Addendum to TSS-17: Aligning WHO's normative and prequalification process

Please note that this is an interim document intended to support the WHO parallel process. The current TSS-17 document will be revised accordingly once any relevant WHO GTB guidelines have been published. In the case no WHO TB guidelines are issued on this topic the addendum will be removed.

INTERIM DOCUMENT TO SUPPORT THE PARALLEL PROCESS

This addendum to "Technical Specification Series document 17: In vitro diagnostic medical devices used for the qualitative detection of Mycobacterium tuberculosis complex DNA and mutations associated with drug-resistant tuberculosis (TSS-17)" is intended to support manufacturers who are applying to Prequalification (PQ) assessment as part of the parallel, coordinated process of WHO Guideline development and the PQ process. Based on current eligibility principles, the in vitro diagnostics (IVD) submitted for PQ assessment must be recommended for use by WHO disease-specific testing guidelines.

The goal of the parallel process is to accelerate access to quality-assured, safe and effective IVDs by coordinating the development of WHO testing guidelines with the PQ assessment of IVDs.

In this specific case the parallel process will be applied to WHO guidelines on classes of MTBC tests and the PQ assessment of class specific IVDs. As a result, PQ may begin assessing products while the testing guidelines are under development, provided that the IVDs first undergo class determination by the disease program and meet the conditions for evidence assessment by the disease program[1].

The upcoming Guideline Development process, led and coordinated by the WHO Global TB Programme, aims to establish evidence-based recommendations on the use of tongue swabs and sputum swabs that are used with near point-of-care (NPOC) nucleic acid amplification tests (NAATs) and low-complexity automated NAATs (LC-aNAATs) for *Mycobacterium tuberculosis* complex (MTBC) with or without drug resistance detection.

The finalized testing guideline is expected to be published in 2026.

As part of the parallel process described above, the PQ IVD assessment team will begin accepting applications for NPOC-NAATs and LCaNAATs utilizing tongue swab and sputum swab specimens starting from 1 October 2025. Please note that, during this phase of the parallel process, only tongue specimens collected by health care professionals (not self-collected) will be accepted as the intended-use specimens.

Manufacturers are required to comply with TSS-17 [2] while also considering the following additional requirements and concepts. The current TSS-17 document will be revised to incorporate these new criteria only after a new WHO GTB guideline that describes use of swabs for TB NAAT testing is published.

[1] Public call for data to inform WHO policy updates on new TB diagnostic samples, tests, and testing strategies.
[2] https://iris.who.int/bitstream/handle/10665/366068/9789240055865-eng.pdf

Note for manufacturers of NPOC Products Using Swab Specimens

For NPOC products with a claim for tongue swabs, it is strongly recommended that the test kit include a swab for collecting tongue specimens.

For all swab-based products (i.e. tongue swabs, sputum swabs), the following applies:

- If the swab is not included in the test kit, the following information about the swab must be provided: manufacturer, product/catalog number, material composition (shaft and tip), dimensions (length, diameter, tip size), swab type (e.g., flocked, foam, polyester), sterilization method, packaging configuration, storage conditions, expiration date).
- If the test kit includes swabs from multiple sources, manufacturers must specify which swab was used in each study.
- If the testing procedure allows storage of the swab-collected specimen in collection/transport media (TM), and the type or volume of TM differs between the analytical and clinical studies, then analytical studies (such as limit of detection (LoD) estimation) must be included in the submission to demonstrate equivalency of the TMs or volumes used.
- The same requirement applies when different swab types are used.

Please review the following information alongside TSS-17. The numbering corresponds to the Table of Requirements (pp. 8-26), Parts 1 & 2.
For all analytical performance studies where TSS-17 requires validation using sputum as the specimen type, please use the claimed specimen type for your product (e.g., tongue swabs, sputum swabs) if sputum is not among the claimed specimen types.

1.4. Precision

1.4.1 Repeatability and reproducibility

Note 12: If the use of sputum swabs or tongue swabs is claimed, the complete testing procedure shall be replicated, including the use of the intended swab type. A defined volume of the specimen shall be applied to the swab in one of the following ways:
a) directly onto the swab, or
b) by placing the swab into a vial containing the specimen and allowing it to absorb the specimen for a specified duration.

The chosen method must be clearly justified, and any variable parameters—such as the volume of specimen applied to the swab (in method a), or the duration of swab immersion (in method b)—must be specified and supported by an appropriate rationale.

Please note that the same principle applies to sections 1.5.1. & 1.5.2.

INTERIM DOCUMENT TO SUPPORT THE PARALLEL PROCESS

1.5. Analytical sensitivity

1.5.1 Limit of Detection for MTBC

1.5.2 Limit of detection for resistance

Please refer to the guidance provided in section 1.4.1 regarding replication of the full testing procedure, including swab application methods and justification of variable parameters.

1.6. Analytical specificity

1.6.1 Potentially interfering substances

These additional endogenous and exogenous substances relevant to tongue swab specimens shall be considered for inclusion in interference testing for IVDs claiming use with this specimen type.

1.6.1.1 Endogenous

- Saliva components

1.6.1.2 Exogenous

- Toothpaste
- Mouthwash
- Throat lozenges
- Cough syrup
- Food and beverages

1.6.2 Cross-reactivity

- Additional risk-based consideration of oral and tongue flora.

1.9. Usability/human factors

1.9.1 Flex studies

These assess the effect of minor, deliberate variations in test parameters on performance, helping define acceptable operating ranges.

- Evaluate the impact of different swab brands or lots on assay performance
- Evaluate the impact of variations in specimen volume and swabbing technique (e.g., saturation time, applied pressure)
- Evaluate the impact of minor changes in the composition or volume of transport media, if relevant.

2.1 Clinical sensitivity and specificity

2.1.1 General requirements for sensitivity and specificity studies

Note 11: Sputum and sputum swabs are regarded as separate specimen types in the context of the clinical study. Therefore, reference testing must be conducted using sputum specimens, not sputum swabs.

INTERIM DOCUMENT TO SUPPORT THE PARALLEL PROCESS