Expert Review Panel for Diagnostic Products: HIV Rapid Diagnostic Tests manufactured in Africa
Frequently Asked Questions

21 November 2023

Reference Number: GF/ERPD/Adhoc 24/08-2023

Please refer to the updated Invitation for Expression of Interest here (update published on 21 November 2023) and to the Letter of Intent template here. This and other invitations can be found on The Global Fund's Expert Review Panel page here.

After reviewing the Invitation for Expression of Interest and this document, should you have any further questions, please contact Dr. Becker-Burgos at the following email address: Rene.Becker-Burgos@theglobalfund.org

1. Target product

a) **Does this ERPD include saliva HIV tests?** Yes, oral fluid HIV self-tests are included.

b) **Is this ERPD targeting only RTDs?** Yes, this pilot is targeted at HIV RDTs (including HIV ST).

c) **What about consideration of malaria tests?** Malaria tests are not included in this pilot; however, as we progress on this HIV RDT work, we will consider opportunities for RDTs in other disease areas following Global Fund's decision to focus on RDT as a product category for supporting capacity building of regional manufacturing. There is an open call for Malaria Rapid Diagnostic Tests for infections of Pf only, Pf/Pv or Pan (GF/ERPD/Adhoc-23/05-2023), that can be found on The Global Fund's Expert Review Panel page here.

d) **Will HIV-Syphilis Duo Test or HIV-Syphilis-HbsAg be included into this ERP?** HIV-Syphilis Duo and HIV-Syphilis-HbsAg are not included in this pilot. There is an open call for Syphilis (Treponema Pallidum) infections (GF/ERPD/Adhoc-14/10-2019) that can be found on The Global Fund's Expert Review Panel page here.

e) **Is there any specification regarding the generation HIV tests?** No. As the ultimate objective is to get approval by WHO PQ, the WHO PQ Technical Specifications on HIV RDTs can be useful guidance.

2. Eligibility

a) **Will regional or national regulatory approval be required prior to submitting for the ERPD process?** Prior regulatory approval is not required to apply to ERPD. It is useful to mention any regulatory approvals that have already been acquired in the relevant section in the product questionnaire as part of the submission.

b) **Do products reviewed by the ERPD still need to go through WHO PQ?** Yes, a commitment to apply to either WHO PQ or an SRA is required. As specified in the QA policy, the ERPD's advice shall be valid for a period of no more than 12 months. The Global Fund may, at its sole discretion, request the ERPD to consider extending the ERPD recommendation period for up to an additional 12 months if the diagnostic product is not yet WHO-prequalified or SRA-authorized within the ERPD Recommendation Period. Such requests can only be considered based on supporting evidence that the risks for using the product have been reduced and/or the benefits have increased, and substantial progress been made towards WHO prequalification or SRA-authorization.

c) **How do you define "end to end" manufacturing?** End to end manufacturing includes the steps of design, purchase, processing of raw materials, cutting of sheets, assembly, packaging, testing, and final release. Commitment to expand to end-to-end manufacturing of RDTs in Africa within the next 10 years is required as part of submission for this ERPD - find here the template for the Letter of Intent..

d) **Have the eligibility criteria for the ERPD changed since it was first published on 8 August 2023?** Yes, the ERPD eligibility criteria has expanded and now enables tech transfers and partnerships, per the updated Call for EOI from 21 November. If a manufacturer outside of Africa does a tech transfer or partners with an African manufacturer such that the legal manufacturer of the finalized RDT (with unique name and product code) is the African manufacturer and at least some of the manufacturing steps take place in Africa, then the product is eligible for ERPD assessment.

e) **For an originator located outside of Africa with an original product WHO PQed (case 1 on the call for EOI of 8 August 2023) is there any fast-track option for PQ change notification?** Please reach out to WHO (diagnostics@who.int) for questions on PQ change notification. Also, please note that the Call for EOI has been updated on 21 November 2023 and the eligibility revised. Please find updated here [insert Revised Call for EOI]

f) **I am a manufacturer with headquarters outside of Africa, but am planning to move packaging of the product into an African country, can I apply to ERPD?** If a manufacturer is located outside of Africa, the product has WHO PQ and the packaging of the product or any other manufacturing step is completed in Africa by that same manufacturer, then the manufacturer is not eligible for ERPD and should apply for a WHO PQ change notification ("change in manufacturing site of PQ product"). If the product is not yet WHO prequalified, then the manufacturer can apply to ERPD. If a manufacturer outside of Africa does a tech transfer or partners with an African manufacturer such that the legal manufacturer of the finalized RDT (with unique name and product code) is the African manufacturer and at least some of the manufacturing steps take place in Africa, then the product is eligible for ERPD assessment.

g) **Are final products eligible for the ERPD assessment if they use sub-assemblies, such as uncut sheet/membranes, which are sub-supplied from a manufacturer commercializing a product which is already WHO prequalified?** Yes, submissions for such final product are eligible for this invitation to an ERPD assessment provided

that the legal manufacturer of the IVD is based in Africa.

h) **I am a manufacturer located outside of Africa, our HIV products are pre-qualified by WHO already, and via technology transfer with our local partner in Africa, we intend to manufacture the product in Africa. Are we eligible for this ERPD?** Yes, if the legal manufacturer of the finalized RDT (with unique name and product code) is the African manufacturer.

i) **What is the rationale for excluding tech transfer/ partnerships to produce an RDT that has been previously WHO prequalified from the ERPD process?** Please note that the ERPD eligibility was updated on 21 November 2023 and tech transfer and partnerships between manufacturers are now encouraged.

j) **If a manufacturer that already has a WHO PQed product does a tech transfer with an African manufacturer, e.g., to produce finished RDTs from uncut sheets, is the product eligible for ERPD?** Yes.

k) **If a manufacturer supplies an assembled test to be packaged by an African manufacturer, is the final product eligible for ERPD?** Yes, provided that the legal manufacturer of the IVD is based in Africa.

l) **How will the big international established manufactures be restricted from setting up a shop in Africa to be defined as "African" manufacturer?** Rebranding of a product from an internationally established manufacturer, which is already prequalified by WHO-PQ, is not in the scope of this ERPD. To be eligible through a tech transfer, the legal manufacturer must be in Africa.

m) **Given that tech transfers for products from manufacturer that are already WHO PQed are eligible for ERPD, how will decision-makers have visibility of which prequalified products are based on the same design and materials of the ERPD-listed products?** WHO will ensure that PQ Public Reports for all prequalified products and the list of prequalified IVDs include information to clearly identify products having the same design and components. Similarly, the Global Fund will ensure that products on the ERPD list are identified as “tech transfer” products linked to a specific WHO prequalified product.

3. Submission

a) Who should submit the ERPD? OEM company or finished product supplier? The ERPD should be submitted by the legal manufacturer.

b) **Is there any requirement for clinical studies (e.g., number of specimens, number of regions etc.)?** There are no explicit requirements for an ERPD submission. As the final objective is an approval by WHO PQ or an SRA, the corresponding documents from WHO PQ can be used as guidance, e.g., the WHO PQ Technical Specifications on HIV RDTs.

c) Can we submit the product questionnaire for review while the clinical study is still ongoing? Does it have to be submitted before the application? A product questionnaire can be submitted while the clinical study is not fully completed, and it must be submitted with the application. However, the clinical data joined within the questionnaire should already provide some information on the clinical performance of products, including the full study protocol and preliminary (interim) study data. Please be advised that an ERPD submission without any clinical data will not be accepted for

review.

d) **If there is a product with the same raw material and production method as the WHO PQ approved product and via tech transfer it starts being manufactured by an African manufacturer, is it possible to obtain an ERPD listing only by submitting equivalence evaluation data with WHO PQ approved product? We plan to use the existing analytical performance data, clinical data, and stability data which were submitted for WHO PQ approval for the original product for the ERPD submission.** No, product validation and evidence of performance must be generated using the actual product submitted to the ERPD. For any analytical or clinical studies in progress at the time of ERPD submission the study protocol and any interim data available should be submitted for review.

e) What is the Product Conformity required? The ERPD assessment is not a regulatory approval. However, conformance to general quality, safety and performance standards and guidance (ISO, CLSI, etc.) applicable to IVDs is required. Applicants are requested to provide a list of standards and guidance the product complies with.

f) **Can we submit the product questionnaire for review with the preliminary stability study (e.g., real time) data with a mention that the studies are ongoing?** Yes, please also provide the study protocol and any interim results that are available at the time of submission.

g) What are the certification bodies accepted in order to demonstrate compliance with the QMS requirements of ISO 13485? Compliance with the requirements of ISO 13485:2016 should be demonstrated by an appropriate certification body such as the ones accredited within the Founding Members of the Global Harmonization Task Force (GHTF) or by a national accreditation body member of ILAC.

h) **For how long will this EOI be open?** This is ad-hoc ERP-D without any deadline for submission.

4. Outcome & procurement

a) **Can I reapply to ERPD if the product is assessed as Risk Category 3 or 4?** For Risk Category 4, the manufacturer may reapply after substantial improvements, taking into account the feedback received from the ERPD. For Risk Category 3, the expectation is that the manufacturer continues in the process and makes ongoing improvements to manufacturing and quality assurance. As a result, there may be an improvement in the risk category while still in the process without a new application. Few months before the end of the validity period, the manufacturer will be asked to provide updated information which will be an opportunity to improve the risk category.

b) **Will the list of submitted products be shared or just once a product gets a favorable result does it go on the list of products eligible for GF procurement?** Only products that get Risk Category 1 and 2 are added to the “List of HIV Diagnostic Test Kits and Equipment Classified According to the Quality Assurance Policy’, which can be found here.

c) Will details about where the manufacturing of the products covered by the ERPD review is taking place be publicly available, especially if some manufacturing steps are performed outside Africa? ERPD dossiers are confidential, so no information is disseminated prior to an assessment. Once the submission is considered

satisfactory to grant a risk category 1 or 2, the product is listed with the name of all manufacturing sites. As to the Letter of Intent, it will be shared with a limited set of partners (e.g., PEPFAR, Unitaid) - up to the company if that information is in it.

d) **If the product achieves Risk Category 1 or 2, what are the next steps before an order is placed using Global Fund funds?** For contracting arrangements with Global Fund, there are two pathways to add the product to Wambo.com as detailed below. Once the product is added to the list of eligible products and Wambo.org, GF Principal Recipients can procure the product using GF funds after requesting a no-objection letter from the Fund Portfolio Manager.
    a. Direct Framework Agreement: Manufacturer participates in Global Fund's RDT tender; tenders are launched periodically. Global Fund and manufacturer enter a multi-year Framework Agreement specifying the Terms and Conditions, product range, and prices. Note that the next Global Fund RDT tender is tentatively planned for Q4 2023.

    b. Indirect Agreement with Global Fund's Procurement Service Agent (PSA): Pathway is available when a product becomes eligible in the middle of Global Fund's procurement cycle to allow immediate procurement of a product. PSA and manufacturer enter a contract, which enables Global Fund to purchase the product.

e) How will PEPFAR use the ERPD assessment? PEPFAR will use a favorable ERPD as a first step towards procurement eligibility. To be considered for PEPFAR procurement a HIV RDT product must receive a favorable ERPD outcome, however a favorable ERPD rating does not guarantee procurement or set volumes. If a product receives a favorable ERPD rating through this process, the next step will be to engage with the applicable manufacturers to discuss in country registration/eligibility, national algorithms, pricing, incoterms, and production capacity.

f) **How is the report generated by ERP on a specific RDT, will or could influence the WHO PQ process of that product?** The manufacturer agrees in the ERPD questionnaire that the materials are disclosed to the WHO PQ Team who will coordinate the ERPD assessment. The PQ assessment will be based on the PQ product dossier, performance evaluation and site inspection. The risk assessment conducted by the ERPD will not have a direct bearing on establishing whether the product meets prequalification requirements as the ERPD report is based only on manufacturer's information submitted with the questionnaire. However, it is expected that information submitted for the same product to either process is consistent.

g) **Will the EPRD process influence country specific algorithms in any way?** Products made available through the ERPD process expand the options available for countries to review during the verification studies for national algorithms. National algorithms are owned by countries and the timelines for those processes and associated product uptake vary country by country.

h) **What will be the role of national regulatory authorities after the ERPD review and approval? How much of the evaluations will the NRAs be doing so that it does not diminish this effort to promote local manufacturing?** Based on GF QA Policy, all products procured with GF funding should be approved by National Regulatory Authorities. ERPD reports are shared with suppliers. Manufacturers can use this report to support their application to National Regulatory Authorities.

i) **Most countries require at least WHO PQ before they will consider evaluating an HIV RDT in-country, let alone adopting one for routine public sector use. What**

has been the engagement with country program directors and National Regulatory Authorities on the acceptability and feasibility of this ERPD pathway for African-manufactured products without PQ? Engagement by partners with Country Program Directors and NRAs is ongoing to ensure that ERPD assessed products can be considered for inclusion in national algorithms. National algorithms are owned by countries and the timelines vary by country.

j) **Are GF and PEPFAR willing to accept higher pricing?** The GF's tender evaluation considers the overall value of a supplier's offer, including total landed costs and contribution to strategic priorities, which means some pricing arbitrage can be acceptable. PEPFAR considers many different factors in making procurement awards, pricing is one important factor amongst several other factors. Consideration of total landed cost which includes freight and logistics in the total cost is evaluated before making any procurement decisions or awards.

k) **Does the GF have a target of how much it will procure from regional manufacturers?** The GF procurement follows value for money principles and plans to increase procurement from regional manufacturers that meet the required eligibility criteria. To date, the GF is procuring 11% ITNs, 18% Antimalarials and over 70% general medicines in the Africa continent.

l) **What is an SRA?** This abbreviation stands for "Stringent Regulatory Authority". For further information, see the document on the WHO PQ website https://apps.who.int/iris/bitstream/handle/10665/350642/9789240033146-eng.pdf, and the Global Fund's Quality Assurance Policy https://www.theglobalfund.org/en/sourcing-management/quality-assurance/ & https://www.theglobalfund.org/en/sourcing-management/

m) **How long does it take to get ERPD review letter and Homepage listing after the EOI submission?** On average 6 months average but it depends on the number of applications received

5. Partnership

a) How is GF and PEPFAR going to push procurement through manufacturers who make the substantial investment needed to enter into African manufacturing? PEPFAR's numbers show that, while relatively few self-tests have been procured historically, they have not come from the only company currently already manufacturing in Africa. Where is the incentive for manufacturers to make this investment, how can they be sure that they will see a return on their investment to ensure the sustainability of a long-term commitment to local and regional manufacturing? At the policy level, partners continue to work with WHO to ensure there is clear guidance to countries on HIV testing, including for HIV self-testing and use of blood and oral products. At the programmatic level, partners will provide technical assistance to countries to expand use of high quality, efficient and effective tools. At the operational level, partners will continue to work with manufacturers to collaborate on demand forecasting and capacity building to ensure optimized access to affordable, quality assured products. There is also an expectation that manufacturers will create demand for their products at the country level and do direct marketing in both the public and private sectors within countries. Manufacturers should not rely solely on donors for marketing of HIV products.

b) **What is the role of African Medicine Agency (AMA)? How will Global Fund use the current structures in Africa for facilitated approvals of IVDs in Africa**? While

AMA is being operationalized and the scope of its prioritized activities are being clarified, WHO shall engage nominated experts from NRAs of the Region to participate in WHO product evaluation activities. This will promote awareness, trust and capacity building which are important in building the capacity of AMA to take up its roles as defined in the treaty. Global Fund is also engaging with the Africa Medicines Regulatory Harmonization (AMRH) program of Africa Development Agency-New Partnership for Africa's Development (AUDA-NEPAD) on additional collaboration avenues.

6. Available Support

a) **My manufacturing facility doesn't currently comply with the GMP requirements. What support is available? How can we access it?** Compliance with GMP / QMS requirements is essential for IVD manufacturing. The investment required to strengthen QMS varies by manufacturer, and it tends to be cross-cutting and affects many aspects of production and the business. Most RDT manufacturers located in jurisdictions with limited IVD manufacturing regulatory oversight can expect to increase QA/QC staff to improve and document production and quality control processes. That said, frequently manufacturers couple facility and new equipment upgrades with investments in QMS. As a first step, engaging skilled professionals with expertise in QMS, RDT manufacturing/business is recommended. A gap analysis can be developed, with a plan for investment and strengthening. Manufacturers can approach the WHO Local production and technical assistance team to seek support. Partners, including FIND, can make recommendations.

b) **We are supplying HIV tests for several years, and we want to be a partner of a local manufacturer and share our know-how to produce RDT's in Africa. How can Global Fund support outside manufacturers to meet the right partner in the continent in order to manufacture locally?** Partners encourage tech and know-how transfer between manufacturers; in the past year, several partners have convened several manufacturer meetings to facilitate such introductions. Going forward, Africa CDC will be conducting a mapping/landscaping and partners will look for opportunities to facilitate introductions between international and African manufacturers.

c) **To ensure capacity is built for local manufacturers already situated in Africa: What support, in terms of technical expertise and strategic partnerships, can be provided now? Are there opportunities or partnerships with institutions that can help develop the necessary technical expertise? Are there initiatives and support aimed at capacity building and training for local manufacturers to enhance their skills and capabilities in rapid test production, including the reagents and biological materials? Is there ongoing research and development related to HIV rapid tests and their biomarkers in the region?** FIND and Unitaid opened a call in Q3 2023 to support African manufacturing, and many of the activities noted above would be eligible for support. For example, FIND can facilitate introductions to skilled professionals and technical experts depending on the African manufacturers' needs. Funding may support manufacturing capacity expansion; strengthening QMS, commercial and manufacturing operations; and product development. Technical assistance to support tech transfers, product development, QMS, market analysis and business development is also possible.