, samples positive for poliovirus will generally grow faster, within 7 days. Hence the target for VI of ≤7 days for positive specimens]
- Note that negative samples will be confirmed during the VI step and will not proceed for further testing.

- This slide illustrates how **countries with full lab capacity** can reach the timeliness of detection **target of 35 days** for samples positive for WPV/VDPV (reaching **31 days** is even possible)

- The intervals are as follows:

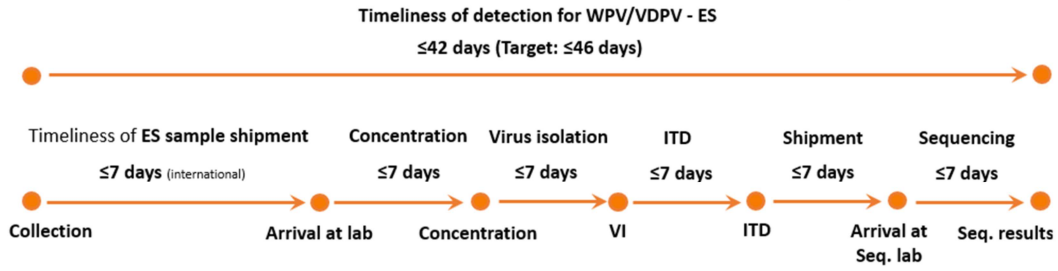
    - Domestic transport to the lab: completed within **3 days** of sample collection

- Concentration: performed within **7 days** of receipt at the lab
- Virus isolation (**VI**): completed within another **7 days**
- Intratypic differentiation (**ITD**): completed within **≤7 days**
- When the same lab handles both ITD and sequencing, no additional shipment is needed, and sequencing results are obtained within **7 days**

→ **Timeliness of detection** for positive ES samples is thus achievable **within 35 days of collection** – and even within 31 days. [3+(4*7)=31]

Countries without full laboratory capacity (target: ≤ 46 days)

The overall timeframe for positive ES samples in countries without full laboratory capacity is longer due to the need for one to two international shipments. Where the laboratories can reduce VI to ≤7 days and perform sequencing in ≤7 days, final results can be obtained in 42 days. The GPSAP sets the **target at ≤46 days**.



VI = Virus isolation, ITD = Intratypic differentiation

- This slide illustrates how **countries without full lab capacity** can achieve a timeliness of detection **target of 46 days** for samples positive for WPV/VDPV (reaching **42 days** is even possible).
- Note that negative samples will be confirmed during the VI step and will not proceed for further testing.

- The intervals are as follows:

  - Without full lab capacity, international shipment is needed: completed within **7 days** of collection
  - Concentration: performed within **7 days** of receipt at the lab
  - Virus isolation (**VI**): completed within another **7 days**
  - Intratypic differentiation (**ITD**): completed within **≤7 days**
  - When a different lab is needed to handle sequencing, additional international shipment is needed: **≤7 days**

- Sequencing results can be obtained within **7 days**

→ **Timeliness of detection** for positive ES samples is thus achievable **within 46 days of collection** – and even within 42 days. [6*7=42]

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The impact of **Direct Detection** on Timeliness of Detection

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The 3 steps in the current polio diagnostic algorithm

- The current polio diagnostic algorithm for AFP cases includes the following 3 steps:

    1. **Virus isolation (VI)**
    2. **Intratypic differentiation (ITD)**
    3. **Sequencing**

- Most samples will be negative by step 1. 'VI' and therefore will not need steps 2. 'ITD' and 3. 'Sequencing'.

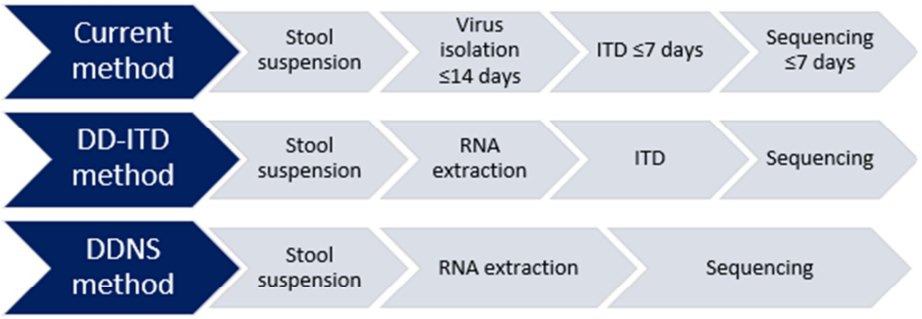
The 2 direct detection methods being validated

2 direct detection (DD) methods for testing AFP stool samples are currently being validated by the Global Polio Laboratory Network (GPLN):

- **Direct detection with intratypic differentiation** (**DD-ITD**)
  - The virus isolation step is eliminated.
  - Samples are extracted and tested using ITD, followed by sequencing of some positive samples; Sabin 1 and 3 are not sequenced.
- **Direct detection by nanopore sequencing** (**DDNS**)
  - The virus isolation and ITD testing steps are eliminated.
  - All samples are extracted and sequenced, provided amplification is successful.

Polio diagnostic algorithms

Poliovirus diagnostic algorithms: Current method and DD methods under validation



Samples skip the VI step

Samples skip the VI step and the ITD testing step

Fig. D5., GPSAP
Source: WHO.

RNA = ribonucleic acid

The impact of direct detection on timeliness of detection

- **Benefit**: The removal of the VI step, under both DD methods, could save 7 to14 days in laboratory processing time for positive samples, hence speed up outbreak response.
- **However**: The removal of the screening by VI means that the volume of samples that need to be tested by ITD and/or sequenced would increase. The target of 7 days for sequencing may therefore need to be increased.

Once DD methods are validated, the Global Polio Laboratory Network (GPLN) will establish timeliness targets for each of the new steps: ribonucleic acid (RNA) extraction, ITD (for DD-ITD), and sequencing.