WHO Emergency Use Assessment and Listing for EVD IVDs
PUBLIC REPORT

Product: STANDARD™ Q Ebola Zaire Ag
EUAL Number: EAE 0444-117-00

Abstract

In order to respond to the urgent need for quality-assured in vitro diagnostics in the event of Ebola Virus Disease (EVD) outbreak, WHO has established a WHO Emergency Quality Assessment Mechanism of In Vitro Diagnostics (IVDs) for EVD. It consists of 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.

STANDARD™ Q Ebola Zaire Ag with product code 05EZ10 (CE-marked version) manufactured by SD Biosensor Inc. 16, Deogyeong-daero 1556beon-gil, Yeongtong-gu, Suwon-si, Gyeonggi-do, 16690, Republic of Korea was listed as eligible for WHO procurement on 8 September 2015. This public report was amended on 20 February 2019 to reflect the inclusion of the latest Instructions for Use and an update to the product name.

Intended use: STANDARD Q Ebola Zaire Ag is a chromatographic immunoassay for the presumptive qualitative detection of Ebola Zaire virus disease in whole blood, plasma or serum from individuals with signs and symptoms of Ebola virus infection in affected areas in conjunction with relevant epidemiological risk factors. This assay is intended for professional use, only for an initial screening test.

Intended user: Professional use only.

Principle STANDARD Q Ebola Zaire Ag test device has 4 pre-coated lines, “T1” (Test line 1), “T2” (Test line 2), “T3” (Test line 3) and “C” (Control line). Mouse monoclonal antibodies specific to Zaire Ebola virus glycoprotein (GP) and mouse monoclonal antibodies specific to Zaire Ebola virus nucleoprotein (NP) and mouse monoclonal antibodies specific to Zaire Ebola virus viral matrix protein (VP40) are on the test region (“T1”, “T2” and “T3”) separately. Mouse monoclonal antibodies specific to Zaire Ebola virus GP, NP and VP40—colloid gold conjugate reacts with the Zaire Ebola virus in the specimen. They move along the membrane chromatographically to the test region (“T1”, “T2” and “T3”) and form a visible line as the antibody-antigen-antibody gold particle complex with high degree of sensitivity and specificity. Three test lines and control line in the result window are not visible before applying any specimen. The control line is used for procedural control and should always appear if the test procedure is performed correctly.
The STANDARD™ Q Ebola Zaire Ag kit contains sufficient reagents to process 25 specimens or quality control samples. The kit contains the following:

<table>
<thead>
<tr>
<th>Components of STANDARD™ Q Ebola Zaire Ag kit</th>
<th>25 Tests/Kit</th>
<th>05EZ10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test Device</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Positive Control swab</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Negative Control swab</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Control swab extraction buffer (0.3ml/tube)</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Disposable dropper</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Disposal bag</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Instructions for use:</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

Materials required but not provided:

<table>
<thead>
<tr>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Timer or watch</td>
</tr>
<tr>
<td>Materials required for venipuncture whole blood specimen collection</td>
</tr>
<tr>
<td>Materials required to obtain a fingerstick whole blood specimen</td>
</tr>
</tbody>
</table>

Storage:
Store the test kit at 2 to 40°C. Do not freeze the kit components.
*Note: When kit is stored at refrigerator, all kit components must be brought to room temperature (15 to 40°C) minimum 30 minutes prior to use.

Background information

SD Biosensor Inc. submitted an expression of interest for WHO emergency quality assessment of STANDARD™ Q Ebola Zaire Ag on 9 February 2015.

1. Product dossier assessment

SD Biosensor Inc., submitted documentation in support of safety and performance for STANDARD™ Q Ebola Zaire Ag as per the “Invitation to Manufacturers of Ebola Virus In Vitro Diagnostics to Submit an Expression of Interest (EOI) for Emergency Assessment by WHO”.¹ The information submitted in the product application was reviewed by WHO staff and external experts (reviewers) appointed by WHO. The findings of the reviews were reported in accordance with “Emergency Quality Assessment Mechanism of In Vitro Diagnostics for Ebola Virus Protocol for the Review of Documentary Evidence of Safety, Quality and Performance” (document number WHO PQDx_0188 v0.2).

Safety and performance documentation assessment conclusion: acceptable.

¹ Invitation to manufacturers of Ebola virus in vitro diagnostics to submit an Expression of Interest (EOI) for emergency assessment by WHO. Accessed on 24 November 2014 at http://www.who.int/diagnostics_laboratory/141002_revised_invitation_to_mx_of_ebola_virus_diagnostics_rc.pdf?ua=1
2. Review of quality management documentation

To establish the eligibility for WHO procurement, SD Biosensor Inc. 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 SD Biosensor Inc. 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

The STANDARD™ Q Ebola Zaire Ag kit was assessed in a blinded, cross-sectional study to aiming at determining the comparative performance of several antigen detection tests for EVD. The performance evaluation was conducted in two separate arms, one prospective, using fresh, whole blood specimens and a retrospective arm on a selected set of archived, de-identified plasma specimens. Results were compared to conventional molecular testing with RT-PCR using the RealStar Filovirus Screen RT-PCR Kit 1.0 (altona Diagnostics GmbH) as benchmark assay. The archived specimens were selected to reflect representative populations seen in 1) passive case-finding (i.e. EVD identified in symptomatic patients who have arrived at a treatment center) and 2) active case-finding (i.e. EVD identified in individuals actively sought by healthcare workers from among case contacts and other at-risk individuals in the field). There was no study-related follow-up and study results were not used for patient care.

Retrospective specimens were obtained from: EU Mobile Lab (Hastings), Nigeria Mobile Laboratory (Kambia), PHE Laboratories (Kerrytown, Port Loko, Makeni). Whole blood specimens were collected from the Public Health England (PHE) laboratory in Makeni, Sierra Leone.

A total of 446 initial patient specimens were selected, comprising 100 fresh whole blood specimens and 346 stored plasma specimens.

Performance of the STANDARD™ Q Ebola Zaire Ag kit when compared with the RealStar Filovirus Screen RT-PCR Kit 1.0 (altona Diagnostics GmbH):

<table>
<thead>
<tr>
<th>Performance</th>
<th>Number tested</th>
<th>Performance (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity on whole blood and plasma</td>
<td>126</td>
<td>84.9% (78.6–91.2)</td>
</tr>
<tr>
<td>Specificity on whole blood and plasma</td>
<td>289</td>
<td>99.7% (99.1–100.0)</td>
</tr>
</tbody>
</table>

Laboratory evaluation conclusion: acceptable.
Scope and duration of procurement eligibility

The STANDARD™ Q Ebola Zaire Ag kit with product code 05EZ10 manufactured by SD Biosensor Inc. 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, SD Biosensor Inc. must engage in post-market surveillance activities to ensure that the product continues to meet safety, quality and performance requirements. SD Biosensor Inc. 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

Participation in further WHO coordinated studies as requested.
Labelling

1. Instructions for Use
**PREPARATION OF CONTROL**

Insert each control swab(Positive) or (Negative) into the control swab extraction buffer(s) and seal the swab(s) for at least ten seconds. Remove the swabs.

**PROCEDURE OF THE TEST (REFER TO FIGURE ON BACK PAGE)**

1. Allow all kit components and specimen to come to room temperature (15 - 30°C) before testing.
2. Remove all kit components from the foil pack prior to use, and place it on a flat, dry surface.
3. As the test begins to work, you will purple color move across the result window in the center of the test device. Read the test result at 20 ± 10 minutes. Do not read after 30 minutes.
4. After test is done, discard used test components into the disposal bag(s).

**INTERPRETATION OF THE RESULTS (REFER TO FIGURE ON BACK PAGE)**

### [Negative result]

- A color appears on the control ("C") line only.

### [Positive result]

- Zaire Ebola virus Glycoprotein(GP) Positive
  - The presence of two color lines ("C" and "T") within the result window no matter which line appears first, indicates Zaire Ebola virus infection.
- Zaire Ebola virus Nucleoprotein(NP) Positive
  - The presence of two color lines ("C" and "T") within the result window no matter which line appears first, indicates Zaire Ebola virus infection.
- Zaire Ebola virus VP40 Positive
  - The presence of four color lines ("C", "T1", "T2", and "T3") in the result window no matter which line appears first, indicates Zaire Ebola virus infection.

### [Invalid result]

- If the control ("C") line color fails to appear, the result might be considered invalid. It is recommended that the sample need to be retested.

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**COLLECTION, STORAGE AND PREPARATION OF SPECIMEN**

**[Whole blood]**

- Collect the venous whole blood into the anticoagulant such as heparin, EDTA and sodium citrate tube.
- The capillary whole blood sample must be tested within one minute immediately after collection.

**[Serum or Plasma]**

- Serum or plasma are collected into the collection tube (NOT containing anticoagulants such as heparin, EDTA and sodium citrate) by venipuncture, leave to settle for 30 minutes for blood coagulation and then centrifugate the blood at 1,000g for 10 minutes.
- Remove the supermatant and then use the supernatant for testing.

[Plasma]

- Collect the whole blood into the collection tube (containing anticoagulants such as heparin, EDTA and sodium citrate) by venipuncture and then leave to settle for 30 minutes for blood coagulation, and then centrifugate at 1,000g for 10 minutes to get plasma supernatant.
- If test is not composed immediately, it should be refrigerated at 2 - 8°C up to six days.

- Store the specimen, store at -20°C or lower dry-ice storage, shelf life up to 36 months.
- If the serum or plasma specimens are kept in refrigerator or freezer, bring to room temperature (15 - 30°C) for 30 minutes prior to use.

**[Precautions]**

- Hemolyzed samples can lead to impaired test results. If a specimen is found to be hemolyzed, do not use the specimen.
- Use separate disposable dropper for each specimen in order to avoid cross-contamination of specimens which could cause erroneous results.
- Disodium citrate solution is not compatible with these test kits.
- Discard alcohol swab if package is pierced or damaged.
- Serum specimen and plasma specimen containing supermatant may yield inconsistent test results. Such specimens must be clarified by centrifugation at 1,000g for 10 minutes at 4°C prior to assay.
- There is a possible risk of false positive results when capillary whole blood is used as a specimen type instead of venous whole blood.
- Inappropriate collection and handling for venous and capillary whole blood can produce incorrect results.

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**STANDARD Q Ebola Zaire Ag**

STANDARD™ Q Ebola Zaire Ag

**READ INSTRUCTIONS CAREFULLY BEFORE YOU PERFORM THE TEST**

**EXPLANATION OF THE TEST**

**[Principle]**

- Standard Q Ebola Zaire Ag test device has 4 pre-coated lines, "T1"(Test line 1), "T2"(Test line 2), (T3) and "C"(Control line).
- "T1" and "T2" are specific to Zaire Ebola virus Glycoprotein (GP), and mouse monoclonal antibodies specific to Zaire Ebola virus nucleoprotein(NP) and mouse monoclonal antibodies specific to Zaire Ebola virus VP40.
- "C" is the test region ("T1", "T2" and "C") separately. Mouse monoclonal antibodies specific to Zaire Ebola virus GP, NP and VP40 – colloid gold conjugate react with the Zaire Ebola virus in the specimen. They move along the test region and interact immunologically with the test region ("T1", "T2" and "T3") and form a visible line as the antibody-antigen-antibody gold complex with high degree of sensitivity and specificity. Three test lines and control line in the result window are not visible before applying any specimen.
- The control line is used for procedural control and should always appear if the test procedure is performed correctly.

**[Intended use]**

- Standard Q Ebola Zaire Ag is a chromatographic immunomagnetic test for the presumptive qualitative detection of Zaire Ebola virus disease in whole blood, plasma or serum from individuals with signs and symptoms of Ebola virus infection in affected areas in conjunction with relevant epidemiological risk factors. This assay is intended for professional use, only for an initial screening test.

**MATERIALS PROVIDED / ACTIVE INGREDIENTS OF MAIN COMPONENTS**

**[Standard Q Ebola Zaire Ag includes]**

<table>
<thead>
<tr>
<th>No</th>
<th>Materials</th>
<th>25 Tests/Kit</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Test Device</td>
<td>100-vs.150 tubes</td>
</tr>
<tr>
<td>2</td>
<td>Positive Control Swab</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>Negative Control Swab</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>Control swab extraction buffer (0.2ml/tube)</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>Disposable dropper</td>
<td>25</td>
</tr>
<tr>
<td>6</td>
<td>Disposable bag</td>
<td>25</td>
</tr>
<tr>
<td>7</td>
<td>Instructions for use</td>
<td>1</td>
</tr>
</tbody>
</table>

### [Active ingredients of main components]


**2. Control swab components:** Mouse monoclonal anti-Zaire Ebola virus GP (0.33±0.1μg) / Test Line “2” (as main component); Mouse monoclonal anti-Zaire Ebola virus VP40 (0.65±0.1ug) / Control Line (as main component). Mixture of Reconstituted Zaire Ebola virus glycoprotein, nucleoprotein and matrix protein-antigen (C. 382±2μg). Nitrocellulose membrane (25x±4.0 x 0.8mm). Cartridge pad (7x1.4 x 4.0 x 0.8mm). Sample pad (18x2.6 x 4.0 x 0.8mm).

**3. Zaire Ebola Ag Positive Control Swab:** Reconstituted Zaire Ebola virus GP (0.50±0.1μg) / Test Line “1” (as main component), Reconstituted Zaire Ebola virus NP (0.50±0.1μg) / Control Line. Reconstituted Zaire Ebola virus VP40 (0.50±0.1μg) / Test Line “3” (as main component). 1/10 of Zaire Ebola virus Positive swab extract buffer (100 µl/Tube).

**[PREPARATION OF CONTROL]**

- 1/10 of Zaire Ebola virus Positive swab extract buffer and 1/10 of Zaire Ebola virus Negative swab extract buffer (100 µl/Tube).

### LIMITATIONS OF THE TEST

The following precautions should be followed when interpreting results of this test must be followed strictly when testing.

1. This test is limited to the detection of Zaire Ebola virus glycoprotein, nucleoprotein and matrix viral protein in the specimen. Detection of other species (Sudan, Bundibugio, Tai Forest) of Ebola virus is not confirmed yet.
2. Incubation period of Zaire Ebola virus infection is 2 - 21 days after exposure to Zaire Ebola virus. For patients having shown symptoms for 3 days in a line, it is confirmed that the sampling sample viral load could be below the limit of detection. If the test result is negative and clinical symptoms are persistent, additional follow-up test using other clinical methods is recommended after 3 days from the first. A negative result does not necessarily mean that there is no possibility of Zaire Ebola virus infection.
3. Test is useful as an initial screening test of Zaire Ebola virus infection, but it should not be used as the sole criterion for the diagnosis of Zaire Ebola virus infection. More specific and appropriate diagnosis methods should be performed in order to obtain the confirmation of Zaire Ebola virus infection.

### INTERNAL QUALITY CONTROL

1. Internal Quality control: The test device has Test Lines and Control Line on the surface of the test device. All Test Lines and Control Line in the result window are not visible before applying any specimen. The Control Line is used for procedural control. Control line should always appear if the test procedure is performed correctly.

2. External Quality control:
   - [1) Control Procedures: Positive and negative control swabs should be tested according to the [Preparation of Control] and [Procedure of the Test].
   - [2) Specification: - Zaire Ebola Ag Positive control swabs should be interpreted as test line “1”, “2” and “3” positive.
   - Zaire Ebola Ag Negative control swabs should be interpreted as negative.

### PERFORMANCE CHARACTERISTICS

1. Internal evaluation(Table-1): Limit of detection: LOD of STANDARD Q Ebola Zaire Ag is 12.5 ng/ml for recombinant Zaire Ebola virus GP, 50ng/ml for recombinant Zaire Ebola virus NP and 50ng/ml for recombinant Zaire Ebola virus VP40.

2. Reproducibility has been demonstrated by studies (within-run, between-run and batch-to-batch) with in-house reference panels. All values were identical to reference panel acceptance criteria.

| Table-1. Limit of detection of STANDARD Q Ebola Zaire Ag |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| **Concentration** | **STANDARD Q Ebola Zaire Ag** |
| 3500 ng/ml | Positive | Positive | Positive | Positive |
| 1500 ng/ml | Positive | Positive | Positive | Positive |
| 250 ng/ml | Positive | Positive | Positive | Positive |
| 62.5 ng/ml | Positive | Positive | Positive | Positive |
| 31.3 ng/ml | Weak Positive | Positive | Positive | Negative |
\textbf{INTRODUCTION}

1. First, open the package and look for the following:
   (1) Device Test
   (2) Positive Control Swab
   (3) Negative Control Swab
   (4) Control swab extraction buffer (3.3ml/tube)
   (5) Disposable dropper
   (6) Disposable bag.
   (7) Instructions for use.

2. Open the foil pouch and look for the following:
   - Result window
   - Sample port

\textbf{PREPARATION OF CONTROL}

Insert each control swab (Positive or Negative) into the control swab extraction buffer and swirl the swab for at least ten seconds. Remove the swab.

\textbf{TEST PROCEDURE}

1. Add 3 drops (about 100μL) of specimen into the sample port.

2. Read the test result at 20-30 minutes. Do not read after 30 minutes.

\textbf{INTERPRETATION OF THE RESULTS}

\textbf{[Negative Result]}

- One line “C” in result window.

\textbf{[Positive Result]}

- \( \text{GP Positive} \quad \text{Two lines “C” and “T1” in result window.} \\
\text{NP Positive} \quad \text{Two lines “C” and “T2” in result window.} \\
\text{VP40 Positive} \quad \text{Two lines “C” and “T3” in result window.} \\
\text{GP, NP and VP40 Positive} \quad \text{Four lines “C”, “T1”, “T2” and “T3” in result window.} \\
\text{[Invalid Result]} \\
- No control “C” line in result window.
- It is recommended that the specimen need to be retested.

\textbf{REFERENCES}

- Laboratory guidance for the diagnosis of Ebola Virus Disease in WHO 19/09/14

\textbf{BIBLIOGRAPHY}

2. World Health Organization (WHO), Personal protective equipment for use in a fluvirus disease outbreak - Rapid advice guideline.