WHO Emergency Use Assessment and Listing for EVD IVDs
PUBLIC REPORT

Product: Xpert® Ebola Assay
Number: EA 0020-019-00

Abstract

In order to respond to the urgent need for quality-assured in vitro diagnostics in the ongoing Ebola Virus Disease (EVD) outbreak in West Africa, WHO has established the Emergency Use Assessment and Listing for EVD IVDs. It consists of a review of any existing evidence of safety and performance; a desktop review of selected manufacturing and quality management systems documentation and limited laboratory evaluation of the product.

**Xpert® Ebola Assay** with product code GXEBOLA-10 manufactured by Cepheid AB, Röntgenvägen 5, Solna, 171 54, Sweden was listed as eligible for WHO procurement on 8 May 2015.

**Xpert® Ebola Assay**
The Xpert Ebola Assay is a real-time reverse transcription polymerase chain reaction (RT-PCR) test intended for the qualitative detection of RNA from the Ebola Zaire virus (detected in the West Africa outbreak in 2014) in EDTA venous whole blood from individuals with signs and symptoms of Ebola virus infection.

The Xpert Ebola Assay is an automated test for qualitative detection of the Zaire strain of the Ebola virus. The assay is performed on the Cepheid GeneXpert Instrument Systems.

The GeneXpert Instrument Systems automate and integrate sample purification, nucleic acid amplification, and detection of the target sequence in simple or complex samples using real-time reverse transcription PCR. The systems consist of an instrument, personal computer, and preloaded software for running tests and viewing the results. The systems require the use of single-use disposable GeneXpert cartridges that hold the real-time reverse transcription PCR reagents and host the real-time reverse transcription processes. Because the cartridges are self-contained, cross-contamination between samples is minimized.

The Xpert Ebola Assay includes reagents for the detection of Zaire Ebola virus total nucleic acids in specimens as well as a sample adequacy control and an internal control and to ensure adequate addition of sample, processing of the target and to monitor presence of inhibitor(s) in the RT and PCR reactions. The Probe Check Control (PCC) verifies reagent rehydration, PCR tube filling in the cartridge, probe integrity and dye stability.

The Xpert Ebola Assay kit contains sufficient reagents to process 10 specimens or quality control samples. The kit contains the following:

- GeneXpert Ebola Assay Cartridges with Integrated Reaction Tubes (10)
- Freeze-dried Bead 1, Bead 2, and Bead 3 (1 of each per cartridge)
- Rinse Reagent (0.5 mL per cartridge)
- Elution Reagent (2.0 mL per cartridge)
- Binding Reagent (2.0 mL per cartridge)
- Ebola Sample Reagent Box - Sample Reagent (1 per kit)
- Lysis Reagent - Guanidinium Thiocyanate (10 x 2.5 mL per bottle)
- Disposable 1 mL Transfer Pipettes (5 bags of ten)
- CD

**Materials Required but Not Provided**

- GeneXpert Dx System or GeneXpert Infinity Systems (catalog number varies by configuration): GeneXpert Instrument, computer with proprietary GeneXpert Software Version 4.4a or higher, Xpertise 6.2 or higher, barcode scanner, and operator manual
- Printer: If a printer is required, contact Cepheid Technical support to arrange for the purchase of a recommended printer.
- Disposable Swabs (catalog # SWAB/E-50)
- Chlorine Bleach

**Storage**: Store the Xpert Ebola Assay cartridges and reagents at 2–28 °C.

**Shelf-life upon manufacture**: 6 months

**Background information**


1. **Product dossier assessment**

   Cepheid AB was granted Emergency Use Authorization by the U.S Food And Drug Administration for the Xpert® Ebola Assay in March 2015. The information submitted to FDA and the outcome of the review was considered sufficient to fulfil requirements for eligibility for procurement by WHO.

   Safety and performance documentation assessment conclusion: acceptable.

2. **Review of quality management documentation**

   To establish the eligibility for WHO procurement, Cepheid AB was asked to provide up-to-date information about the status of their quality management system.
Based on the review of the submitted quality management system documentation, it was established that sufficient information was provided by Cepheid AB to fulfil the requirements described in the “Invitation to manufacturers of Ebola Virus In Vitro Diagnostics to submit an Expression of Interest (EOI) for Emergency Assessment by WHO”.

Quality management documentation assessment conclusion: acceptable.

3. Laboratory evaluation

A limited analytical evaluation of the Xpert® Ebola Assay was conducted by the Bernhard Nocht Institute for Tropical Medicine (BNITM) in Hamburg, Germany which is a WHO Collaborating Centre for Arbovirus and Haemorrhagic Fever Reference and Research. The limit of detection (LOD) of the assay was verified and compared to the RealStar® Filovirus Screen RT-PCR Kit 1.0 (altona Diagnostics GmbH) using simulated specimens generated by spiking cell culture supernatants containing infectious Ebola virus strain Makona into whole blood of a healthy donor. The evaluation of the Xpert® Ebola Assay was performed on the GeneXpert-IV System.

The 95% limit of detection of the assay was found to be 82.0 RNA copies/reaction, 95% CI 39.7 to 3193.6 copies/reaction.

Laboratory evaluation conclusion: acceptable.

Scope and duration of procurement eligibility

The Xpert® Ebola Assay with product code GXEBOLA-10 manufactured by Cepheid AB Limited is considered to be eligible for WHO procurement. The assay may be used to test symptomatic individuals for EVD. This listing does not infer that the product meets WHO prequalification requirements and does not mean that the product is listed as WHO prequalified.

As part of the on-going requirements for listing as eligible for WHO procurement, Cepheid AB must engage in post-market surveillance activities to ensure that the product continues to meet safety, quality and performance requirements. Cepheid AB is required to notify WHO of any complaints, including adverse events related to the use of the product within 7 days. Furthermore, WHO will continue to monitor the performance of the assay in the field.

WHO reserves the right to rescind eligibility for WHO procurement, if additional information on the safety, quality and performance comes to WHO’s attention during post-market surveillance activities.

Commitment to WHO

As a requirement to listing, the manufacturer is required to participate in the WHO collaborative study for the assessment of the suitability of an interim standard for Ebola virus nucleic acid amplification tests.