Invitation to Manufacturers

4th April 2022

Manufacturers of Diagnostic Products Are Invited to Submit An Expression of Interest For Product Evaluation by the Global Fund Expert Review Panel for Diagnostic Products

Closing Date: not applicable (open Call)

Reference Number: GF/ERPD/Adhoc-21/04-2022

TB Diagnostic Tests employing:

- Nucleic Acid Amplification based Technologies (NAAT)
- Lateral Flow Mycobacterial lipoarabinomannan (LAM) tests for TB
- Interferon-Gamma Release Assay (IGRA)
- Next-Generation Sequencing (NGS)

01 Background

The Global Fund to Fight AIDS, Tuberculosis and Malaria (the "Global Fund") is one of the major funder of diagnostic products and related laboratory items for the diagnosis and management of HIV/AIDS, tuberculosis and malaria. Unitaid and the Global Fund support the procurement of large amounts of these products. In March 2011, the Global Fund established the Global Fund Quality Assurance Policy for Diagnostic Products ("the QA Policy"). The Global Fund revised its QA Policy for Diagnostic Products in May 2017 to reflect new WHO recommendations or guidelines and the Global Fund policy on co-infection and co-morbidities[1].

[1] Available at: https://www.theglobalfund.org/board-decisions/b37-dp12/

The application of nucleic acid amplification tests (NAAT) has revolutionized rapid and accurate diagnostic testing for most pathogens. The general accuracy and rapid time to detection make NAATs an essential tool for the TB community to rapidly and accurately diagnose TB and MDR TB. In addition, some NAATs are suited to be used as a follow-on test for the rapid detection or resistance to other key drugs such as fluoroquinolones. In the fourth edition of the Unitaid landscape report on TB diagnostics[2] the pipeline of NAATs in development was presented as being highly promising, especially with molecular tests targeting intermediate laboratories and peripheral-level facilities.

In 2015, WHO Global TB Programme (GTB) evaluated one Lateral Flow-Lipoarabinomannan (LF-LAM) Ag rapid diagnostic test (RDT) for the diagnosis of active tuberculosis in people living with HIV resulting in the release of the WHO policy guidance[3] and in 2019 issued a policy update on LF-LAM tests[4].The test is suitable for use at the patient bedside and the first point of care test for TB. Furthermore, it is a non-sputum-based test which has advantages in patients that cannot produce sputum.

The WHO Global TB Programme currently recommends that either a tuberculin skin test (TST) or interferon-gamma release assay (IGRA) can be used to test for TB infection[5]. The former is an in-vivo test widely used for many years while the latter is an in-vitro test using *Mycobacterium tuberculosis* specific antigens.

Several companies have developed NGS TB assays that are poised to revolutionize DR-TB testing and support rapid identification of optimal DR-TB treatment regimens. These NGS assays are on the pathway to WHO evaluation for clinical use.

The products in the pipeline described in the Unitaid landscape on TB diagnostics offer important potential solutions but require field evaluations to generate evidence for policy as well as quality assessment required for procurement. In addition, the operationalization of WHO recommendations for the diagnosis of TB[6] requires scaling up and a sufficient expansion in the number of quality-assured products meeting the Global Fund and Unitaid quality assurance policies to improve access to TB diagnostics and finding missing cases (roughly 36% of people with active TB are missed each year). Access to some of these diagnostic products is of critical importance, especially when market entry may be pending comprehensive reviews associated with stringent regulatory assessment, WHO GTB programme assessment or World Health Organization (WHO) prequalification. Consequently, the assessment by the Expert Review Panel for Diagnostics (ERPD) has been put in place, as described in the QA Policy[7].

02 The Expert Review Panel for Diagnostic products (ERPD)

The ERPD is a **mechanism to review the risks and benefits associated with procurement and use of diagnostic products that may have a high public health impact but is not yet recommended by the WHO GTB programme or have not yet undergone a stringent regulatory assessment**, either by the WHO Prequalification of In-Vitro Diagnostics Programme or by **regulatory authorities of the Founding Members of the Global Harmonization Task Force (GHTF)**[8] when stringently assessed (high-risk classification). The ERPD is not intended to replace the WHO GTB programme recommendation, WHO prequalification programme or stringent regulatory assessment, but to provide an interim solution for a time-limited period, in anticipation of the completion of a stringent review process.

[2] Available at: http://unitaid.org/assets/2017-Unitaid-TB-Diagnostics-Technology-Landscape.pdf
[3] Available at: https://www.who.int/tb/publications/use-of-lf-lam-tb-hiv/en/
[4] Available at: https://www.who.int/tb/publications/2019/diagnose_tb_hiv/en/
[5] Available at: https://apps.who.int/iris/bitstream/handle/10665/260233/9789241550239-eng.pdf
[6] Available at: https://www.who.int/tb/areas-of-work/laboratory/policy_statements/en/
[7] Available at: https://www.theglobalfund.org/en/sourcing-management/quality-assurance/diagnostic-products/
[8] The founding members of the Global Harmonization Task Force (GHTF) include U.S., Japan, EU, Canada, and Australia.

Thus, the ERPD mechanism may help to expedite access to innovative diagnostic products, if the associated risks are deemed to be less than the potential benefits.

Among innovative diagnostic products of potential interest for the countries supported by the Global Fund, Unitaid and other stakeholders, the diagnostics products selected in the present invitation for an Expression of Interest have been identified as a priority.

The Global Fund and Unitaid are issuing this invitation for an Expression of Interest, inviting manufacturers of the selected category of diagnostic products to submit their product information (as specified in the product questionnaire) for review. Once a submission is accepted by the Global Fund, an independent panel of technical experts will conduct an analysis of the potential risks and benefits linked to the procurement and use of such diagnostic products which have not yet been prequalified by WHO, recommended by the WHO GTB programme or authorized for use through a stringent regulatory review.

The ERPD is hosted by WHO and operates in accordance with its Terms of Reference. The ERPD then advises the Global Fund, Unitaid and other partners, as relevant, on the use of grant funds for procurement of such diagnostic products for a time-limited period and under specific conditions.

The complete process - the invitation to submit an Expression of Interest, followed by the submission of the diagnostic product questionnaire by the manufacturers to the Global Fund, the ERPD review and the subsequent communication of the results to the manufacturers by the Global Fund - takes a maximum of six months.

03 Purpose of this invitation

The purpose of this invitation is to invite manufacturers to submit their product dossier to the ERPD to determine the acceptability for procurement and use of their diagnostic products as per the scope of product categories described in this document. This invitation applies only to diagnostic products (e.g. test reagent kits) that can (1) at least provide qualitative results at clinical decision points; and (2) which are not yet prequalified by WHO or authorized for use through a stringent regulatory review; and (3) which are not yet recommended by the WHO GTB programme.

04 Scope of the present invitation to submit an expression of interest

The present invitation focuses on diagnostic tests for TB testing. Any diagnostic test included in the expression of interest should meet the following:

For NAAT based technologies:

- using NAAT assays for TB diagnostics including TB drug susceptibility testing

For LF-LAM Ag Rapid Diagnostic Tests:

- using lateral flow technologies or similar for TB diagnostics and
- using a rapid test format that can be used at point-of-care

For IGRA based Tests:

- IVDs using immune response-based methods for diagnosis of TB infection

For NGS based Tests:

- IVDs using Next-Generation sequencing technologies for TB drug susceptibility testing

05 Eligibility criteria

Manufacturers must meet the following criteria in order to be eligible for ERPD review.

i. The diagnostic product has a dossier already under review by the WHO Prequalification of In-Vitro Diagnostics Programme, WHO GTB programme or is undergoing a stringent regulatory approval process;

OR

The aforementioned product has not yet been submitted to the WHO Prequalification, WHO GTB programme or has not yet been stringently assessed and approved by a regulatory authorities of the Founding Members of the Global Harmonization Task Force (GHTF) but the manufacturer can provide a signed "Letter of Commitment" either to (1) submit to the WHO Prequalification of In Vitro Diagnostics Programme, (2) submit to the WHO GTB programme or (3) engage in a stringent regulatory approval process through one regulatory authorities of the Founding Members of the Global Harmonization Task Force (GHTF) after a successful ERPD review[9];

AND

ii. The aforementioned product is manufactured at a site that is compliant with the requirements: ISO 13485:2016 or an equivalent quality management system (ISO 13485) recognized by an appropriate body (e.g. recognized certification body by a regulatory authorities of the Founding Members of the Global Harmonization Task Force (GHTF) or successfully assessed by WHO Prequalification);

06 Submission of documents for ERPD review

All manufacturers interested in submitting applications for review by the ERPD are requested to submit the following information and material for each diagnostic product proposed for review:

- A cover letter expressing interest in submitting the product to the ERPD for review and indicating the authorized contact for the manufacturer;
- Where appropriate, a letter from the WHO Prequalification of In-Vitro Diagnostics Programme, WHO TB Programme or a stringent regulatory authority confirming that the submission for the said diagnostic product is currently under review for the intended use or - in the absence of such a confirmation letter - a letter of commitment from the manufacturer;
- One of the following documents, substantiated by the most recent inspection reports:
  - i. An ISO 13485 certificate; or
  - ii. A certificate ensuring that the product (reagents and equipment) is manufactured at a site that is compliant with ISO 13485 requirements; or
  - iii. an equivalent quality management system recognized by a regulatory authorities of the Founding Members of the Global Harmonization Task Force (GHTF); or
  - iv. a letter from WHO ensuring that the manufacturing site has been inspected by the WHO Prequalification of In-Vitro Diagnostics Programme and found compliant with WHO prequalification requirements.
- A completed product questionnaire, which can be found on the Global Fund website[10].

[9] For example: Conformity assessments as of European Directive 98/79/EC article 9 paragraph 2

[10] Available at: https://www.theglobalfund.org/en/sourcing-management/quality-assurance/expert-review-panel/

07 Confidentiality

All information provided by manufacturers will be received by the Global Fund, kept confidential in accordance to the Global Fund's rules and shared with the ERPD members for the purpose of facilitating their review of the submission and provision of advice to the Global Fund under a confidentiality agreement with WHO as coordinating entity.

Review outcomes and advice provided by the ERPD, in connection with this Expression of Interest, will be shared with and used by the Global Fund, Unitaid and the following partners as the basis for procurement decisions: Médecins sans Frontières (MSF), UNICEF and USAID.

08 Eligibility

The Global Fund Quality Assurance will review all submissions for completeness. All the documents listed in section 6 and specifically detailed in the Diagnostic Product Questionnaire must be included by the applicant. Incomplete submissions will not be forwarded to the ERPD for review.

09 Instructions for submission

Submission should be submitted by electronic means (either via email or web based download service) together with a hard copy of the duly signed questionnaire, cover letter and letter of commitment (accompanied by an electronic copy on CD or a USB key). Files should be named to reflect their content as mentioned in this letter (e.g. "Cover letter.pdf", "annex A.pdf", "annex B.pdf").

There is no deadline for submitting an Expression of Interest as long as the invitation is published on the Global Fund website (submissions are accepted at any time until closure of this call). Information of the closing will be published on the Global Fund website 3 months in advance.

All submissions should be addressed with the reference number GF/ERPD/Adhoc-21/04-2022 and be sent by mail to the following address:

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Should you have any further questions, you may contact René Becker-Burgos at the following email address: Rene.Becker-Burgos@theglobalfund.org