World Health Organization

The assessment process for listing of Performance Evaluation Laboratories in connection with WHO prequalification of in vitro diagnostics

Information for candidate laboratories

Prequalification Unit
In Vitro Diagnostics Assessment Team

The assessment process for listing of performance evaluation laboratories in connection with WHO prequalification of in vitro diagnostics: information for candidate laboratories

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1. Introduction

1.1 Prequalification if in vitro diagnostics

The World Health Organization's (WHO) prequalification of in vitro diagnostics (IVDs) programme is coordinated through WHO's Regulation and Prequalification Department. WHO prequalification of IVDs is a comprehensive assessment of the safety, quality and performance of individual, commercially available IVDs through a standardized procedure[1] aimed at determining whether a product meets WHO's prequalification requirements. The purpose of the WHO prequalification assessment for IVDs[2] is to provide guidance to interested WHO Member States, United Nations agencies and other international organizations in their procurement decisions. Focus is placed on IVDs for priority diseases and their suitability for use in resource-limited settings.

Two types of prequalification assessment (i.e., full prequalification assessment and abridged prequalification assessment) can take place, depending on the regulatory version submitted and evidence from a previous stringent review by a Recognized Stringent Regulatory Authority[3]. WHO will determine the appropriate type of prequalification assessment at the time of its review of the pre-submission form.

The full prequalification assessment process consists of the following components:

- review of a full product dossier
- performance evaluation, including operational characteristics
- manufacturing site(s) inspection
- labelling review.

The abridged prequalification assessment consists of the following components:

- review of an abridged product dossier
- performance evaluation, including operational characteristics
- manufacturing site(s) inspection
- labelling review.

1.2 Performance evaluation for prequalification assessment

The performance evaluation component mentioned above is essential for the independent verification of the performance and operational characteristics of IVDs submitted for WHO prequalification assessment. As part of the performance evaluation, the IVD product is evaluated against pre-determined acceptance criteria established by WHO. More information on performance evaluations for WHO prequalification assessment can be found through this link[4].

The performance evaluation of an IVD submitted for WHO prequalification assessment is conducted, in accordance with standardized WHO performance evaluation protocols, by one or more laboratories that have been designated by WHO for conducting performance evaluation for one or several types of IVDs

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[1] Please refer to the *Overview of the WHO Prequalification of In Vitro Diagnostic Assessment* document (available at https://extranet.who.int/prequal/sites/default/files/document_files/21-01-27-Overview-DX-Prequalification-Requirements-PQDx_007-v9.pdf), and to the documents referenced therein and/or relating thereto.

[2] Prequalification does not imply any approval by WHO of the product and manufacturing site(s), as this responsibility lies with the national regulatory authorities. Moreover, prequalification does not constitute any endorsement or warranty by WHO of the fitness of any product for a particular purpose, including its safety, quality or performance.

[3] For more information about what constitutes a "Recognized SRA", please refer to document PQDx_173 "Abridged prequalification assessment"

[4] https://extranet.who.int/prequal/vitro-diagnostics/performance-evaluation

(each such designated laboratories is hereinafter referred to as a "Performance Evaluation Laboratory" or "PEL")[5].

The manufacturer of the IVD submitted for WHO prequalification assessment must choose one of the following two performance evaluation options, and must indicate its choice in the pre-submission form:

- **Option 1:** Performance evaluation is commissioned by WHO and carried out by an evaluating site (including a PEL) listed by WHO; or
- **Option 2:** Performance evaluation is commissioned by the manufacturer and carried out by a PEL listed by WHO.

Candidate laboratories wishing to become a PEL may apply to List 1 for evaluations commissioned by WHO (option 1), to List 2 for evaluations commissions by manufacturers (option 2), or to both.

1.3 Assessment of candidate laboratories

A formal mechanism to assess whether candidate laboratories are suitable to become PELs has been developed and is implemented by WHO.

WHO's assessment process of candidate laboratories wishing to be listed as a Performance Evaluation Laboratories consists of the following:

- receipt by WHO of a complete Expression of Interest (EOI) from the candidate laboratory;
- the candidate laboratory's due completion, signature and return to WHO of the "Terms of Reference for Performance Evaluation Laboratories" together with all of its Annexes;
- stage 1 audit: Review by WHO of the candidate laboratory's EOI and specific quality management system (QMS) documentation;
- stage 2 audit: On-site (or remote, under special circumstances) audit by WHO of the candidate laboratory to assess its compliance with WHO requirements and with internationally recognized standards;
- if applicable, submission and implementation by the candidate laboratory to WHO, and WHO's review of, a Corrective Action Plan (CAP) to address any non-conformances raised by WHO during the abovementioned Stage 2 audit.

WHO requirements for candidate laboratories are based on the principles laid out in international standards and guidelines referenced in this document and other aspects relevant to prequalification. The various stages of the assessment aim at verifying the candidate laboratory's compliance with these requirements.

If WHO determines that the candidate laboratory successfully meets WHO's requirements and international standards that are relevant/necessary to act as a PEL, then the candidate laboratory will be listed by WHO as a Performance Evaluation Laboratory.

2 Scope and intended audience

This document has been prepared to provide candidate laboratories with an overview of the process used by WHO to assess whether candidate laboratories having submitted an EOI are suitable to be listed as Performance Evaluation Laboratories to conduct performance evaluations of in vitro diagnostics (IVDs) for WHO prequalification purposes.

Candidate laboratories wishing to apply to be listed as a Performance Evaluation Laboratory should fully and carefully read this document before submitting their EOI, so that they can be aware of and prepared

[5] In exceptional cases, where no PELs are designated for a specific analyte, WHO may outsource the performance evaluation to other designated laboratories.

for all stages of the assessment. In addition, candidate laboratories are strongly encouraged to read the information about performance evaluations for WHO prequalification assessment that can be found on this link[6], the "Terms of Reference for Performance Evaluation Laboratories" set out in Annex 1 (as well as its Annexes) to understand the expected role as PEL, and the *Overview of the WHO Prequalification of In Vitro Diagnostic Assessment* document cited above for further information about WHO's prequalification assessment programme.

3 Definitions and abbreviations

3.1 Definitions

Audit	Systematic, independent and documented process for obtaining audit evidence and evaluating it objectively to determine the extent to which the audit criteria are fulfilled. [reference 1 definition 3.9.1]
Auditor	Person with the demonstrated personal attributes and competence to conduct an audit. [reference 1 definition 3.9.9]
Audit findings:	Results of the evaluation of the collected audit evidence against audit criteria. NOTE: Audit findings can indicate either conformity or nonconformity with audit criteria or opportunities for improvement. [reference 1 definition 3.9.5]
Audit plan	Description of the activities and arrangements for an audit**.** [reference 1 definition 3.9.12]
Audit scope	Extent and boundaries of an audit NOTE: The audit scope generally includes a description of the physical locations, organizational units, activities and processes, as well as the time period covered. [reference 1 definition 3.9.14]
Audit team	One or more auditors conducting an audit, supported if needed by technical experts**.** [reference 1 definition 3.9.10]
Competence	Demonstrated personal attributes and demonstrated ability to apply knowledge and skills. [reference 1 definition 3.1.6]
Corrective Action	Action to eliminate the cause of a detected nonconformity or other undesirable situation [reference 1 definition 3.6.5]
Desktop review	An audit technique used under circumstances of low risk or low residual risk, for example, where an extension of range is required to an existing method and equipment, or a new test method is requested using an existing measurement platform.
Evidence	Records, statements of fact or other information, which are relevant to the audit criteria and verifiable. [reference 1 definition 3.9.4]
Extraordinary event or circumstance	A circumstance beyond the control of the laboratory, commonly referred to as "Force Majeure" or "act of God". Examples are war, strike, riot, political instability, geopolitical tension, terrorism, crime, pandemic, flooding, earthquake, malicious computer hacking, other natural or man-made disasters. [IAF ID 3:2011]
Nonconformity	Non-fulfilment of a requirement. [reference 1 definition 3.6.2]

[6] https://extranet.who.int/prequal/vitro-diagnostics/performance-evaluation

Major nonconformity	Non-fulfilment of a requirement that compromises results, or a re-occurrence of a previously raised minor nonconformity or a non-fulfilment of any regulatory requirement.
Minor nonconformity	Non-conformance against those observations that indicate that although the organization has failed to conform to the prescribed requirements, the failure has no immediate or imminent effect on results.
Observation	Remark made that is directed towards continual improvement of the Quality Management System.
Performance evaluation	Performance evaluation including evaluation of operational characteristics of a product for the purpose of the prequalification assessment process.
Quality management system	Management system to direct and control an organization with regard to quality. [reference 1 definition 3.2.3]
Remote audit	Audit of the physical location or virtual site of a conformity audit body, using electronic means. Note: A virtual site is an online environment allowing persons to execute processes, e.g. in a cloud environment. [ISO/IEC 17011:2017]
Technical expert	Person who provides specific knowledge or expertise to the audit team**.** [reference 1 definition 3.9.11]
Performance Evaluation Laboratories	Laboratories that have successfully undergone the assessment process described in this document and which are listed by WHO to undertake, in accordance with standardized WHO performance evaluation protocols, performance evaluations of in vitro diagnostics submitted for WHO prequalification assessment.

3.2 Abbreviations

CAP	Corrective action plan
EOI	Expression of interest
IEC	International Electrotechnical Commission
ISO	International Organization for Standardization
IVD	In vitro diagnostic
PEL	Performance Evaluation Laboratory
QMS	Quality management system
TOR	Terms of Reference
WHO	World Health Organization

4 The assessment process

WHO requirements for listing of PELs are specifically related to performance evaluations for WHO prequalification of IVDs. The assessment of candidate laboratories will evaluate their ability to undertake performance evaluations of IVDs according to the relevant standardized protocol, as well as the laboratory's compliance with the principles of ISO/IEC 17025:2017 [4] and ISO 15189:2022 [5, 6]. Additional references relating to good practice for laboratories performing IVD evaluations, including other relevant ISO standards, will be utilized during the audit. The auditing process is based on the principles outlined in ISO 19011:2018 [7]. The assessment process will follow the guiding principles set out in Ammex 2.

4.1 Expression of Interest

The candidate laboratory must complete an EOI and provide WHO with all requested supporting documentation, as described in document *PQDx_250 Expression of Interest Submission Form for Performance Evaluation Laboratories*[7]. The documentation must be provided in English.

In addition to general information about the laboratory and the laboratory's QMS, the laboratory will be required to specify the analyte(s) for which it is applying and to provide specific information about this or these analyte(s).

The laboratory will also be required to specify whether it is applying for List 1 (i.e. evaluations commissioned by WHO; option 1 above), List 2 (i.e. evaluations commissioned by the manufacturer; option 2 above) or both. Laboratories are encouraged to apply for List 1 initially, in order to gain experience in conducting performance evaluations commissioned by WHO in connection with a prequalification assessment, before expanding to List 2. The assessment process is similar for List 1 and List 2.

4.2 Signature of the Terms of Reference and associated contractual documents

Upon reception of the EOI, WHO will provide the candidate laboratory with a copy of the Terms of Reference for Performance Evaluation Laboratories (hereinafter, the "Terms of Reference" or "TORs") which are set out in Annex 1 hereto, together with the annex(es) thereto, which contain terms and conditions: (i) applicable to the assessment process for candidate laboratories wishing to be listed as a PEL, and (ii) applicable to laboratory and its work, should the laboratory be listed as a PEL.

In order for the assessment process to proceed in respect of a candidate laboratory wishing to be listed as a PEL, the candidate laboratory must first return to WHO duly completed, signed and dated originals of the Terms of Reference and the contractual documents associated therewith, namely the Confidentiality Undertaking (Annex 1 to the TORs) and, if applicable, a Material Transfer Agreement. For the avoidance of doubt, the assessment process in respect of a candidate laboratory will not proceed unless and until WHO has received the Terms of Reference and other contractual documents associated therewith, duly completed, signed and dated by the candidate laboratory.

4.3 Screening of the Expression of Interest

After WHO has received from the candidate laboratory its EOI, as well as its completed, signed and dated TORs and contractual documents associated therewith, WHO will screen the EOI submission for completeness. If the application is incomplete, the candidate laboratory will be requested to provide supplemental information to complete the application within a specified deadline, to be established by

[7] The EOI form can be found using the following link:
https://extranet.who.int/prequal/sites/default/files/document_files/220414_PQDx_250_v2.0_EOI_Submission_Form.docx

WHO. The laboratory will be given one opportunity to provide the missing information or documentation within the specified deadline. In the event of non-compliance, the application will be rejected on grounds of incompleteness.

EOIs that are considered complete following screening will advance to Stage 1 Audit, as described in section 4.4 below. WHO will inform the candidate laboratory in writing about the outcome of the EOI screening.

WHO reserves the right to reject applications if the number of existing PELs for the relevant analyte(s) and/or in the relevant region is considered sufficient by WHO. The analyte(s) for which Expressions of Interest are sought are specified on the following website:

https://extranet.who.int/prequal/vitro-diagnostics/performance-evaluation-laboratories

4.4 Stage 1 Audit: Desktop review of the information provided with the EOI

For the Stage 1 audit, WHO will review the EOI submission form and attachments to establish the laboratory's ability to comply with applicable WHO requirements.

The Stage 1 audit is a desktop audit. During this audit, WHO will review general information about the laboratory's QMS documentation, including the quality manual, relevant standard operating procedures for the specific validated/verified methodology(ies), relevant validation/verification reports and proficiency testing evaluation reports of the specific method(s), organogram, and floor plan. WHO will also review the ability of the candidate laboratories to conduct the performance evaluation(s) as described in the relevant performance evaluation protocol, including access to specimens.

Any deficiencies in the documentation submitted that are identified in the desktop review will be communicated to the candidate laboratory in writing. The laboratory will be given one opportunity to provide clarification or additional documentation within the deadline specified by WHO. In the event of non-compliance, the application will be cancelled. In certain cases, WHO may agree, in its sole discretion, to permit the candidate laboratory to provide further clarification or information during the Stage 2 audit.

A letter describing the outcome of the Stage 1 audit will be sent by WHO to the laboratory. A satisfactory outcome of the Stage 1 audit is a pre-condition for the candidate laboratory and its application to proceed to a Stage 2 audit. Any applications from candidate laboratories which have not successfully passed the Stage 1 audit: (a) will not undergo any further reviews and (b) will be cancelled by WHO.

4.5 Stage 2 Audit: On-site audit of the laboratory

The Stage 2 audit is the on-site audit to verify the candidate laboratory's effective implementation of an effective QMS and to confirm the ability of the laboratory to conduct performance evaluations of specific types of IVD(s). The specific objectives of the Stage 2 audit are:

- to verify the information supporting the claims presented in the candidate laboratory's EOI submission and other Stage 1 audit documentation;
- to determine the effectiveness of the implemented QMS in meeting appropriate quality standards and the laboratory's own requirements.

In connection with the Stage 2 audit (whether on-site or remote; see below), the candidate laboratory will provide WHO with full access to the following:

- all organizational units, activities and processes of the laboratory associated with specified IVD performance evaluations;
- all information, documents, and records from all levels of the laboratory's QMS, for sampling and review;
- the laboratory's personnel at all levels, for the purposes of conducting interviews and discussions with persons selected by the auditor. Such interviews and discussions will form part of the audit process.

Due to extraordinary events or circumstances such as those leading to very limited international travel, WHO may determine that an on-site audit is not possible, and in such cases resort to remote audit. WHO will inform the candidate laboratory in writing whenever the use of remote audits replaces a scheduled on-site audit.

4.5.1 Roles and responsibilities during a Stage 2 Audit

4.5.1.1 Responsibilities of WHO

WHO is responsible for the following activities associated with the Stage 2 audit.

- Provide the laboratory with the auditors' *curriculum vitae* and afford the laboratory to review and object to any particular auditors on the grounds of conflict of interest.
- Request all auditors to complete all relevant confidentiality and conflict of interest documentation.
- Plan and prepare the audit.
- Define the scope of the audit.
- Prepare and submit the audit plan, working documents, and briefing documents to the audit team and laboratory's contact person.
- Supervise the travel arrangements for the auditors.
- Communicate any challenges regarding the audit to the laboratory's management prior to or during the audit.
- Prepare and present the draft audit report to the laboratory's management at the closing meeting on the final day of the audit.
- Submit the final Stage 2 audit report to the laboratory.
- Follow-up on nonconformities with a request for a detailed corrective action plan (CAP) from the laboratory.
- Communicate the outcome of the Stage 2 audit to the laboratory.

4.5.1.2 Responsibilities of the laboratory

Responsibilities of the laboratory will be communicated to the laboratory prior to the audit. In general, the laboratory's responsibilities in connection with a Stage 2 audit include:

- confirm audit dates;
- provide an official invitation letter to all the members of the audit team to facilitate applications for visas;
- inform WHO in writing of any major changes to the QMS since the Stage 1 audit was performed and provide WHO with the current version of the QMS at least one week prior to the Stage 2 audit;
- inform WHO, in writing and before the audit, if the laboratory's documentation is not in English and arrange for the translation of such documentation and/or the presence of a translator, if and as requested by WHO;
- submit to WHO in writing the current Quality Manual, if it was revised since the Stage 1 audit;
- inform WHO in writing of any issues that may affect an effective and efficient audit process;
- fully cooperate with the auditors to ensure an effective and efficient audit process that achieves the audit objectives;
- identify and communicate to WHO in writing the name and contact details of a contact person responsible for coordinating and facilitating the audit process on behalf of the laboratory;
- inform relevant employees and other personnel about the objectives and the scope of the

audit, and ensure that the laboratory's employees and personnel fully cooperate with WHO to ensure an effective and efficient audit process;

- appoint employees or personnel of the laboratory responsible to accompany members of the audit team;
- ensure that auditors are aware of health, safety and other applicable requirements;
- provide on-site resources for the audit team (such as meeting rooms for the opening and closing meeting and a meeting space for auditors to meet privately during the audit), to ensure an effective and efficient audit process; and
- provide WHO with full access to the laboratory's employees, personnel, facilities, documents, records, and other evidence as requested by the auditors in a timely manner to ensure an effective and efficient audit process that also meets the audit timetable.

4.5.1.3 WHO audit team

The WHO audit team will have experience and knowledge in laboratory QMS, performance evaluations and the specific IVDs. Normally an audit team will consist of two members, including a WHO staff member and an external auditor appointed by WHO.

Prior to the site audit, WHO will inform the laboratory of the identity of the proposed audit team members and will provide the laboratory such team member's *curriculum vitae*, with an aim to ensure that there are no conflicts of interest that may compromise the audit. For a period of one week following the date on which WHO informs the laboratory of the audit team's composition, the laboratory will have the opportunity to express to WHO, in writing, concerns regarding any of the auditors prior to the site audit. If the laboratory communicates to WHO, in writing, any such concerns within the abovementioned one-week period, then WHO and the laboratory will make good faith efforts to resolve such concerns in a mutually acceptable manner. If the laboratory does not communicate to WHO, in writing, any such concerns within the abovementioned one-week period, then the audit will proceed with the proposed audit team composition.

All members of the audit team are obliged to act according to the requirements of the WHO International Civil Service Commission "Standards of Conduct for the International Civil Service" [8]. In addition, WHO will request all members of the audit team to complete a Declaration of Interests and sign, and comply with, a Confidentiality Undertaking.

4.5.2 Logistics for the audit

4.5.2.1 Dates and time allocated for the audit

The dates and time allocated for the audit are to be agreed upon by the audit team and laboratory.

It is the responsibility of the laboratory to ensure that during the audit, the laboratory is performing routine testing for the relevant analyte(s) and the key personnel for the QMS and laboratory activities are present.

WHO will provide the laboratory with the audit plan at least one week before the audit, which will include details of the audit to be conducted using information from the submitted documentation on the QMS, including the quality manual. The audit plan is intended as a guide only and will be flexible to permit changes in emphasis based on information gathered during the audit.

The audit plan (see example in Annex 3) will include:

- the audit's scope and purpose
- identification of audit team members
- date and place of audit
- expected time and duration of each audit activity, including meetings to be held with the laboratory's management team.

4.5.2.2 Language for the on-site audit

The audit will be conducted in English. Translation needs will be discussed with the laboratory as required. In the event that translation is needed, then the laboratory will be responsible for arranging for such translation, and the laboratory will be responsible for covering all costs associated with such translation.

4.5.2.3 Travel and accommodation arrangements

WHO is responsible for the travel and accommodation arrangements of the audit team and all associated costs with the audit team. However, the laboratory will generally be asked to provide advice for these arrangements. Upon WHO's request, the laboratory will promptly provide an official invitation letter to all members of the audit team to facilitate applications for visas, if applicable.

4.5.2.4 Prerequisite requirements for remote audits, if applicable

In case an on-site audit is not possible and WHO decides to replace such an on-site audit with a remote audit, the laboratory shall ensure that the following requirements are in place in order to carry out such remote audit:

- access to internet through a fast, reliable internet connection (e.g. Fibre or 4G/5G);
- a contingency plan for internet connection during the audit in case of failure of the main access to internet;
- suitable video conferencing or communication software (e.g., MS Teams, Zoom, Skype, etc.), and associated computer network to enable communication with the laboratory as necessary, including opening and closing meetings, as well a live on-line video witnessing (not pre-recorded) of the activities that need to be witnessed as part of the audit;
- a secured and structured system for sharing documentation (e.g. Dropbox or similar); and
- the audit team members must have access to the laboratory contact person at all times, and the rest of the laboratory's staff must be available, as and when needed by WHO, for interview purposes.

In addition to the requirements listed above, the laboratory must prepare a short video clip (not longer than 10 minutes) or a live video tour showing the laboratory, the layout of equipment, air-conditioning, lighting, benches or other workspaces, windows, the receipt of samples, equipment or samples for testing.

In addition to the remote audit, follow-up on-site audit(s) may be conducted by WHO, as and when WHO deems it necessary and appropriate to do so.

4.5.3 Meetings during the audit

4.5.3.1 Opening meeting

The opening meeting of the audit (approximately 1 hour 15 total) is held to exchange information between the audit team and the laboratory's team on the audit process, and to confirm the audit scope, objectives, and plan as well as the availability of the laboratory's responsible persons on-site.

Audit team (45 minutes approximately)

The audit team will:

- introduce the audit team;
- explain the functions and responsibilities of the WHO audit team;
- make sure that the Attendance Register is completed;
- present the WHO Prequalification programme and the performance evaluation for the analyte(s) in scope;
- explain the purpose, and objectives of audit;

- confirm the audit plan including:
    - the areas/activities of facility to be covered
    - requirement for access to selected documents, records, reports
    - working hours and break times;
- introduce the methods to be used for the auditing and classification of findings;
- establish official communications links between the laboratory and the audit team;
- allow the laboratory personnel to ask clarifying questions regarding the process;
- allow the audit team to seek clarifications from and about the laboratory.

Laboratory (30 minutes approximately)

The laboratory will:

- introduce key staff members;
- provide an organigram (with photographs if possible) and a written list with contact details for key personnel during the audit process;
- provide a brief overview of the QMS;
- provide a brief overview of the laboratory particularly for the testing of the IVDs to be evaluated;
- inform the audit team of any changes since the submission of information about the laboratory to WHO;
- provide an activity schedule including shifts (if applicable) for the audit days;
- organize a tour of the laboratory;
- provide an overview of the safety regulations.

4.5.3.2 Meeting of auditors

The audit team will meet as necessary throughout the audit, with the following meetings to take place as a minimum:

- discussion of findings: during the course of the audit, the audit team will confer regularly and informally regarding the progress of the audit;
- daily summary: At the conclusion of each day (or at the beginning of the following day) of the audit, the audit team will present a brief summary of the day's activities and findings;
- audit summary: At the conclusion of the audit process on the last day of the audit, the audit team will meet to discuss their findings in detail;
- preparation of on-site draft audit report: the auditors will then assist the lead auditor in summarizing any nonconformities found at the audit.

4.5.3.3 Daily wrap-up meeting

The laboratory staff may be invited to discuss the outcomes and any issues of concern (potential nonconformities) identified during the audit, at the end of every audit day. This meeting allows the laboratory to discuss/clarify any issues of concern. If the laboratory contests a nonconformity, the laboratory must promptly provide WHO, in writing, a rationale therefor, including supporting evidence.

4.5.3.4 Closing meeting

The audit team and laboratory management may meet prior to the closing meeting, if required. The closing meeting concludes the audit and will be held in the presence of the audit team and the management team of the laboratory. Other staff members of the laboratory may be invited by the management, as appropriate.

The outcome of the audit (including areas covered and not covered, and limitations to the audit) will be presented during the closing meeting. The audit team will summarise the findings and issues of concern in the order of significance and present the list of nonconformities that will be rated for severity

in a format of a draft audit report.

A CAP in the form of an Excel spreadsheet will be presented by the audit team. The laboratory must use such CAP form to start the process of correcting the findings raised.

4.5.4 Records and documentation to be submitted

For on-site audits, the list of records/documents required to be submitted by the laboratory will be provided by the audit team at the beginning of the audit. The laboratory must provide the audit team with complete and correct copies of all records/documents identified in such list during the audit.

For remote audits, the audit team will provide the laboratory with a list of records/documents required to be submitted by the laboratory at least two weeks before the remote audit. The laboratory must submit electronically (into Dropbox or similar) complete and correct copies of all records/documents identified in such list at least one week prior to the start of the remote audit. In the event that English is not the language in which the records/documents are available, the audit team will provide the list of required records/documents three weeks before the audit and the laboratory must electronically submit complete and correct copies of the requested records/documents (in the original language, preferably in Word format) at least two weeks prior to the start of the remote audit.

Failure to submit the required records/documents within the required time period may result in the postponement of the remote audit. For on-site audits, failure to submit the required records/documents during the audit will be considered as a non-conformity.

4.5.5 Issuance of the final report of the on-site audit

The final audit report will be issued by WHO within 60 days of the conclusion of the on-site visit or remote audit, as applicable. If an audit report cannot be issued within this time, the laboratory will be notified by WHO about the delay.

4.5.5.1 Content of the reports

The final audit report will describe the main findings, non-conformities and issues of concern identified during the audit and summarize the general outcome of the audit. It will also contain specific information on the nonconformities observed by the auditors during the audit.

4.5.5.2 Reports with no requirements

If the audit team did not find any issues of concern or nonconformities as part of the audit, WHO will notify the laboratory by letter of successful completion of the Stage 2 audit. Such letter should not be considered or construed by the laboratory as an indication that the laboratory will be included in WHO's list of PELs.

For the avoidance of doubt, in the event that WHO determines to include the laboratory in WHO's list of PELs, then WHO will provide the laboratory with a separate notification letter to that effect.

4.5.5.3 Reports with requirements (relating to nonconformities)

The final audit report will include a description of the nonconformities found during the audit, their severity, the findings that contributed to each such nonconformity, and the relevant internal QMS document or specific requirement in the standard (individual clause or subclause). The severity of nonconformities will be classified into major findings, minor findings or observations.

The laboratory must take all necessary and appropriate actions to address, to WHO's satisfaction, all of the major and minor nonconformities found during the audit, before WHO may be in a position consider including the laboratory in its PEL listing.

4.5.6 Laboratory corrective action plan

A proposed CAP shall be submitted, in writing, by the laboratory to WHO within one month after receipt of the final audit report using the CAP Excel spreadsheet provided by WHO. For each nonconformity identified during the audit, the proposed CAP must include:

- immediate action taken, where applicable
- root cause analysis
- proposed corrective action
- timeline to correct the nonconformity
- person(s) responsible within the laboratory.

The proposed CAP will be reviewed by the audit team for acceptance of, or comments concerning, the proposed corrective action. WHO may request the laboratory to provide, within a specified timeframe, additional documents or information in connection with the proposed CAP; in such event, the laboratory will have a maximum of two opportunities to supply WHO with the necessary documents/information to address nonconformities in a timely manner, usually within one month of WHO's request. In certain cases, however, the nature of some nonconformities may require an extended time period to correct, and WHO may give consideration to justifiable requests for an extension of time to respond. If the laboratory fails to respond timely or adequately to requests for submission of additional or new information relating to nonconformities, the laboratory's application for PEL listing may be terminated by WHO.

Once the CAP has been accepted by WHO, the laboratory must timely provide WHO with all necessary and appropriate documentary evidence of its implementation. The timeline for providing evidence of the corrective action taken will depend on the timeline proposed by the laboratory, and agreed by WHO, as part of the CAP.

4.5.7 Stage 2 audit outcome

Before finalizing the Stage 2 audit, all nonconformities must have been appropriately addressed and corrected by the laboratory.

Following WHO review of the initial CAP and associated evidence of implementation, one of the following outcomes may occur:

- If the CAP and evidence of its implementation are acceptable to WHO, WHO will notify the laboratory by letter that the Stage 2 audit and follow-up are complete. Such letter should not be considered or construed by the laboratory as an indication that the laboratory will be included in WHO's list of Performance Evaluation Laboratories. For the avoidance of doubt, in the event that WHO determines to include the laboratory in WHO's list of PELs, then WHO will provide the laboratory with a separate notification letter to that effect.
- If the CAP is acceptable to WHO, but evidence of its implementation cannot be reviewed remotely, a follow-up audit may be scheduled to verify effective implementation within 12 months after the CAP is accepted. The laboratory will have only one opportunity for follow-up audit for verification of implementation of the CAP.
- If the CAP and/or its implementation are not acceptable to WHO (including, but not limited to, because the laboratory is unable to properly address and correct the nonconformities), the laboratory's application may be terminated by WHO depending on the severity and number of the nonconformities.

5 Outcome of the assessment

5.1 Reporting and communication of the results of the assessment

The laboratory will receive a letter from WHO informing it of the outcome of the overall assessment of the laboratory in connection with its application for listing as a PEL.

WHO reserves the right to share the laboratory's EOI and related information with interested governments, national regulatory authorities and other relevant authorities of WHO Member States (all of the foregoing, collectively, "Authorities"), subject to WHO entering into an appropriate confidentiality undertaking with each such Authority.

As WHO is responsible for the prequalification assessment programme as well as for the assessment process for listing of Performance Evaluation Laboratories in connection with WHO Prequalification of In Vitro Diagnostics programme, WHO shall have full and exclusive ownership of any and all findings, outcomes, results and/or reports arising from or relating to the WHO prequalification assessment process and/or the aforementioned assessment process for PEL listing. Thus, WHO shall be entitled to use and publish any such findings, outcomes, results and/or reports in its sole discretion, subject always, however, to the protection of any commercially sensitive confidential information of the manufacturer and/or laboratory, as applicable. Confidential information in this context means:

- confidential intellectual property, know-how, and trade secrets (including, e.g. formulas, processes or information contained or embodied in a product, unpublished aspects of trademarks, patents, etc.); and
- commercial confidences (e.g. structures and development plans of a company).

In addition to and notwithstanding any of the foregoing, WHO reserves the right to use, publish, issue, share with relevant Authorities of WHO Member States, with UN agencies and with other relevant intergovernmental and/or international organizations, and/or make publicly available (in each case, in accordance with the provisions of this document, including provisions regarding the protection of any commercially sensitive information of the manufacturer and/or the laboratory, as applicable) any findings, outcomes, reports, notices and/or results— whether in draft or final form, and whether positive or negative— arising from or relating to the WHO prequalification assessment process and/or WHO's assessment of laboratories in connection with their potential or actual listing as Performance Evaluation Laboratories, and including any confidential information to which WHO may gain access in the course of the aforementioned prequalification process and/or PEL assessment process.

For the avoidance of doubt, the cancellation or withdrawal, at any time and for any reason, of an application for a laboratory to be listed as a PEL will not prejudice or otherwise affect any of WHO's rights described in this Section 5.1. Similarly, the suspension or delisting, at any time and for any reason, of any laboratory as a PEL will not prejudice or otherwise affect any of WHO's rights described in this Section 5.1.

5.2 Successful assessment

If WHO is satisfied that the assessment process is complete with respect to a candidate laboratory wishing to be listed as a PEL, and that such laboratory satisfactorily meets all requirements applicable to PELs, then such laboratory will be included in the WHO list of Performance Evaluation Laboratories.

The list of PELs will be published on the WHO website[8] and will specify the name and address of the laboratory, details of the authorized contact(s), analyte(s) that the laboratory is listed for and whether the laboratory is listed on List 1 and/or List 2.

[8] The list of PELs is available on the following website: https://extranet.who.int/prequal/vitro-diagnostics/prequalified/performance-evaluation-laboratories

The laboratory will receive a letter of listing from WHO informing it of the outcome of the overall assessment. Once a laboratory is listed as a PEL, the laboratory will be responsible for maintaining compliance with its status as a PEL, including but not limited to by (i) complying with the provisions and obligations set forth in the Terms of Reference, Confidentiality Undertaking and, if applicable, Materials Transfer Agreement; and (ii) fulfilling its annual reporting, reporting of changes and re-inspection commitment as described in section 6 below.

The decision to include the laboratory in the list of PELs is made upon information available to WHO at the time of the assessment. This decision is subject to change on the basis of new information that may become available to WHO.

5.3 Cancellation of the application

WHO reserves the right to cancel the laboratory's application at any time or stage of the PEL assessment process if:

- the laboratory's EOI does not contain all of the required information or does not meet WHO requirements; and/or
- the laboratory is not able to, or fails to, provide the required or requested information within the deadlines specified by WHO; and/or
- the laboratory is unable to meet WHO's requirements to be listed as a PEL including, without limitation, evidence of an effective quality management system and/or evidence of the ability to conduct the performance evaluation as per the relevant protocol(s); and/or
- the laboratory is not able to, or fails to, implement any corrective actions which WHO may require within a specified deadline; and/or
- the information supplied is inadequate to complete the assessment in a timely manner.

In case of cancellation of an application, the laboratory will not be allowed to re-apply to become a PEL for a period of time determined by WHO, usually one year from the date of notification of cancellation, unless otherwise agreed by WHO.

5.4 Withdrawal from the assessment

WHO provides the applicant laboratory with the right to withdraw its application to become a PEL at any time or stage. To exercise this right of withdrawal, the applicant must provide WHO with written notice thereof. In this case, the candidate laboratory will not be allowed to re-apply to become a PEL for a period of time determined by WHO, usually one year from date of notification of withdrawal, unless otherwise agreed by WHO.

6 Duration of the validity of listing as a PEL

WHO will reassess laboratories included in the WHO list of PELs at intervals determined by WHO using a risk-based approach. If, as a result of this reassessment, it is found that a laboratory no longer meets WHO requirements, such laboratory will be removed from the list of PELs. Failure of the laboratory to participate in the reassessment procedure will also lead to delisting of the laboratory from the WHO list of PELs.

In addition, WHO reserves the right to delist a laboratory that has been designated as PEL if such laboratory either fails to timely and/or completely deliver the agreed work to WHO; and/or fails to comply with the performance evaluation protocol. In this event, WHO will inform the laboratory and provide a reasonable opportunity during thirty (30) days to cure the relevant failure.

6.1 Annual reporting

Each laboratory listed as a PEL is required to submit to WHO, in writing, an annual report using the template PQDx_381 "*Template Performance Evaluation Laboratory Annual Report*" provided by WHO. The laboratory must include the following information as part of each annual report:

- a summary of the performance evaluations for WHO prequalification assessment conducted by the laboratory during the past 12 months;
- a summary of the laboratory's latest completed internal audit, with corrective actions implemented or in progress;
- a summary of the laboratory's latest annual management review, with corrective actions implemented or in progress, for agenda items relevant to prequalification evaluations;
- summary performance reports of the laboratory's relevant annual external quality assessment/proficiency testing; and
- the laboratory's current certification/accreditation.

For the avoidance of doubt, the laboratory must submit to WHO an annual report each and every year following the year on which such laboratory becomes listed as a PEL, regardless of whether or not the PEL conducted any performance evaluations for WHO prequalification assessment in the preceding year. The laboratory's annual report for the previous calendar year must be submitted to WHO, in writing, no later than 28 February of the following year to which the annual report relates. The information provided as part of the annual report will, among other things, inform WHO's decision regarding the frequency of the re-audits described under Section 6.3 below.

6.2 Submission of changes

Upon providing WHO with prior written notice thereof in accordance with this section, a laboratory that has been listed as a PEL may decide to implement the following changes:

- temporarily or permanently de-list one or several of the analytes that such laboratory is listed for; and/or
- restrict or expand such laboratory's listing to List 1 and/or List 2;

provided that, for the avoidance of doubt, such decision shall take effect as of a date determined by WHO.

The abovementioned changes, as well as any change in contact details of the laboratory and any other change that will or may impact the laboratory's capacity as a PEL (including but not limited to a significant re-organization, loss of accreditation, changes in legal status or entity, changes in the quality management system, etc.) must be reported to WHO using the document PQDx_334 *Change request form for Performance Evaluation Laboratories.* Based on the nature of the change, WHO may decide to conduct a re-audit of the laboratory and/or to suspend and/or withdraw the laboratory's listing as a PEL.

6.3 Re-audits

Re-audits of a laboratory that has been listed as a PEL will be routinely conducted by WHO to verify the laboratory's ongoing compliance with WHO requirements and relevant standards; such re-audits will either be a partial or full audits.

Mandatory re-audits will occur every three to five years after laboratory's initial listing as a PEL, unless an earlier re-audit is deemed necessary by WHO.

Depending on the risk assessed by WHO based on the initial Stage 2 audit and CAP, as well as the laboratory's annual reports, WHO may decide that the re-audit will take place as an on-site or a remote audit.

Re-audits will focus on verifying the laboratory's effective implementation of the CAP and on-going compliance of the quality management systems. The re-audit will also verify that the performance evaluations that have been conducted by the laboratory for WHO's prequalification assessment since the laboratory was listed as a PEL meet WHO requirements and international standards. This will include the review of records of at least one performance evaluation conducted by the laboratory for WHO's prequalification assessment.

For remote audits, the required records/documents for the re-audit will be requested by the auditors at least 2 weeks before the re-audit begins. The laboratory must provide the audit team with complete and correct copies of all records/documents identified in such list at least one week prior to the audit.

As with the initial audit, an audit report will be shared with the laboratory, which will list the nonconformities identified during the re-audit, if applicable.

Depending on the nature and severity of the nonconformities identified during the re-audit, one of the following outcomes may occur, as determined by WHO in its sole discretion:

- the laboratory may be permanently or temporarily removed or suspended from the list of PELs;
- the laboratory may be invited to submit a CAP within one month after receipt of the final audit report and CAP submission, and review of such CAP will be as described in section 4.5.6; or
- if no non-conformities are identified, the laboratory's listing as a PEL will be maintained with no further action.

7 Resolution of Disputes

Any and all claims or disputes arising from or in connection with WHO's assessment of a candidate laboratory to determine whether it can be listed as a PEL—including, but not limited to, any rejection, termination or suspension of an application and/or any decision whether or not to include a laboratory in the list of PELs (hereinafter, collectively, "Disputes") must be submitted by the laboratory, in writing, to WHO's Director of Regulation and Prequalification (RPQ) Department, with a copy to the PQT-IVD Team Lead.

WHO's Director of RPQ, or one of his/her authorized representatives, will acknowledge in writing receipt of the relevant Dispute and will conduct an investigation into the Dispute within 30 days of receipt. Following the investigation, WHO's Director of RPQ, or one of his/her authorized representatives, will provide a written response to the laboratory that submitted the Dispute. If the laboratory is dissatisfied with the written response, then it must object in writing to WHO within 30 days of the date of WHO's aforementioned written response. In the event that the laboratory does not object to WHO in writing within such 30-day period, then the content of WHO's written response (including, without limitation, any findings or decisions contained therein) will be final and can no longer be challenged by the laboratory in any way. However, if the laboratory does object to WHO in writing within such 30-day period, then the Dispute will be referred to WHO's Director-General for his or her decision which will be final and binding on the parties.

8 Privileges and Immunities of WHO

By virtue of WHO's status as a Specialized Agency of the United Nations, WHO, its officials and experts performing missions for WHO (including, e.g. assessors and inspectors) enjoy privileges and immunities under national and international laws and conventions, including without limitation: (i) the Convention on the Privileges and Immunities of the Specialized Agencies, adopted by the General Assembly of the United Nations on 21 November 1947 (the "1947 Convention"), and (ii) the United States' International Organizations Immunities Act of 1945 and Executive Order 9698 relating thereto (collectively, the "IOIA"). Nothing contained in or in connection with this document and/or any assessment process described hereunder will constitute or be deemed as a waiver of any of the privileges or immunities which WHO, its officials and/or experts performing missions for WHO enjoy pursuant to the 1947 Convention, the IOIA or otherwise under any national or international law, convention or agreement, and/or as submitting WHO, its officials and/or experts aforesaid to any national court jurisdiction.

9 References

1 ISO 9000:2015 Quality management systems — Fundamentals and vocabulary. Geneva, Switzerland; 2015. International Organization for Standardization.

2 ISO 18113-1:2022. In vitro diagnostic medical IVDs - Information supplied by the manufacturer (labelling) - Part 1: Terms, definitions and general requirements. Geneva, Switzerland; 2022. International Organization for Standardization.

3 Information and documents on laboratory accreditation can be found on the ILAC (International Laboratory Accreditation Cooperation): www.ilac.org - [website] [Accessed 23 May 2016]

4 ISO/IEC 17025:2017 General requirements for the competence of testing and calibration laboratories; Geneva, Switzerland. 2017. International Organization for Standardization/ International Electrotechnical Commission.

5 ISO 15189:2022 Medical laboratories — Requirements for quality and competence. Geneva, Switzerland; 2022. International Organization for Standardization.

6 ISO/TR 22869:2005 Medical laboratories — Guidance on laboratory implementation of ISO 15189:2003. Geneva, Switzerland; 2005. International Organization for Standardization.

7 ISO 19011:2018 Guidelines for quality and/or environmental management systems auditing. Geneva, Switzerland; 2018. International Organization for Standardization.

8 WHO International Civil Service Commission "Standards of Conduct for the International Civil Service" [webpage] [Accessed 19 May 2016] http://icsc.un.org/resources/pdfs/general/standardsE.pdf

10 Revision history

Version	Date	Summary of changes	Prepared by/ reviewed by
V1.0	23 May 2016	Original version	
V2.0	December 2022	Change WHO Prequalification Evaluating Laboratories to Performance Evaluation Laboratories; Add more detailed introduction including Prequalification of IVD,	AL Page

		Performance evaluation and Assessment; Add abbreviations and definitions; Add more detailed Assessment process; Clarify Outcome of the assessment and Validity of listing as a PEL; Added Resolution of disputes; Added Privileges and immunities of WHO; Added Terms of Reference as Annex 1	
V2.1	9 November 2023	Add ISBN, copyright page and barcodes; Minor editing	AL Page / JF Flandin

11 Annexes

11.1 Annex 1. Terms of Reference

Terms of Reference for Performance Evaluation Laboratories (PELs)

Collaborating with WHO in connection with WHO's Prequalification of IVDs Assessment

Background/Context:

The World Health Organization (WHO) prequalification of in vitro diagnostics (IVDs) assessment programme is coordinated through WHO's Regulation and Prequalification Department. WHO prequalification of IVDs is a comprehensive assessment of the safety, quality and performance of individual, commercially available IVDs through a standardized procedure[9] aimed at determining whether a product meets WHO's prequalification requirements. The goal of the WHO prequalification assessment for IVDs is to provide guidance to interested Member States, United Nations agencies and other international organizations in their procurement decisions. Focus is placed on IVDs for priority diseases and their suitability for use in resource-limited settings.

The full prequalification assessment process includes the following components:

- review of a full product dossier
- performance evaluation, including operational characteristics
- manufacturing site(s) inspection
- labelling review.

An abridged prequalification assessment includes the following components:

- review of an abridged product dossier
- performance evaluation, including operational characteristics
- manufacturing site(s) inspection
- labelling review.

The performance evaluation component mentioned above is essential for the independent verification of the performance and operational characteristics of IVDs submitted for WHO prequalification assessment. Pursuant to Section 8.4.2 of the standardized procedure applicable to the WHO prequalification of IVDs:

- The performance evaluation of an IVD submitted for WHO prequalification assessment is conducted, *inter alia*, by one or more laboratories which are designated by WHO for conducting performance evaluation for one or several types of IVDs submitted for WHO prequalification assessment (each such designated laboratory is hereinafter referred to as "Performance Evaluation Laboratory" or "PEL"). A formal mechanism to assess the suitability of these laboratories has been developed and implemented by WHO; and
- The manufacturer of the relevant IVD submitted for WHO prequalification assessment must choose one of the following two performance evaluation options in its pre-submission form:
    - **Option 1:** Performance evaluation commissioned by WHO and carried out by an evaluating site (including a PEL) listed by WHO; or
    - **Option 2:** Performance evaluation commissioned by the manufacturer and carried out by an evaluating site (including a PEL) listed by WHO.

[9] Please refer to the *Overview of the WHO Prequalification of In Vitro Diagnostic Assessment* document (available at https://extranet.who.int/prequal/sites/default/files/document_files/21-01-27-Overview-DX-Prequalification-Requirements-PQDx_007-v9.pdf), and to the documents referenced therein and/or relating thereto.

Assessment of Candidate Laboratories for Designation as a PEL:

The undersigned laboratory (hereinafter, the "Undersigned") wishes to collaborate with WHO as a Performance Evaluation Laboratory, or PEL. The Undersigned hereby acknowledges that assessment of candidate laboratories for designation as a PEL consists of the following steps[10]:

- receipt of a complete expression of interest (EOI) from the candidate laboratory wishing to be designated as a PEL;
- the Undersigned's signature and return to WHO of fully and duly completed, signed and dated originals of the following documents:
    - these Terms of Reference for Performance Evaluation Laboratories;
    - confidentiality Undertaking (Annex 1 hereto); and
    - *Applicable for IVDs for HIV serology testing:* Materials Transfer Agreement (to be provided by WHO separately, where applicable).
- stage 1 audit: Review by or on behalf of WHO of the candidate laboratory's EOI and specific quality management system (QMS) documentation;
- stage 2 audit: On-site (or remote, under special circumstances) audit by or on behalf of WHO of the candidate laboratory to assess its compliance with internationally recognized standards and its fulfillment of WHO requirements;
- submission by the candidate laboratory of a Corrective Action Plan (CAP) to address any non-conformances raised by WHO during the abovementioned Stage 2 audit;
- review by WHO of the candidate laboratory's Corrective Action Plan (CAP) to non-conformances raised during the Stage 2 audit;
- if WHO determines that the candidate laboratory successfully meets WHO requirements and international standards necessary to act as a PEL, then the candidate laboratory will be listed by WHO as a designated Performance Evaluation Laboratory.

The Undersigned hereby agrees to fully cooperate with WHO in its assessment of the Undersigned as a candidate PEL, and to provide WHO with all relevant documents and information which are necessary for WHO to assess and determine whether the Undersigned can be successfully designated as PEL.

The Undersigned acknowledges and agrees that the Undersigned's signature of these Terms of Reference and/or any other Contractual Documents shall not be construed or interpreted as any promise, commitment or guarantee by WHO: (i) that the Undersigned, once assessed, will be successfully designated as a PEL; and/or (ii) that the Undersigned, once designated as a PEL, will continue to be listed or designated as a PEL (please refer to the provisions below regarding withdrawal/removal of designation as a PEL).

Terms of Reference for PELs:

The Undersigned hereby acknowledges and agrees that, in the event that the Undersigned is successfully designated by WHO as a PEL, then in close coordination with the WHO Prequalification Unit - In Vitro Diagnostics Assessment Team (WHO PQ-IVD), the Undersigned will:

1. Upon request from either WHO PQ-IVD (for option 1 performance evaluations) or the relevant manufacturer (for option 2 performance evaluations), the Undersigned will conduct the performance evaluations for the types of tests for which the Undersigned is designated as a PEL under the following list: https://extranet.who.int/prequal/vitro-diagnostics/prequalified/performance-evaluation-laboratories. For the avoidance of doubt, the

[10] Please refer to *The Assessment Process for Listing of Performance Evaluation Laboratories in connection with WHO Prequalification of In Vitro Diagnostics*)

Undersigned will conduct each performance evaluation subject to and in accordance with: (i) the relevant evaluation protocol provided by WHO; (ii) the provisions of these Terms of Reference, the Confidentiality Undertaking and, if applicable, the Materials Transfer Agreement (collectively, the "Contractual Documents") signed by the Undersigned; and (ii) the budget[11], timeline and other particulars agreed in writing with WHO (under option 1) or with the relevant manufacturer (under option 2);

2. Designate and communicate to WHO the Undersigned's principal investigator (PI) who will be responsible for the Undersigned's conduct of the performance evaluations, from among the contacts listed in the list referenced above (i.e., the PI usually being the first contact);
3. Obtain and maintain in full force and effect any applicable national and/or international licenses, permits, authorizations, accreditations, documentation and/or other recognition which are necessary or required for the Undersigned to perform its activities and obligations as a PEL, including national ethics approval where required;
4. Adhere to and comply with all applicable laws, statutes, rules, regulations and other legal or ethical requirements;
5. Strictly adhere to and comply with the terms and conditions contained in the performance evaluation protocol provided by WHO PQ-IVD and in the Contractual Documents;
6. Communicate with WHO, in a prompt and timely manner, in case of any doubt or question about the protocol, these Terms of Reference or any other Contractual Documents, and/or any issues or difficulties encountered during the conduct of the performance evaluation;
7. Conduct all trainings which are necessary for the Undersigned's employees, consultants and/or contractors to appropriately discharge the Undersigned's activities and obligations as a PEL including, without limitation, the performance evaluations;
8. Ensure availability of all specimens and panels that are necessary for the conduct of the performance evaluations, as defined in the evaluation protocols provided by WHO;
9. Communicate with the manufacturer to facilitate shipment of the kits and/or shipment and installation of equipment needed for the evaluation;
10. Ensure storage of equipment and IVD kits received by or on behalf of the Undersigned for the performance evaluations, in accordance with the storage conditions stated in the product instruction for use;
11. Keep accurate and complete records of the conduct and results of the performance evaluations;
12. Conduct an analysis of the data and results arising from each performance evaluation and prepare draft reports of such analysis and results. For the avoidance of doubt, WHO shall be responsible for: (i) distributing such draft report(s) to the manufacturer in question; and (ii) preparing and distributing the final report(s) of the aforementioned analysis, and the Undersigned agrees to reasonably cooperate with and assist WHO, upon WHO's request, in the preparation of such reports;
13. Ensure that the Undersigned and/or any employees, consultants, contractors or other third parties collaborating with the Undersigned shall not disclose, make available or otherwise transmit to any manufacturers or other parties (except for WHO) any raw data or results arising from or relating to any performance evaluation, except as expressly authorized in the relevant protocol provided by WHO or as WHO may otherwise expressly approve in writing;
14. Share all of the raw data, results and draft reports of each performance evaluation with WHO PQ-IVD (regardless of whether option 1 or option 2 applies), and with the relevant manufacturer (but only if option 2 applies), immediately after completion of the performance evaluation;

[11] The budget shall be based on reasonable, direct, out-of-pocket, not-for-profit costs and expenses of the Undersigned.

15. Respond to questions from WHO PQ-IVD and the relevant manufacturer during review of the draft report;
16. Archive all source data, data analysis records, draft and final reports, correspondence, and other relevant information and materials including, but not limited to, information and materials comprising the "study file" (as defined in the *Guide for PELs*), for a period of 5 years after the final report of each performance evaluation;
17. In accordance with the Confidentiality Undertaking annexed hereto, treat as "confidential" all documents, reports, materials and information about the IVDs under evaluation, as well as all data and information relating thereto, which are provided to or otherwise obtained by the PEL through its participation in the WHO prequalification performance evaluations;
18. In agreement and in collaboration with WHO, participate in the preparation of manuscripts for the publication of the results of the performance evaluation; it being agreed that, with respect to any such manuscripts and publications: (i) they shall be subject always to the protection of any confidential information of WHO and/or third parties collaborating with it; (ii) they shall be made pursuant to and in accordance with WHO's Open Access Policy, available at https://www.who.int/about/policies/publishing/open-access; (iii) payment of applicable open access fee will be discussed on a case-by-case basis; and (iv) authorship and acknowledgement of data contributors will follow the International Committee of Medical Journal Editors standards (http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html);
19. Declare, through the Undersigned's PI, to WHO all possible conflicts of interest related to the work described in these Terms of Reference by providing a Declaration of Interest to WHO for each performance evaluation;
20. Submit to WHO an annual report using the template provided by WHO by 28 February each year;
21. Ensure that the Undersigned's employees and contractors adhere to and comply with the terms and conditions of these Terms of Reference and the other Contractual Documents;
22. Ensure that any agreements entered into by the Undersigned with any manufacturer in connection with the Undersigned's work as a PEL are consistent, in all material respects, with the terms and conditions of these Terms of Reference and the other Contractual Documents;
23. Ensure that if any portion of the Undersigned's work relating to the performance evaluation, including but not limited to testing, data analysis and/or report drafting, is subcontracted or otherwise outsourced to any laboratories or third parties, then the Undersigned will promptly disclose any such agreements to WHO (under options 1 and 2) and to the manufacturer (only under option 2). For the avoidance of doubt, notwithstanding any such subcontracting or disclosure, the Undersigned will remain primarily and directly responsible vis-à-vis WHO and the manufacturer for the performance of the work subcontracted or otherwise outsourced to any third parties;
24. Except as otherwise agreed in writing with WHO pursuant to an Agreement for the Performance of Work (APW) and/or with the relevant manufacturer, the Undersigned will bear all costs and expenses arising from its designation and/or activities as a PEL;
25. Ensure ongoing compliance with WHO requirements applicable following the Undersigned's designation as a PEL. In connection with the foregoing, the Undersigned agrees to undergo mandatory re-assessment by WHO to verify the Undersigned's ongoing compliance with WHO requirements and relevant standards, which shall take place every three to five years (or sooner, if deemed necessary by WHO) after the Undersigned has been designated/listed as a PEL; and
26. Promptly inform WHO in writing if the Undersigned wishes to temporarily or permanently de-list one or several of the analytes that the Undersigned is listed for and/or to restrict or expand its listing to List 1 and/or List 2 at any time after the Undersigned is listed as a PEL.

In addition to the foregoing, the Undersigned acknowledges and agrees that WHO may, at any time, withdraw the designation of the Undersigned as a PEL and remove/delist the Undersigned from the list referenced above, in the event that the Undersigned either (i) fails to timely and/or completely deliver the agreed work (including, without limitation, the results of the performance evaluations) to WHO; and/or (ii) fails to comply with the provisions or obligations under the performance evaluation protocol or any of the Contractual Documents; provided, however, that prior to withdrawing the Undersigned's designation as a PEL and removing/delisting the Undersigned as described, WHO shall provide the Undersigned with prior written notice of, and a reasonable opportunity during thirty (30) days to cure the relevant failure.

The Undersigned hereby agrees that any claim or dispute arising from or relating to these Terms of Reference and/or the Undersigned's assessment, designation and/or activities as a PEL (collectively "Dispute") shall, unless amicably settled, be subject to a conciliation. In the event the Dispute is not resolved by conciliation, the Dispute shall be settled by arbitration. The arbitration shall be conducted in accordance with the modalities to be agreed upon by the Undersigned and WHO or, in the absence of agreement, with the rules of arbitration of the International Chamber of Commerce. The Undersigned and WHO shall accept the arbitral award as final.

Nothing contained in or relating to these Terms of Reference and/or the Undersigned's assessment, designation and/or activities as a PEL will be construed as a waiver of any privileges and immunities enjoyed by WHO under national or international law, and/or as submitting WHO to any national court jurisdiction.

The undersigned laboratory has caused its duly authorized representative to sign, as of the date set forth below, this document in two (2) originals in the English language in order to evidence such laboratory's agreement with and acceptance of these Terms of Reference.

SIGNED FOR AND ON BEHALF OF THE UNDERSIGNED LABORATORY:

Full Legal Name of Entity: _____
Signature: _____
Full Name of Authorized Representative: _____
Title/Position of Authorized Representative: _____
Date: _____
Mailing Address: _____
_____
Telephone Number: _____
Email Address: _____

[Annexes follow on the next pages]

ANNEX 1
CONFIDENTIALITY UNDERTAKING

1. The World Health Organization (WHO), acting through its Department of Regulation and Prequalification, has access to certain information relating to WHO's prequalification programme and/or to in vitro diagnostics (IVDs) undergoing assessment under WHO's prequalification programme, which information WHO considers to be confidential, non-public and/or proprietary to itself or to third parties collaborating with it (collectively, the "Information"). For the avoidance of doubt, the term "Information" includes, without limitation: (i) any confidential, proprietary or non-public information about WHO's prequalification programme (including, but not limited to, the performance evaluations conducted in connection therewith) and/or the IVDs submitted for WHO prequalification assessment, in each case, that is communicated by or on behalf of WHO to the Undersigned, whether in oral, visual or written form; and (ii) any data, outputs, findings and/or results arising from or relating to: (A) the assessment and/or reassessment, as applicable, of the Undersigned by WHO to determine whether it should be listed in the first place and/or continue to be listed as a Performance Evaluation Laboratory ("PEL"), and/or (B) the performance evaluations of IVDs submitted for WHO prequalification assessment including, without limitation, any such performance evaluations that are conducted by the Undersigned.

2. The Undersigned may, in WHO's sole discretion, gain or have access to the Information in the course of: (i) the Undersigned undergoing an assessment by WHO to determine whether it should be designed as a Performance Evaluation Laboratory; and/or (ii) the Undersigned's participation as a PEL and/or conduct of performance evaluations of IVDs submitted for WHO prequalification assessment.

3. WHO is willing to provide the Information to the Undersigned, or arrange for the provision of the Information to the Undersigned, solely for the purposes of enabling the Undersigned to: (i) conduct (in accordance with the technical procedures, protocols and requirements determined by WHO) performance evaluations of IVDs submitted for WHO prequalification assessment, and (ii) discharge the Undersigned's responsibilities in connection with its collaboration with WHO as a PEL, as set forth in the *Terms of Reference for WHO Performance Evaluation Laboratories*, a copy of which has been provided to the Undersigned (such purposes are hereinafter collectively referred to as "the Purpose"); provided, however, that the Undersigned undertakes to treat the Information as strictly confidential and proprietary, and to disclose it only to persons who have a need to know such Information for the Purpose and who are bound by obligations of confidentiality and non-use which are substantially the same as those contained in this Undertaking.

4. The Undersigned undertakes to treat the Information as strictly confidential and proprietary to WHO or third parties collaborating with WHO, and agrees to take all reasonable measures to ensure that the Information shall not be used, copied, disclosed or otherwise transmitted, whether in whole or in part, other than as expressly permitted in this Undertaking, except that the Undersigned shall not be bound by any such obligations if and to the extent the Undersigned is clearly able to demonstrate that the Information:

   a) was known to the Undersigned prior to any disclosure by or on behalf of WHO to the Undersigned (as evidenced by written records or other competent proof);

   b) was in the public domain at the time of disclosure by or on behalf of WHO to the Undersigned;

   c) becomes part of the public domain through no fault or breach of the Undersigned or of any third party to which the Undersigned disclosed the Information pursuant to paragraph 3 above; or

   d) becomes available to the Undersigned from a third party not in breach of any legal obligations of confidentiality (as evidenced by written records or other competent proof).

5. The Undersigned further undertakes not to use the Information for any benefit, gain or advantage, including but not limited to trading in securities or having others trading in securities on the Undersigned's behalf, giving trading advice or providing Information to third parties for trade in securities.

6. The Undersigned also undertakes not to communicate any of the activities, deliberations and/or decisions related to WHO's prequalification programme (including, but not limited to, any performance evaluations of IVDs submitted for WHO prequalification assessment) to any entities or persons outside of WHO, except as otherwise expressly agreed in writing by WHO.

7. If requested to do so by WHO, the Undersigned agrees to promptly return to WHO any and all copies of the Information, except that the Undersigned may retain one copy of the Information for the purpose of determining its continuing obligations hereunder; provided, however, that such copy of the Information shall remain subject to the confidentiality and non-disclosure obligations contained in this Undertaking.

8. The Undersigned furthermore agrees that any and all rights in the work performed by the Undersigned in connection with or as a result of: (a) the Undersigned's collaboration with WHO as a PEL, and/or (b) any performance evaluations of IVDs submitted for WHO prequalification assessment that are conducted by the Undersigned, shall be exclusively vested in WHO. The Undersigned hereby irrevocably and unconditionally assigns all such rights to WHO and waives any moral rights attached to such work. The Undersigned understands and agrees that WHO reserves the right (a) to revise such work, (b) to use such work in a different way from that originally envisaged, or (c) not to use or publish such work at all.

9. The obligations of the Undersigned shall survive the termination of the Undersigned's collaboration with WHO as a PEL.

10. Any dispute arising from or relating to this Undertaking, including its validity, interpretation, or application shall, unless amicably settled, be subject to a conciliation. In the event the dispute is not resolved by conciliation, the dispute shall be settled by arbitration. The arbitration shall be conducted in accordance with the modalities to be agreed upon by the Undersigned and WHO or, in the absence of agreement, with the rules of arbitration of the International Chamber of Commerce. The Undersigned and WHO shall accept the arbitral award as final.

11. Nothing in this Undertaking, and no disclosure of Information to the Undersigned pursuant to its terms, shall constitute, or be deemed to constitute, a waiver of any of the privileges and immunities enjoyed by WHO under national or international law, or as submitting WHO to any national court jurisdiction.

Acknowledged and Agreed for and on behalf of [INSERT FULL LEGAL NAME OF THE ENTITY SIGNING THIS UNDERTAKING]

Signature: _____

Name: _____

Title: _____

Date: _____

11.2 Annex 2. Principles relating to the WHO audit

Independence

The auditors, that include WHO staff and QMS and technical experts, shall be impartial and free from influences that could affect their objectivity.

Audit objectives and scope

The audit objectives and scope shall be defined in a general audit plan provided to the laboratory and agreed upon with the laboratory prior to the audit. Modification of the plan may occur, to accommodate the laboratory processes and to follow audit trails depending on the observations made at the time of the audit.

Roles and responsibilities

Roles and responsibilities of all personnel involved in the audits shall be clearly defined so that expectations can be met and accountableness maintained.

Resources

Resources shall be adequate in terms of competent auditors, expertise as deemed necessary, time allocation and access to external technical and other information. The resources utilized shall ensure that the audit results are highly reliable.

Competence of the audit team

The audit team shall consist of auditors with appropriate skills, education and experience in QMS auditing and IVDs.

Consistency of procedures

The audit procedure shall be performed according to defined guidelines (ISO 19011:2018) using a WHO format to ensure consistency for all audits.

Confidentiality and standard of conduct

The auditors shall maintain confidentiality with regard to information and documentation related to the audit and the laboratory/organization and shall comply with the defined WHO standards of conduct. Within these considerations, the audit process is to be transparent to all participants.

Audit results and conclusions

The results and conclusions of the audits shall be consistent and accurate subject to the normal limitations of an audit, noting that the objective evidence collected during the audit is generally a sample.

Quality system

Audits are conducted in compliance with the relevant auditing standards

11.3 Annex 3. Example of audit plan

The table below is an example of an audit plan for a WHO audit of a laboratory. Times may be modified to better comply with the daily routine. Length of the site visit will vary according to audit requirements and composition of the audit team.

Name of Laboratory		ALE- *xxx*
Dates		
Audit Team		

Day	**Time**	**Audit Scope**
Day 1	9.00 – 10.15	Opening meeting as per Opening meeting agenda. Introduction of personnel and overview of audit by WHO; overview of laboratory processes, key staff and QMS by the laboratory.
	10.15 – 10.30	Facility tour
	10.30 – 12.30	Horizontal Audits (includes 15-minute break) QMS: Management responsibility including interviewing of senior management. • Organization and Management System • Document Control / Record Control • External Services and supplies • Service to the customer and complaints • Control of nonconforming work • Improvement • CAP • Internal Audits • Management Reviews
	12.30 – 13.15	Lunch break (on-site)
	13.15 – 16.45	Audit (continued)
	16.45 – 17.00	Daily wrap up meeting: Auditors report briefly to laboratory personnel on day's findings
Day 2	All day	Short opening meeting to schedule activities Audit continued as above and as required including breaks Daily wrap up meeting
Day 3	09.00 – 10.00	Discuss requirements to conduct the performance evaluation

Day 3	10.00 – 17.00 (including lunch break)	Assessment of technical competence. This includes the Observations of performance of tests / vertical audits and interviews. Technical audit includes but is not limited to: • Personnel • Accommodation and environment • Pre-examination (sourcing and handling of panels) • Methods & method validation • Ensuring Quality of examinations • Equipment • Reporting the results
Final day	9.00 – 12.00	Audit (continued)
	12.00 – 12.45	Lunch break (on-site)
	12.45 – 15.00	Prepare draft on-site report
	15.00 – 16.00	Closing meeting: present audit outcome and draft report and discuss findings with laboratory

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