WHO PREQUALIFICATION TEAM:
DIAGNOSTICS

World Health Organization

Invitation to manufacturers of in vitro diagnostics for Monkeypox virus nucleic acid detection to submit an application for emergency use listing by WHO.

1 Introduction

Mpox has been reported in the Democratic Republic of the Congo (DRC) for more than a decade, and the number of cases reported each year has increased steadily over that period. In July 2022, the multi-country outbreak of mpox was declared a Public Health Emergency of International Concern (PHEIC) as it spread rapidly via sexual contact across a range of countries where the virus had not been seen before. That PHEIC was declared over in May 2023 after there had been a sustained decline in global cases. However, last year, reported cases again increased significantly in DRC, and mpox continues to affect people around the world. The detection and rapid spread of a new clade (Clade Ib) of Monkeypox virus in eastern DRC, its detection in neighbouring countries that had not previously reported mpox, and the potential for further spread within Africa and beyond has prompted the renewal of its classification as a PHEIC as of 14. August 2024.

The WHO Emergency Use Listing (EUL) Procedure is primarily used during a PHEIC. The EUL process is based on an essential set of available quality, safety and performance data. The EUL procedure for IVDs to detect Monkeypox virus is intended to expedite the availability of IVDs needed in PHEIC situations and, in that context, to assist interested UN procurement agencies and Member States in determining the acceptability of using specific products for time limited procurement.

2 Purpose of this invitation for EOI

The purpose of this Expression of Interest (EOI) is to invite manufacturers to submit IVDs for Monkeypox virus nucleic detection for review by WHO through an emergency assessment mechanism.

3 Product categories included in this EOI

- IVDs for the detection of mpox nucleic acid (multiplex assays, detecting more than one non-variola Orthopox virus targets, at least one target must be Monkeypox virus specific)
- Differentiation of Monkeypox virus clades I and II is preferred but not required.

Contact diagnostics@who.int for further information.

4 Submission of applications

Applicants are strongly encouraged to contact WHO as early as possible to discuss specifics of the application. Applications are accepted **only** from legal manufacturers. Rebranded products are outside

the scope of EUL assessment and hence not accepted for assessment.[1] All manufacturers interested in submitting applications for review are requested to follow the steps below:

4.1 Pre-submission meeting

Manufacturers who are interested in an EUL submission are invited to contact diagnostics@who.int to arrange a pre-submission meeting/call. Please note that applications will not be accepted without prior consultation with WHO.

4.2 Application letter (see Annex 3 Application letter model in the Emergency Use Listing Procedure document[2])

The manufacturer is requested to submit an application letter to WHO's Director of Regulation and Prequalification Department (RPQ), Dr Rogerio Pinto de sá Gaspar (gasparr@who.int), with a copy to the PQT/IVDs Assessment Team Lead, Ms Irena Prat (prati@who.int), the mpox EUL IVD focal point, Dr Ute Ströher (stroheru@who.int) and diagnostics@who.int.

The application letter should include

- The product name and product code,
- Name and address of the legal manufacturer,
- Title and name of the authorized contact for the EUL assessment,
- Sites of manufacture,
- Information on whether the National Regulatory Authority (NRA[3]) has issued an authorization for emergency use or equivalent.

WHO will acknowledge receipt of the application letter by e-mail; the acceptance of an application will also be confirmed by email.

Once the product has been accepted for review under the EUL procedure, a product dossier will be requested.

4.3 Essential data requirements for IVD EUL:

The EUL procedure includes the following:

- **Quality Management Systems Review and Plan for Post-Market Surveillance**: review of the manufacturer's Quality Management System documentation and specific manufacturing documents;
- **Product Dossier Review**: assessment of the documentary evidence of safety and performance.
- WHO reserves the right to conduct an **independent laboratory evaluation** of all EUL-listed IVDs or to require the manufacturers to participate in the blinded testing of their EUL-listed products via a performance panel. The same can also apply to products that are under EUL assessment.

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[1] A rebranded product is identical in every respect to the product manufactured by the original manufacturer, except that the product is labelled with the "rebranded" product name and product code and bears the rebrander's name. Such products are also known as original equipment manufacturer (OEM) products.

[2] https://extranet.who.int/pqweb/key-resources/documents/emergency-use-listing-procedure-eul

[3] The NRA of the country where the manufacturer is located.

Instructions on the essential data/validation requirements for IVDs to be submitted will be available in the near future on the following webpage: https://extranet.who.int/prequal/vitro-diagnostics/emergency-use-listing-procedure . The instructions are subject to change as more is learnt about mpox, and the risk-benefit profile mpox IVDs. Any updates will be published on our website as they become available. Furthermore, manufacturers are invited to consult the target product profiles that outline desirable and minimally acceptable profiles for different mpox IVD categories[4] and "Diagnostic testing for the monkeypox virus (MPXV) - Interim guidance"[5] . The EUL submission structure must follow the format prescribed in the respective instructions document.

4.4 Submission of updates

Manufacturers are required to inform WHO of any planned changes to the IVD and submit additional information on the development of the product, particularly if it may affect the product's benefit/risk assessment.

5 Submission

The information on how to apply is provided in the presubmission call.

6 Process for assessment

The assessment will consider all evidence of the quality, safety and performance of IVDs that is made available to WHO for review.

7 Process for listing

Upon making a decision whether or not to grant a recommendation (acceptance or nonacceptance) for emergency use listing of the assessed product, WHO will (without prejudice to any confidential information of the applicant/manufacturer) publish information about the product in a public report available on a dedicated portal of the WHO website. This may include negative assessment outcomes.

Subject to the protection of commercially sensitive confidential information, WHO will publish on the WHO website and make publicly available the following information in connection with the assessment process:

- the names of products and of manufacturers that have applied for EUL, the product code(s) submitted for EUL and the EUL status of each application;
- a WHO EUL public report summarizing the findings of the EUL assessment; and
- any negative outcomes of the EUL assessment.

In addition, WHO reserves the right to share full reports with the relevant authorities of any interested Member State of the Organization and interested United Nations agencies.

8 Post – listing activities

Subject to inclusion of the product in the WHO EUL list, any reportable changes to the product (as defined in the WHO guidance document PQDx_121 v2 *"Reportable WHO Prequalified In Vitro Diagnostic Medical*

[4] https://www.who.int/publications/i/item/9789240076464
[5] https://www.who.int/publications/i/item/WHO-MPX-Laboratory-2024.1

Device"[6] must be reported to WHO. In addition, the listing status of the product may be reconsidered in light of a review by WHO of the change information. WHO reserves the right to ask for further information to support the change.

After a product has been listed, the manufacturer is required to also take into consideration the post-market surveillance activities (as defined by WHO guidance "*Post-market surveillance of in vitro diagnostics*" ISBN 978 92 4 150921 3 https://www.who.int/health-topics/substandard-and-falsified-medical-products/safety-info-medical-devices-in-vitro-diagnostics). In addition, the listing status of the product may be restricted or revoked by WHO in light of its review of post-market surveillance information.

WHO EUL listing in the context of a public health emergency is granted for a period of 12 months and may be renewed, upon request from the manufacturer, provided that the information requested by WHO is submitted within agreed timelines.

9 Contact information

Please refer to the EUL webpage https://extranet.who.int/prequal/vitro-diagnostics/emergency-use-listing-procedure

Any inquiries should be addressed to: diagnostics@who.int

[6] https://iris.who.int/bitstream/handle/10665/251915/WHO-EMP-RHT-PQT-2016.01-eng.pdf;jsessionid=830C82950055325AF37A0A8302BE4623?sequence=1