Global Polio Laboratory Network

Guidance Paper 7

Evaluation and Adoption of New Polio Diagnostic Methods and Procedures

Document version (date)	Description of substantive revisions
Version 1 (May 2021)	
Version 2 (May 2023)	The rationale for a revised version is (i) to provide clarity on some criteria, and (ii) to expand criteria's narrative for more specificity.

Evaluation and Adoption of New Polio Diagnostic Methods and Procedures by the *GPLN's Small Working Group on development and evaluation of new methodologies, diagnostic reagents and approaches to testing*

The Global Polio Laboratory Network (GPLN), is a laboratory network of 145 laboratories spanning all WHO regions with the purpose to detect and identify polioviruses in human specimens or environmental samples, while complying with poliovirus containment requirements, in support of the Global Polio Eradication Initiative (GPEI). The success of the GPLN in providing consistent and robust results for the GPEI has been achieved through broad validation and standardization of methods and procedures. The GPLN has provided programmatic support structures at global and regional level; laboratory capacity building, both human and material; training and technical assistance; logistic networks; quality assurance, quality control and safety protocols; and annual accreditation. The laboratories within the GPLN are accredited by WHO, on a yearly basis, to perform the methods and report the results as described in the Polio Laboratory Manual. The other key to sustaining the quality of the results over more than three decades has been the continual evolution of methods using new technologies that are broadly applicable and assuring their successful adaptation in all GPLN laboratories.

The GPLN *ad hoc* Small Working Group on development and evaluation of new methodologies, diagnostic reagents and approaches to testing (aka GPLN SWG) is the guiding group for poliovirus diagnostics within the GPLN. It consists of GPLN stakeholders with extensive knowledge of laboratory procedures and processes within the laboratory network of each WHO region. The SWG leverages the experience and knowledge of each region to plan and implement technical and operational improvements, review QA/QC parameters, and respond to issues facing the GPLN through different stages of polio eradication globally. Within this context, new methods and procedures, along with supporting information, are reviewed and assessed for diagnostic validity, performance and programmatic feasibility and feedback provided for implementation in the GPLN. The SWG may determine a method to be either recommended or accepted, or not recommended or not accepted for use by and within the GPLN.

Changes and updates to recommended methods can be grouped into two categories: minor or major changes. Minor changes are updates to current assays or algorithms (e.g., ITD 4.1 to ITD 5.0) that do not fundamentally change laboratory procedures, reporting, or referral patterns, and have minimal impact on procurement of supplies and reagents. Major changes are anything that has the potential to significantly change the routine procedures and/or processes of the GPLN (e.g., molecular genotyping replacing serotyping) and often represent significant cost and time investments for successful implementation. Although minor changes are carefully weighed, analyzed, and discussed, the potential for disruption is minimal and will not be the focus of this document.

The SWG classifies a method as either **accepted** or **recommended** based on specific criteria. A WHO GPLN **accepted method** fits the criteria listed in BOX 1. To be classified as an **accepted method** the SWG must be satisfied that the results reviewed were reliable and not inferior to current results. Accepted methods are methods from which the results are accepted by GPLN SWG, but the methods will not be endorsed or recommended, indicating that no mandatory support from the GPEI or the GPLN is implied. An accepted method can be utilized in designated laboratories or regions, but due to, cost, complexity, or applicability will not be supported, by the GPEI or the GPLN financially or through provision of consumables, reagents and equipment. Laboratories using accepted methods are responsible for documentation of QA/QC protocols, including proficiency testing, and must meet annual accreditation requirements specified by the SWG. New methods should never increase the risk for employees or the risk of poliovirus release into the environment.

BOX 1: Criteria to accept a New Method in the GPLN

1. Proof of concept

Data from pilot-testing a finalized protocol must show non-inferiority relative to existing recommended poliovirus diagnostic methods (refer to point 3). These data must include quantitative assessment (e.g. Limit of Detection) of the new method.

- The new method should add programmatic value compared to the existing methods.
- To gauge the programmatic value, a detailed concept note must be provided to the SWG stating:
  (i) the background to the development of the method;
  (ii) Specific aspect(s) of the method that add value to poliovirus diagnostics;
  (iii) Advantages over existing methods; and
  (iv) Suitability for implementation in the GPLN. This should include, but not be restricted to, potential challenges to implement the method and availability of real-time mentoring and troubleshooting, while acknowledging the varied levels of competency in the Network.

2. Programmatically relevant data

The new method should provide data that:

(i) Can be analysed by the Laboratory performing the test;
(ii) Can be reported in a standardized format; and
(iii) Is relevant to the national program for action when needed (refer to Guidance paper number 5).

3. Analytical and diagnostic non-inferiority and non-inferiority in parallel testing or testing known reference standard materials

An improvement or non-inferiority compared to current methods must be shown by parallel testing against an existing recommended method in several GPLN laboratories that were selected in consultation with the SWG.

The following criteria must be met for the SWG to accept the results of the parallel testing:

(i) The proposed method is tested in parallel with the recommended method in multiple laboratories with varied and broad experience and resources. An adequate number and variety of samples should be tested to identify issues or changes that may negatively affect or limit the implementation of the method The type of materials to be tested, e.g., stool samples versus RNA and the design of the study, e.g. prospective or fresh samples versus retrospective or stored samples should be clearly stated;
(ii) Establish a comprehensive and decipherable process to identify discordant results arising from the head-to-head comparison with a recommended method. For example, robust statistical analysis of the overall results should be presented in 2 by 2 tables with reference to sensitivity, specificity, positive predictive value, negative predictive value etc., as well as breaking down results by Poliovirus serotype and intra-type;
(iii) Approaches to analyse potential false positives or false negatives should be clearly defined, and additional studies planned to help understand discrepancies;
(iv) All sources of variability, within and between laboratories performing the parallel testing are identified and their impact on the outcomes of the new method evaluated and reported; and
(v) Based on the poliovirus positivity rate, the SWG may define the number and type of samples to be tested during parallel testing to achieve statistical significance.

4. Diagnostic algorithms

Diagnostic algorithms for sample testing, analysis, reporting and referral must be provided for the new method.

(i) A minimum requirement for the diagnostic algorithm(s) should be defined and used for the pilot and parallel testing studies;
(ii) The algorithm used during the pilot-testing of the new method should be compared to the algorithm being used for the recommended method; and
(iii) Both algorithms should be adaptable and the final algorithm for the new method should be implementable.

5. QA/QC procedures

- To ensure reliable and reproducible results, a comprehensive QA/QC procedure for the new method must be submitted to the SWG for approval.
- The QA/QC system should include:
  - (i) Detailed SOPs covering all aspects of testing procedures;
  - (ii) A description of the positive and negative controls;
  - (iii) A comprehensive description of troubleshooting procedures for all possible results;
  - (iv) A sustainable proficiency testing scheme, including details on the provider; and
  - (v) A detailed description of the potential accreditation approaches.

6. Reagent availability

If the accepted method is meant to be disseminated within the GPLN, then criteria in Box 2 point 1 should apply.

7. Training

If the accepted method is meant to be disseminated within the GPLN, all materials and protocols then used to train the personnel to perform the new method should be compared to items used for training to perform the recommended methods.

A WHO-GPLN **recommended method,** as described in the WHO Polio Laboratory Manual, fits all the criteria for an "accepted method" (listed in BOX 1) and must meet the additional requirements specified in BOX 2.

BOX 2: Additional Criteria for a new method to be Recommended

1. **Global reagents/equipment availability and logistics**
   - (i) Reagents, consumables and necessary equipment are globally available, with at least two independent suppliers.
   - (ii) Alternative reagents (e.g., enzymes, NA extraction kits) and equipment should be continuously tested, validated and reported to the GPLN-SWG; and
   - **(iii)** Streamlined procurement should be possible through the WHO system.
2. **Algorithm**
   - (i) The diagnostic algorithms for sample testing, analysis, and/or referral are provided and will work broadly within the GPLN; and
   - (ii) The introduction of a new/adapted algorithm should not disrupt work practices recommended by the GPLN.
3. **Workflow**
   - (i) The work can be performed by currently available GPLN personnel and/or sustainable support for recruitment of staffing needs are identified; and
   - (ii) The potential disruptions of the routine workflow introduced by the new algorithm are identified and contingency planning for adequate corrective action is proposed.
4. **Cost-benefit analysis**
   - (i) A cost-benefit analysis (e.g. burden of laboratory time/capability/expertise of personnel/resources needs) has been performed and is in favor of the new method; and
   - (ii) Mid and long-term resource needs of the new method are identified, quantitated and evaluated.
5. **Training**
   - (i) A Plan for training of GPLN trainers is available and endorsed by the SWG; and
   - (ii) A training curriculum and standard materials and protocols are available to the GPLN.

6. Implementation

(i) A Pilot testing within representative GPLN laboratories has been performed, including assessment of implementation requirements, and results are approved by the GPLN SWG.

(ii) An implementation plan is prepared, with defined timelines, training workshops, budget and monitoring/evaluation mechanisms.

7. Quality assurance program

A comprehensive quality assurance program managed by the GPLN, including a quality control plan, process evaluation and monitoring, supply of reagents and procedures (proficiency testing, accreditation checklist), is available and feasible.

8. Support

(i) Financial support for implementation of the new recommended method is, or can be, secured/provided.

(ii) At least one Global Specialized Laboratory (GSL) is committed to continuous monitoring, evaluation, further development/adaptation of the method and provision of corrective actions as needed. A commitment by the GSL is to be formally secured, including through an accountability framework.

Most of the additional criteria for a new method to become a recommended method is summarized in Table 1 and does concern the diagnostic quality of the method. The diagnostic quality should be based on non-inferiority relative to the existing recommended method. The additional criteria aim at managing worldwide implementation of the new method and sustained performance of the global polio surveillance system.

Last, it is important to reiterate that the overarching goal of this guidance paper is to structure and orient the necessary interactions between (i) the entity aiming to get a new method accepted or recommended by the GPLN and (ii) the GPLN-SWG.

Table 1. Comparison of requirements for new accepted and recommended methods.

	Accepted	Recommended
Proof of concept	X	X
Programmatically relevant data	X	X
Analytical non-inferiority	X	X
Non-inferiority in parallel testing	X	X
QA/QC procedure	X	X
Reagent availability	X	X
Clear compatible algorithm		X
Workflow		X
Cost-benefit analysis		X
Training	X	X
Implementation		X
Quality assurance program		X
Support		X

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