FAQ: TB Diagnostics – GTB Recommendations and PQ

No.	Question	Answer
1	**Topic: WHO Global TB programme class recommendations and WHO Prequalification (PQ) product assessments**	
1.1	What are going to be the classes of TB IVDs that will be assessed by PQ?	The WHO Global TB programme (GTB) will establish diagnostic classes of tests and provide policy recommendations. The new classes will be determined based on emerging needs, technology developments and supporting evidence.
1.2	What products will WHO PQ Dx review?	The Prequalification (PQ) Unit will assess technologies that fall within classes that have a positive GTB recommendation. All current classes will be included in the scope of PQ product reviews. However, due to time and capacity for these changes, the transition will take place in a stepwise approach with prioritization of high use and impact technologies first.
1.3	Is it the manufacturer's choice to put an existing product through PQ assessment?	Submission for PQ assessment is a voluntary process. However, manufacturers interested in participating in procurement within UN agencies and other agencies relying on WHO prequalification as their quality assurance criterion will need to submit IVDs for PQ assessment. The current TB diagnostic assessment process for TB IVDs will evolve into a two-step mechanism which focuses on the evaluation of classes of TB diagnostic technologies for WHO recommendation through WHO GTB while WHO PQ will evaluate each specific product brand for quality, safety and performance within the product intended use. The WHO/PQ and WHO/GTB are working together on a smooth transition for TB IVDs from the current procurement eligibility mechanism to prequalification listing based WHO procurement eligibility. This will be done in a stepwise approach.
1.4	How is the WHO PQ Dx review different from the WHO GTB GDG process/ recommendation?	Please refer to Table 1 in the document below for a comprehensive comparison of the two processes: https://extranet.who.int/pqweb/sites/default/files/documents/210211_PublicAnnouncement_TB_%20in-vitro-diagnostics.pdf
2	**Topic: Prequalification and Global TB programme Processes**	
2.1	What is the difference between an abridged	The implementation of the IVDR will not change the WHO processes for the evaluation of classes and/or PQ assessment. Prequalification will follow either a full or an abridged assessment pathway depending on

	and full assessment and how does that relate to the CE IVD regulations?	the existing evidence of recognized regulatory reviews. For more information please refer to the documents at the links below: https://extranet.who.int/pqweb/sites/default/files/documents/21-01-27-Overview-DX-Prequalification-Requirements-PQDx_007-v9.pdf https://extranet.who.int/pqweb/sites/default/files/documents/210112_PQDx_173-v4_AbridgedPQ_assessment.pdf
2.2	Will GTB continue to have GDGs to change the strength or scope of recommendations for previously recommended classes of IVDs?	Yes, GTB will continue to hold Guideline Development Group meetings to either generate new recommendations or update existing recommendations when relevant. The latter would occur where evidence in the existing policy was limited to specific population groups, sample types or other aspects. If new evidence supports the expansion of the policy recommendation, an update of the recommendation would be made. Alternatively, the recommendation may remain, but the strength of a recommendation may increase, if for example, new evidence indicates greater impact on patient important outcomes for which evidence was lacking previously.
2.3	When can a supplier submit their product for review? What needs to happen from WHO PQ Dx side before a product can be submitted?	There are three pre-conditions for submission of a PQ application: • a WHO/GTB recommendation • a confirmation by WHO/GTB that a specific product belongs to a product class for which a WHO recommendation exists • the prequalification eligibility includes the product class and PQ technical specifications are published. Once a product is confirmed by GTB to belong to a product class covered by an existing WHO recommendation and the prequalification eligibility includes that product class an application for prequalification assessment can be submitted.
2.4	How will a supplier know when their product can be submitted?	The manufacturer will receive a written confirmation that their product is confirmed by GTB to belong to a product class covered by an existing WHO recommendation and PQ will be informed of the decision.
2.5	Will WHO recommended products go through a full assessment or an abridged assessment?	The decision to undertake a full or an abridged prequalification assessment is taken by the PQ Unit/In Vitro Diagnostics assessment Team at the time of the submission of an application. The applicant is informed of this decision through an official letter.

2.6	How will programmes know that the products they are procuring are WHO PQ Dx approved?	The list of prequalified products will be publicly available on the WHO website along with product specific public reports that capture dossier assessment and performance evaluation outcomes (WHOPAR) and site inspection findings (WHOPIR). In addition, WHO will ensure efficient and transparent communication on its assessment mechanisms.
2.7	What happens if a GTB recommended product does not get approval from WHO PQ Dx?	Both a WHO recommendation (or, for products other than those first in class, a confirmation that a specific product belongs to a product class covered by an existing WHO recommendation) and prequalification listing are mandatory to grant WHO procurement eligibility. If a manufacturer fails to meet prequalification requirements, the necessary corrective actions will have to be implemented prior to re-applying for PQ assessment. The PQ Unit will provide the necessary guidance to the manufacturer. Products recommended by GTB prior to the PQ process being implemented will be given a 6-month period for the PQ submission and a 2-year timeframe to become WHO prequalified. After such time has elapsed, the product will have to be prequalified to continue to be considered eligible for WHO procurement.
3	**Topic: Prequalification Requirements**	
3.1	For new products to be launched, will more documentation or studies be needed than before (current process) to support the GTB evaluation of classes and the PQ product's quality, safety and performance?	For prequalification purposes manufacturers of all products submitted for PQ assessment will have to demonstrate compliance with a set of requirements on quality, safety and performance. These will apply to all products submitted for PQ assessment. While there is a certain overlap between data required for a WHO recommendation and information required for PQ assessments, the overall objective of the two processes is different and, therefore, datasets required for PQ assessment may be different from those reviewed by GTB. Manufacturers are encouraged to review the PQ technical specifications (TSS-17), technical guidance and instructions in advance to be well prepared for PQ assessment. Where data is lacking or inadequate, additional validation studies will be required.
3.2	What will be used by PQ as gold standard for TB?	The prequalification requirements on the comparator assay to be used for product validation purposes will be described in the PQ technical specifications. These will vary based on the product class. For the purposes of the PQ performance evaluation the comparator assay will be defined in the evaluation protocol, which will be shared with the applicant prior to the commencement of such evaluation. The comparator assay will be defined for a specific product class.

<table>
<tr><td>4</td><td colspan="2">Topic: Prequalification Timelines</td></tr>
<tr><td>4.1</td><td>What are the estimated timelines for availability of technical specifications of different classes? And opening of PQ for review of dossiers?</td><td>The Prequalification Unit is developing the PQ technical specifications following a prioritization plan agreed between GTB and PQT. This will allow the development of specifications for product classes in a stepwise approach and the expansion of the PQ eligibility as Technical Series Specifications (TSS) become available. The development of TSS-17 for molecular TB IVDs used for the detection of Mycobacterium tuberculosis complex (MTBC) with or without drug resistance was completed in Q3 2022and WHO is now accepting submissions for prequalification assessment. The development of PQ technical specifications for other classes of TB IVDs will follow and the PQ eligibility will be expanded accordingly. WHO will keep stakeholders updated on the prioritization of product classes and timelines for TSS development.

For molecular TB IVDs the below timelines will apply for PQ assessments and listing:
<table><tr><td>Q3 2022</td><td>Q1 2023*</td><td>Q4 2024**</td></tr><tr><td>TSS-17 published and applications invited
Workshop held for manufacturers</td><td>Deadline for currently endorsed products submissions for PQ assessment</td><td>Deadline for PQ listing of currently endorsed products</td></tr></table>* Unless the manufacturer and the PQ Team have agreed on a different timeframe
** WHO will give due consideration to the progress of each application in the assessment process and may consider extending the procurement eligibility for products close to PQ listing.

WHO will also ensure that procurement eligibility criteria are adjusted taking into account the timelines for PQ specifications development and the opening of the PQ pipeline for specific product classes.</td></tr>
<tr><td>4.2</td><td>Given timelines for PQ can be lengthy, should manufacturers of currently WHO-recommended diagnostics apply for the ERPD if a relevant invitation is posted? Or should they just apply directly for PQ?</td><td>Manufacturers will be invited to apply for PQ assessment as the PQ technical specifications become available and the PQ eligibility is expanded to certain product classes. In the meantime, some donor agencies may consider adopting risk-based quality assurance mechanisms to inform their procurement decisions. The Expert Review Panel for diagnostics (ERPD) is a panel of independent technical experts to advise the Global Fund and UNITAID on the potential risks and benefits associated with the use of diagnostic products that are not yet recommended by WHO GTB and/or not prequalified and/or approved for use after a stringent assessment by a GHTF Founding Member. More information can be found here:
https://www.theglobalfund.org/en/sourcing-management/quality-assurance/diagnostic-products/</td></tr>
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4.3	What are the timelines for WHO PQ Dx review?	Target timelines for PQ assessments are described in a dedicated guidance document which can be found here: https://apps.who.int/iris/bitstream/handle/10665/259168/WHO-EMP-RHT-PQT-2017.05-eng.pdf;sequence=1 Timelines depend on the type of assessment undertaken by WHO (full or abridged) and on the manufacturer's decision to follow option 1 or option 2 for the PQ performance evaluation. In summary, the WHO target deadlines for full assessment are: • 270 WHO calendar days, if the alternative performance evaluation pathway is selected by the manufacturer; and • 350 WHO calendar days, if WHO coordinates the performance evaluation. The WHO target deadlines for abridged assessment are: • 100 WHO calendar days, if the alternative performance evaluation pathway is selected by the manufacturer; and • 180 WHO calendar days, if WHO coordinates the performance evaluation.
4.4	What are the expected impacts on timelines for review by WHO PQ Dx considering their work on EUL for C19 diagnostics?	To manage the large number of applications during the COVID-19 pandemic a prioritization of incoming applications for PQ and emergency use listing assessment was established by WHO. This is a temporary measure aiming at the most efficient use of limited resources and will be adjusted according to future public health needs. More information can be found here: https://extranet.who.int/pqweb/sites/default/files/documents/EUL_IVD_priority_categorization.pdf
5	**Topic: Prequalification Costs**	
5.1	Will there be a possibility to waive fees for IVDs that have a small market in LMICs?	The PQ assessment fee cannot be waived. However, WHO can consider waiving the annual fee provided that an acceptable justification is provided by the applicant.
5.2	What is the expected impact of WHO PQ Dx fees, additional validation studies, additional time to develop a dossier, etc., on current and future	The pricing of tests would need to factor in all costs as is standard practice and the PQ costs ensuring quality, safety and performance are the same as would be expected for any regulatory approval.

	pricing of TB diagnostics?	
5.3	What are the costs associated with WHO PQ Dx submission and listing?	A prequalification assessment fee is charged to a manufacturer once its application has been determined to be eligible for PQ assessment. For a product undergoing full assessment, US$ 5000 is charged for dossier screening and US$ 12,000 for product assessment. For a product undergoing abridged assessment the fee is US$ 8,000. A change assessment fee of US$ 3000 is also charged when changes are submitted for review. Finally, an annual fee of US$ 4000 is levied for each product listed on the WHO List of Prequalified In Vitro Diagnostics. More information can be found at the link below: https://apps.who.int/iris/bitstream/handle/10665/259171/WHO-EMP-RHT-PQT-2017.04-eng.pdf?sequence=1&ua=1
6	**Topic: General and Procurement related**	
6.1	Is the deadline published in the first announcement for 31 December 2022 still valid?	The deadline is now updated, see Table under 4.1. The timelines for other classes of technologies will follow and be adjusted accordingly.
6.2	What will the status be for procurement between the time when a GTB Recommendation is made and the final PQ assessment outcome? What about items recommended by GTB for which the PQ process has not started?	The transition process with existing TB diagnostic products and the new classes of TB diagnostic products that will be added in the future will have a time lag between the published GTB recommendations and final PQ approval. To address this time window, the GTB recommendations which include product classes as well as specific products will be valid for procurement following the release of the guidelines and continue to be so until the PQ process is completed. For example, a specific TSS is planned for release in Q2 2022 which will include timelines set for submission and for the PQ final decision. Up until the final PQ decision, the GTB recommendations will continue to be applicable for procurement. Products will be introduced into the PQ system in a stepwise manner. Products not covered in the released TSS will continue to fall under the previous GTB recommendations and be accepted for procurement. When TSS for that product or class is released, manufacturers have 6 months to enroll in the PQ process, during which time the GTB recommendations are still valid for procurement.
6.3	What is the role of the ERPD in this overall process?	Please refer to the answers provided above. The ERPD is an independent risk-based assessment mechanism which provides advise the Global Fund and UNITAID on the potential risks and benefits associated with the use of diagnostic products that are not yet recommended by WHO GTB and/or

		prequalified by WHO PQ and/or approved for use after a stringent assessment by a GHTF Founding Member. ERPD assessments are handled independently from WHO PQ reviews.
6.4	What is the expected impact on access/availability of new diagnostics if first-in-class products must go through WHO GTB review and then WHO PQ Dx review?	The purpose of the additional PQ step is not to hinder access to diagnostics that impact patient care but rather to provide quality assurance and ongoing monitoring. Appreciating the time lag between the policy recommendation and final PQ review with patient and programme needs, a time window period is provided to allow procurement of the first in class product(s) under the GTB recommendations until the PQ assessments are complete. In order to accelerate the PQ TSSs and the GTB activities, the two departments will closely collaborate in advance to ensure cohesion.