



**Invitation to manufacturers of Ebola virus in vitro diagnostics
to submit an Expression of Interest (EOI) for emergency assessment by WHO
(Originally issued 18 September 2014)
(Revised version issued 02 October 2014)**

1. Introduction

Given the outbreak of Ebola virus disease (EVD) in West Africa, there is an urgent need to scale up confirmed diagnosis of individuals suspected of EVD in order to stop transmission of the virus. Therefore, WHO has established an emergency quality assurance mechanism for review of available in vitro diagnostics (IVDs) for EVD in view of their procurement by WHO and other partners.

2. Purpose of this invitation for EOI

The purpose of this Expression of Interest (EOI) is to invite submissions of IVDs for EVD for review by WHO through an emergency quality assessment mechanism. This invitation applies to products that can provide either a qualitative or quantitative result for the presence or absence of the virus or any analyte that would signal the presence of the virus in order to facilitate clinical decision making.

3. Product categories included in this EOI

- Assays for the detection of Ebola virus antigen using a rapid diagnostic assay format (immunochromatography or immunofiltration).
- Real-time nucleic acid based assays for the direct detection of Ebola virus including extraction and amplification/detection reagents.

4. Submission Requirements

All manufacturers interested in submitting applications for review are requested to submit the following information, **where available**, for each product under consideration:

4.1. Required information:

4.1.1. Instructions for use: The product dossier should contain a complete set of labelling associated with the product. This includes:

- labels
- instructions for use (IFU)
- if applicable, the instrument manual
- any other instructional materials provided to the user.

4.1.2. Product Performance Specification, and Associated Validation and Verification Studies

It is acknowledged that most of the currently available IVDs for EVD are not yet authorised for use based on any stringent regulatory review. Therefore, the manufacturer shall submit, where available, relevant investigations to support the intended use. For each study to be submitted, the following must be provided:

- Study description, study identifier, product identifier (for example, lot numbers), IFU version used, the date of initiation and the date of completion;

- a summary of the study findings including a conclusion that clarifies how the study objectives have been met; and
- the study protocol and full report.

4.1.2.1.1. Specimen type

This section contains information on the types of specimens that can be used with the IVD.

4.1.2.1.2. Analytical performance characteristics

Accuracy of measurement: trueness and precision studies.

Analytical sensitivity: analytical sensitivity of the IVD.

Analytical specificity: interference and cross reactivity studies.

Traceability of calibrators and control material values: traceability of values assigned to calibrators and trueness control materials supplied with the assay (if applicable) and those used for the manufacturing process.

Measuring range of the assay: measuring range of the assay (linear and non-linear measuring systems), including the limit of detection.

Validation of assay cut-off: determination of assay cut-off.

Validation of assay procedure – reading time: reading time (minimum-maximum reading window) claimed in the IFU was determined.

4.1.2.1.3. Stability (excluding specimen stability)¹

Claimed shelf life: stability testing studies to support the claimed shelf life of the IVD.

In-use stability: in-use stability for each component of the IVD.

Shipping stability: shipping stability studies for the IVD.

4.1.2.1.4. Robustness Studies

Robustness (flex) studies are designed to challenge the system under conditions of stress to identify potential device deficiencies, including failures, and determine the robustness of the product.

4.1.2.1.5. Clinical evidence (clinical or diagnostic sensitivity and specificity)

Clinical evaluation – Manufacturer: All performance claims should be supported by well-designed performance evaluations that have been carried out or coordinated by the manufacturer.

Clinical evaluation - Independent study: Details of at least one well-designed independent performance evaluation for the IVD.

4.1.3. Quality management systems requirements

- Provide evidence of implementation a manufacturing quality management system (ISO 13485:2003 certificate and most recent regulatory audit report, quality manual, exclusions or non-applications, list of valid quality management documentation, management review report);
- Details of the production workflow including QC points (in process and final release activities);
- Critical supplier list including supplied products (components / raw materials) and services;
- Details on the experience with the product (when was the product developed and when was it first placed on the market);
- Details on the manufacturing capacity (existing inventory, minimum time to provide finished product, maximum batch size).

¹ Shelf-life, in-use stability and shipping stability information provided under this section must be consistent with the instructions for use and product labels provided within the product dossier.

5. Submission

Interested manufacturers are encouraged to submit expressions of interest for IVDs for EVD by sending the required documentation in hard copy and in electronic copy (CD or DVD) to the following address:

WHO Prequalification Team - Diagnostics

Regulation of Medicines and other Health Technologies

HIS/EMP/RHT/PQT – Diagnostics

World Health Organization

20 Avenue Appia

1211, Geneva 27

Switzerland

The deadline for submission of expressions of interest is 17 October 2014. This deadline may be extended at the discretion of WHO.

6. Process for Assessment

The process for emergency assessment is under preparation and will be published as a separate document. The assessment will take into account all evidence of the quality, safety and performance of IVDs for EVD that is made available to WHO for review.

7. Confidentiality

The assessors will treat all information to which they will gain access during the evaluation, or otherwise in connection with the discharge of their responsibilities in regard to this procedure, as confidential and proprietary to WHO or parties collaborating with WHO in accordance with the terms set forth below.

Assessors will take all reasonable measures to ensure that confidential information:

- Is not used for any purpose other than the assessment activities described in this document; and
- Is not disclosed or provided to any person who is not bound by similar obligations of confidentiality and non-use as contained herein.

8. Contact information

For more information on any of the requirement sections listed above and related references, please follow this link: <http://goo.gl/2j36lz>

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