

WHO Emergency Use Assessment and Listing for Ebola Virus Disease IVDs PUBLIC REPORT

Product: FilmArray Biothreat-E
EUAL Number: EAE 0433-154-00

Abstract

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

FilmArray Biothreat-E with product code **RFIT-ASY-0122** manufactured by BioFire Defense LLC., Salt Lake City, UT 84107, USA was re-listed as eligible for WHO procurement on 13 June 2019.

Intended use:

The FilmArray BioThreat-E test is a qualitative multiplexed nucleic acid-based in vitro diagnostic (IVD) test intended for the presumptive detection of Ebola Zaire virus (detected in the West Africa outbreak in 2014) in whole blood specimens or undiluted urine specimens.

The FilmArray BioThreat-E test is performed on the FilmArray Instrument to detect RNA from the Ebola Zaire virus in specimens from individuals with signs and symptoms of Ebola virus infection in conjunction with epidemiological risk factors.

Testing with the FilmArray BioThreat-E test should not be performed unless the individual has signs and symptoms of infection with Ebola Zaire that meet clinical and epidemiologic criteria for testing suspect specimens.

Test results are for the presumptive identification of Ebola Zaire virus. The definitive identification of Ebola Zaire virus requires additional testing and confirmation procedures in consultation with public health or other authorities for whom reporting is required. The diagnosis of Ebola virus infection must be made based on history, signs, symptoms, exposure likelihood, and other laboratory evidence in addition to the identification of the Ebola Zaire virus. The level of Ebola Zaire virus that would be present in blood or urine from individuals with early infection is unknown. Due to the difficulty in obtaining clinical specimens, this test was evaluated with limited numbers of contrived specimens spiked with inactivated Ebola Zaire virus and limited numbers of blood and urine specimens from individuals infected with the Ebola Zaire virus. Negative results do not preclude Ebola Zaire virus infection and should not be used as the sole basis for patient management decisions.

Intended user:

Clinical laboratory personnel that have been appropriately trained.

Acceptable specimen types:

- Whole Blood
- Urine

NOTE: Urine should not be the sole specimen tested from a patient. If a urine specimen from a patient is tested, it must be tested in conjunction with a whole blood specimen from the patient.

Components of FilmArray Biothreat-E kit with product code RFIT-ASY-0122 (6 tests)	Description of contents sufficient to test 6 specimens
Individually packaged FilmArray BioThreat-E pouches	6
Single-use (1.0 mL) Sample Buffer ampoules	7 x 1.0mL
Single-use freeze-dried protease vials	7
Single-use pre-filled (1.5 mL) Hydration Injection Vials (blue)	7 x 1.5mL
Single-use Sample Injection Vials (red)	7
Individually packaged Transfer Pipettes	7
Instructions for use	1

Materials required but not provided

Name
FilmArray System with computer
FilmArray Pouch Loading Station compatible with the use of the FilmArray Injection Vials (included with FilmArray System)
Bleach
De-ionized water

Optional materials not provided with kit:

Information on how to obtain optional external control material is posted on the BioFire Defense, website at: <http://biofiredefense.com/support/filmarray-support/>

Storage:

Store the test kit, including reagent pouches and buffers at 15-25 °C. Do not refrigerate.

Limitations:

- A subset of the performance data presented in the 'Instruction for Use' was collected using previous versions of the test.
- The FilmArray BioThreat-E Panel may cross-react with high concentrations of members of the *Bundibugyo* and *Tai Forest ebolavirus* species.

Background information

BioFire Defense LLC. submitted an expression of interest for WHO emergency quality assessment of **FilmArray Biothreat-E** on 20 October 2014.

1. Product dossier assessment

BioFire Defense LLC. was granted Emergency Use Authorization by the U.S Food and Drug Administration for the FilmArray Biothreat-E in 25 October 2014. 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, BioFire Defense LLC. 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 BioFire Defense LLC. 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 **FilmArray Biothreat-E** 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 **FilmArray Biothreat-E** was performed on the FilmArray System.

The 95% limit of detection of the assay was found to be 4059 RNA copies/reaction, 95% CI 3272 to 5097 copies/reaction.

Laboratory evaluation conclusion: acceptable.

Commitment to WHO

As a requirement to listing, the manufacturer is required update the current version (RFIT-PRT-0302-03, June 2016) of the instructions for use by 31 December 2019.

Scope and duration of procurement eligibility

The **FilmArray Biothreat-E** with product code **RFIT-ASY-0122** manufactured by BioFire Defense LLC. 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 BioFire Defense LLC. must engage in post-market surveillance activities to ensure that the product continues to meet safety, quality and performance requirements. BioFire Defense LLC. 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.