GeneXpert
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Xpert® Hemorrhagic Fever Panel

REF **GXHF-10**

Instructions for Use

For Use with GeneXpert® Dx System

Cepheid

***In Vitro* Diagnostic Medical Device** IVD Rx only

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Xpert® Hemorrhagic Fever Panel

℞ only

For *In Vitro* Diagnostic Use Only

1. Proprietary Name

Xpert® Hemorrhagic Fever Panel

2. Common or Usual Name

Xpert Hemorrhagic Fever Panel

3. Intended Use

The Xpert® Hemorrhagic Fever Panel, performed on the GeneXpert® Dx system, is an automated multiplex real-time reverse transcription polymerase chain reaction (RT-PCR) test intended for the qualitative *in vitro* detection and identification of RNA from multiple biothreat agents:

- Ebola virus (including Zaire, Sudan, Taï Forest, and Bundibugyo, not differentiated)
- Crimean-Congo hemorrhagic fever (CCHF) virus
- Marburg virus
- Lassa virus

The Xpert Hemorrhagic Fever Panel uses EDTA-treated whole blood specimens collected by venous draw from individuals with signs and symptoms of the suspected infections and/or individuals who are at risk for exposure or may have been exposed to these agents.

The Xpert Hemorrhagic Fever Panel is indicated as an aid in the diagnosis of viral hemorrhagic fevers and results should be used in conjunction with other clinical, epidemiologic and laboratory data, consistent with applicable WHO recommendations[1] and local public health guidelines.

The Xpert Hemorrhagic Fever Panel results are for the presumptive identification of Ebola, CCHF, Marburg, and Lassa viruses. Definitive identification requires additional testing and confirmation procedures in consultation with the appropriate public health authorities for whom reports may be necessary. Positive results do not rule out co-infection with organisms not included in the Xpert Hemorrhagic Fever Panel. The organism(s) detected may not be the definite cause of symptoms. Negative results do not preclude infection with these agents and should not be used as the sole basis for diagnosis, treatment, or other patient management decisions.

Xpert Hemorrhagic Fever Panel is intended to be performed by healthcare professionals trained on the use of the test in laboratories having appropriate personal protective equipment (PPE) and other safety precautions, including personnel trained in the safe handling of diagnostic clinical specimens potentially containing highly infectious agents. Viral hemorrhagic fevers are nationally notifiable diseases caused by biothreat agents and reporting of these diseases should be coordinated with the appropriate public health authorities.

4. Summary and Explanation

Viral hemorrhagic fevers are severe acute viral infections, usually with sudden onset of fever, malaise, headache, and myalgia followed by pharyngitis, vomiting, diarrhea, skin rash, and hemorrhagic manifestations.[2] Viral hemorrhagic fever is generally applied to disease caused by *Arenaviridae* (Lassa Fever), *Bunyaviridae* (Crimean-Congo hemorrhagic fever [CCHF]), *Filoviridae* (Ebola and Marburg).[3]

The nomenclature of the family *Filoviridae*, including the viruses that cause Ebola disease, has changed over time. Recently, the genus name *Ebolavirus* was changed to *Orthoebolavirus*, and the species name Zaire ebolavirus was changed to *Orthoebolavirus zairense*.[4] Additionally, the genus name *Marburgvirus* was changed to *Orthomarburgvirus.*[4]

Viruses that cause hemorrhagic fevers are transmitted by mosquitoes, ticks (CCHF), rodents (Lassa) or bats (Ebola, Marburg). For Ebola and Marburg viruses, humans have been infected from contact with tissues of diseased non-human primates (monkeys and apes) and other mammals, but most human infections have resulted from direct contact with the body fluids or secretions of infected patients. Humans who develop CCHF usually become infected from a tick bite but can also acquire the virus from direct contact with blood or

other infected tissues from livestock or from infected patients. Lassa virus is carried by rodents and transmitted by excreta, either as aerosols or by direct contact. Some viral hemorrhagic fevers have been amplified in hospitals by nosocomial transmission resulting from unsafe procedures, use of contaminated medical devices (including needles and syringes) and unprotected exposure to contaminated body fluids.[2]

Diseases caused by hemorrhagic fever in this group occur in the tropical and sub-tropical regions of the world. Ebola, Marburg, and Lassa fevers occur in parts of sub-Saharan Africa. CCHF occurs in the grassland, shrubland and savanna regions of central Asia and in central Europe, as well as in tropical and southern Africa.[2]

Collecting and performing tests on patient samples potentially containing hemorrhagic fever pathogens presents an extreme biohazard risk and should only be conducted under appropriate biological containment conditions. However, if samples have been inactivated, they can be manipulated in a basic biosafety environment.

5. Principle of the Procedure

The Xpert Hemorrhagic Fever Panel test is an automated test for qualitative detection of Ebola virus (including Zaire, Sudan, Taï Forest, and Bundibugyo, not differentiated), Crimean-Congo hemorrhagic fever (CCHF) virus, Marburg virus, and Lassa virus. The test is performed on the GeneXpert Dx system.

The GeneXpert Dx system automates and integrates sample extraction, nucleic acid purification and amplification, and detection of target sequences from samples by using reverse transcription (conversion of RNA templates into DNA) followed by real-time PCR.

The GeneXpert Dx system consists of an instrument, computer, barcode scanner, and preloaded software for running the tests and viewing the results. Each test requires the use of a single-use disposable GeneXpert cartridge that contains target-specific reagents and carries out the RT-PCR and PCR processes. Because the cartridges are self-contained, the risk of cross-contamination between samples is minimized. For a full description of the system, refer to the *GeneXpert Dx System Operator Manual*.

The Xpert Hemorrhagic Fever Panel test includes reagents for the detection of Ebola virus (including Zaire, Sudan, Taï Forest, and Bundibugyo, not differentiated), Crimean-Congo hemorrhagic fever (CCHF) virus, Marburg virus, and Lassa virus from venous whole blood samples. A Sample Processing Control (SPC), a Sample Adequacy Control (SAC), and a Probe Check Control (PCC) are also included in the cartridge. The SPC is present to control for adequate extraction and processing of the target sequences and to monitor for the presence of inhibitors in the PCR reaction. The SAC ensures that human cells have been added in a cartridge. The PCC verifies reagent rehydration, PCR tube filling in the cartridge, probe integrity, and dye stability.

The results are interpreted by the GeneXpert Dx software from measured fluorescent signals and embedded calculation algorithms and are clearly shown in the View Results. The Xpert Hemorrhagic Fever Panel test provides test results for Ebola, CCHF, Marburg and Lassa. If INVALID, ERROR, or NO RESULT test result is reported, the user is instructed to repeat the test.

6. Reagents and Instruments

6.1. Materials Provided

The Xpert Hemorrhagic Fever Panel test kit contains sufficient reagents to process 10 specimens or quality control samples. The kit contains the following:

Xpert Hemorrhagic Fever Cartridges with Integrated Reaction Tubes in Foil-Sealed Pouches	**10**
• Bead 1, Bead 2 and Bead 3 (freeze-dried)	1 of each per cartridge
• Binding Reagent	2.0 mL per cartridge
• Rinse Reagent	0.54 mL per cartridge
• Elution Reagent	2.0 mL per cartridge
Xpert Hemorrhagic Fever Sample Reagent (in a zip lock bag)	**10 per kit (2.0 mL each)**
Xpert Hemorrhagic Fever Accessory Bag	**2 per kit**
• 1.1 mL Transfer Pipette	12 per bag
• 200 µl Transfer Pipette	12 per bag
CD	**1 per kit**
• Assay Definition File (ADF)	

- ADF Import Instructions (to import ADF into GeneXpert Dx software)
- Instructions for Use

Note Safety Data Sheets (SDS) are available at www.cepheid.com or www.cepheidinternational.com under the **Support** tab.

Note The protein stabilizer of bovine origin in the beads within this product was produced and manufactured exclusively from bovine plasma sourced in the United States. No ruminant protein or other animal protein was fed to the animals; the animals passed ante- and post- mortem testing. During processing, there was no mixing of the material with other animal materials.

7. Storage and Handling

- Store the Xpert Hemorrhagic Fever cartridges at 2–28 °C. If refrigerated, it is recommended to equilibrate the cartridge to room temperature (15-25 °C) before use.
- Do not open a cartridge until you are ready to perform testing.
- Do not use cartridges that have passed the expiration date.
- Do not use a cartridge that has leaked.

8. Materials Required but Not Provided

- GeneXpert Dx System (catalog number varies by configuration): GeneXpert instrument, computer, barcode scanner, Operator Manual and GeneXpert Dx software version 6.5 or higher
- Printer: If a printer is required, contact Cepheid Technical Support to arrange for the purchase of a recommended printer.
- K_2 EDTA tube for collection of venous whole blood sample

9. Materials Recommended but Not Provided

- Absorbent pad
- Blood tube rack

10. Materials Available but Not Provided

External controls in the form of AccuPlex recombinant sindbis virus containing Ebola, Lassa, CCHF and Marburg RNA sequences are available from LGC Clinical Diagnostics (Milford, MA) for optional use with the Xpert Hemorrhagic Fever Panel test.

- AccuPlex™ Viral Fever-ELCM Control Pack (P/N 0505-0410)

11. Warnings and Precautions

11.1. General

- For *in vitro* Diagnostic Use
- For prescription use only
- A healthcare professional, with training in principles and use of infectious disease diagnostics and reporting of results, should carefully interpret the results from the Xpert Hemorrhagic Fever Panel test in conjunction with a patient's signs and symptoms, and results from other diagnostic tests.
- Nationally notifiable disease caused by a biothreat microbial agent must be reported to public health authorities in accordance with local, state, and federal law.
- Treat all biological specimens, including used cartridges, as if capable of transmitting infectious agents. Because it is often impossible to know which might be infectious, all biological specimens should be treated with standard precautions. Guidelines for specimen handling are available from the U.S. Centers for Disease Control and Prevention[5] , the Clinical and Laboratory Standards Institute[6], and the World Health Organization (WHO).[7]
- If infection with Hemorrhagic Fever agents is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, the appropriate public health authority should be contacted for testing.
- Reliable results are dependent on adequate specimen collection, transport, storage and processing. Incorrect test results may occur from improper specimen collection, handling or storage, technical error, sample mix-up or because the number of organisms in the specimen is below the limit of detection of the test. Careful compliance with the Instructions for Use instructions and the *GeneXpert Dx System Operator Manual* are necessary to avoid erroneous results.
- Follow your institution's safety procedures for working with chemicals and handling biological samples.

- Biological specimens, transfer devices, and used cartridges should be considered capable of transmitting infectious agents requiring standard precautions. Follow your institution's environmental waste procedures for proper disposal of used cartridges and unused reagents. These materials may exhibit characteristics of chemical hazardous waste requiring specific national or regional disposal procedures. If national or regional regulations do not provide clear direction on proper disposal, biological specimens and used cartridges should be disposed per WHO [World Health Organization][7] medical waste handling and disposal guidelines.
- Do not allow Xpert Hemorrhagic Fever Sample Reagent, which contains guanidinium thiocyanate, to contact with sodium hypochlorite (bleach) solution. This mixture can produce hazardous fumes that irritate the respiratory tract.
- Bleach, a recommended disinfectant, is corrosive and may cause irritation if it comes into contact with eyes and skin, and it is harmful if swallowed or inhaled.

11.2. Specimen

- Specimen collection and handling procedures require biosafety training and guidance.
- For collection and transport of blood specimens, use only the material listed in Section 13.
- Specimens must be tested before the expiration date of the Xpert Hemorrhagic Fever Panel test kit.
- Maintain proper storage conditions during specimen transport to ensure the integrity of the specimen (see Section 13.2). Specimen stability under shipping conditions other than those recommended has not been evaluated.
- Proper sample collection, storage, and transport are essential for correct results.

11.3. Test/Reagent

- Performance may be impacted when using frozen samples.
- Do not substitute Xpert Hemorrhagic Fever test reagents with other reagents.
- Do not open the Xpert Hemorrhagic Fever test cartridge lid except when adding specimen.
- Do not use a cartridge that has been dropped after removing from the packaging.
- Do not shake or tilt the cartridge. Shaking or dropping the cartridge after opening the lid may yield non-determinate results.
- Do not place the sample ID label on the cartridge lid or on the cartridge barcode label.
- Do not use a cartridge with a damaged barcode label.
- Do not use a cartridge that has a damaged reaction tube.
- Each single-use Xpert Hemorrhagic Fever test cartridge is used to process one test. Do not reuse processed cartridges.
- The single-use disposable pipettes are used to transfer one specimen. Do not reuse disposable pipettes.
- Do not use a cartridge if it appears wet or if the lid seal appears to have been broken.
- Good laboratory practices, including changing gloves between handling patient samples, are recommended to avoid contamination of samples or reagents.
- In the event of a spill of specimens or controls, wear gloves and absorb the spill with paper towels. Then, thoroughly clean the contaminated area with a 1:10 dilution of freshly prepared household chlorine bleach. The final active chlorine concentration should be 0.5% regardless of the household bleach concentration in your country. Allow a minimum of two minutes of contact time. Ensure the work area is dry before using 70% denatured ethanol to remove bleach residue. Allow surface to dry completely before proceeding or, follow your institution's standard procedures for a contamination or spill event. For equipment, follow the manufacturer's recommendations for decontamination of equipment.

12. Chemical Hazards[8,9]

- Signal Word (GHS UN): **Danger**
- **GHS UN Hazard Statements**
  - Harmful if swallowed or if inhaled.
  - May be harmful in contact with skin
  - Causes severe skin burns and eye damage.
  - Harmful to aquatic life with long lasting effects.

- **GHS UN Precautionary Statements**
  - **Prevention**
    - Do not breathe dusts or mists.
    - Wash hands thoroughly after handling. Do not touch eyes.
    - Do not eat, drink or smoke when using this product.
    - Use only outdoors or in a well-ventilated area.
    - Avoid release to the environment.
    - Wear protective gloves, protective clothing, eye protection, face protection.

- **Response**
  - IF SWALLOWED: rinse mouth. Do NOT induce vomiting.
  - IF ON SKIN: Take off immediately all contaminated clothing. Immediately rinse with water for several minutes.
  - IF INHALED: Remove person to fresh air and keep comfortable for breathing.
  - IF IN EYES: Immediately rinse with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
  - Get emergency medical help immediately.
  - Specific treatment, see supplemental first aid instruction.
  - Wash contaminated clothing before reuse.

- **Storage/Disposal**
  - Store locked up.
  - Dispose of contents and container to hazardous or special waste collection point, in accordance with local, regional, national and/or international regulations..

13. Specimen Collection, Transport, and Storage

13.1. Venous Whole Blood Collection

Note Venous whole blood collection or venipuncture should be performed by appropriately trained staff or a phlebotomist.

1. Venous whole blood collected in EDTA tube should be performed according to the manufacturer's instructions.
2. Once the EDTA venous whole blood is collected, verify that the EDTA blood collection tube is labeled with the correct patient ID.

Warning Failing to invert the tube 10 times after blood collection may result in incorrect results.

3. Gently invert the tube **10 times** to ensure the blood is thoroughly mixed (Figure 1).

Note **Do not shake.** Vigorous mixing may cause foaming or hemolysis. Inadequate mixing may result in platelet clumping, clotting, and/or incorrect test results.

Figure 1. 1 Flip Down + 1 Flip Up = 1 Full Invert

13.2. Specimen Transport and Storage

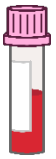
- EDTA-Venous whole blood specimens (VWB) can be stored at room temperature (15–30 °C) for up to 24 hours, refrigerated (2–8 °C) for up to 5 days, or at 31-35°C for 24 hours until testing is performed on the GeneXpert Dx system.
- VWB specimens in **Sample Reagent (SR)** can be stored at room temperature (15–30 °C) for up to 28 hours, refrigerated (2–8 °C) up to 6 days, or at 31-35°C for up to 24 hours until testing is performed on the GeneXpert Dx system.
- Proper specimen collection, storage, and transport are critical to the performance of this test. Inadequate sample collection, improper sample handling, and/or transport may yield a false result. Specimen stability under shipping and storage conditions other than those listed have not been evaluated with the Xpert Hemorrhagic Fever Panel test.
- EDTA whole blood specimens should be free of clots and collected in accordance with standard specimen collection procedures to minimize hemolysis.

14. Procedure

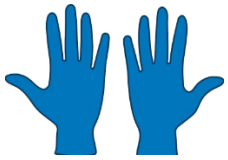
14.1. Preparing the Specimen and Cartridge

Gather the following supplies from your institution (Table 1).

Table 1. Supplies Needed from Your Institution



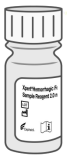
Blood sample in tube



Gloves and appropriate PPE

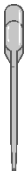
Gather the following supplies from the assay kit (Table 2).

Table 2. Supplies from Xpert Hemorrhagic Fever Panel Test Kit



Xpert® Hemorrhagic Fever Sample Reagent Vial **(clear cap)**

200 uL pipette



1.1 mL pipette

Xpert® Hemorrhagic Fever Cartridge

Important Start the test within 30 minutes of adding the sample to the cartridge.

1. Use **double** gloves when performing this test. Put on clean inner and outer gloves, protective clothing, eye protection, and face shield.
2. Decontaminate the work surface and dispose of biohazard waste according to site/field regulations.
3. Remove a cartridge from the package (it is recommended to equilibrate the cartridge to room temperature [15-25 °C] before use).
4. Inspect the cartridge for damage. If damaged or has signs of leakage, do not use it.
5. Label the cartridge with specimen identification. Write on the side of the cartridge or affix an ID label. Do not put the label on the lid of the cartridge or over the existing 2D barcode on the cartridge.
6. Remove the sample reagent vial from the test kit.
7. Check that the sample reagent vial says **Xpert® Hemorrhagic Fever Sample Reagent**.
8. Open the **200 µL** pipette wrapper, leaving the pipette inside the wrapper.
9. Twist the cap to open the sample reagent vial.
10. Remove and place the cap upside down.
11. Check that the blood tube is fully closed.

Warning Failing to invert the blood tube 10 times may result in incorrect results.

12. Gently invert the blood tube **10 times** to ensure the blood is thoroughly mixed (Figure 2).

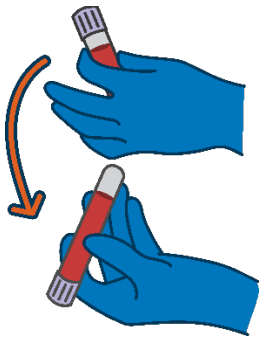


Figure 2. 1 Flip Down + 1 Flip Up = 1 Full Invert

13. Place the blood tube in the test tube rack, if available.
14. Carefully uncap the blood tube.
15. Remove and place the cap upside down on the absorbent pad, if available.

Warning Failing to use the correct pipette may result in incorrect or invalid results.

16. Remove the **200 µL** pipette from the wrapper.
17. Squeeze the top bulb of the pipette until completely flat.

Warning Do **not** let the **bulb** of the pipette or **glove** enter the blood tube. Contamination may occur.

18. While still squeezing the top bulb of the pipette, place the tip in the blood tube (Figure 3).

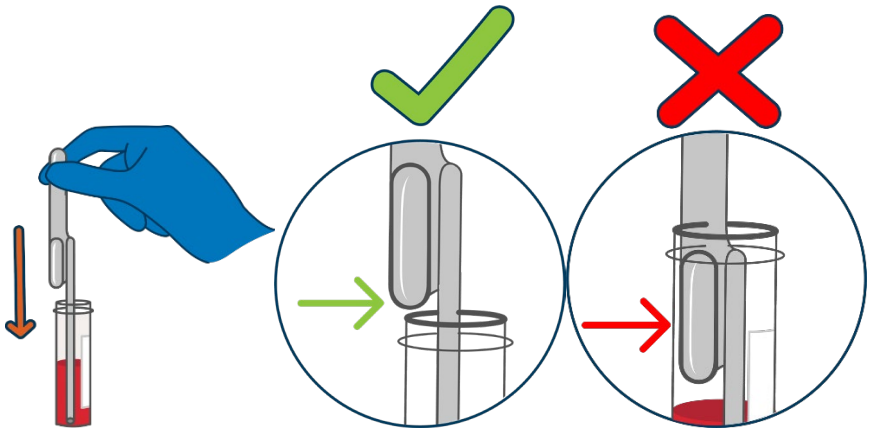


Figure 3. Squeezing Bulb and Placing into Blood Tube Plus Demonstrating Correct Use and Incorrect Pipette Use

Warning Do **not** let the **bulb** of the pipette or **glove** enter the blood tube. Contamination may occur.

19. Place the tip of the pipette **close** to the bottom of the blood tube (Figure 4).

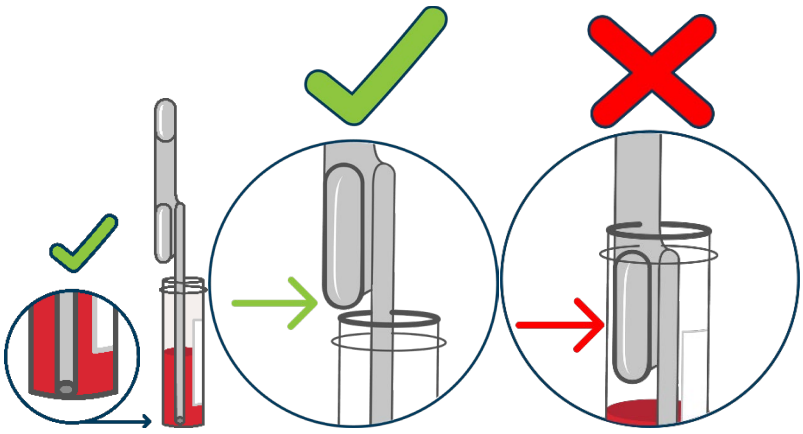


Figure 4. Tip of Pipette Close to Bottom of Blood Tube Plus Demonstrating Correct Use and Incorrect Pipette Use

20. **Slowly** release the top bulb of the pipette until the pipette shaft is completely filled with blood before removing it from the tube. It is OK if blood goes into the overflow reservoir of the pipette.
21. Remove the pipette from the blood tube.
22. Check that the pipette does not contain air bubbles (Figure 5). If air bubbles are present, dispense blood back into the blood tube, keeping the pipette tip above the surface of the liquid while dispensing. Some blood may remain in the overflow reservoir of the pipette. Repeat steps 16-22 with a new **200 µL** pipette.

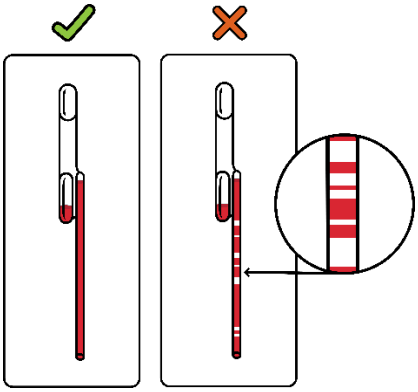


Figure 5. Transfer Pipette (Correct and Incorrect Use)

23. Place the tip of the pipette close to the bottom of the sample reagent vial (Figure 6).

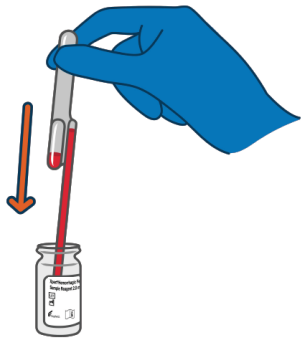


Figure 6. Pipette Into Sample Reagent Vial

24. Squeeze the top bulb of the pipette completely flat to dispense all the blood into the sample reagent vial. Some liquid may remain in the overflow reservoir of the pipette.
25. While still squeezing the top bulb of the pipette, remove the pipette from the sample reagent vial.

Note If there is still liquid inside the pipette, squeeze the top bulb of the pipette into the **sample reagent vial** until the pipette is empty.

26. Check that no blood has **accidentally been drawn back in the pipette**.
27. Discard the pipette in a biohazard container.
28. Twist the cap back on the sample reagent vial.
29. Place the cap back on the blood tube and completely close.

Warning Failing to invert 15 times may result in incorrect results.

30. Invert the sample reagent vial **15 times** (Figure 7).

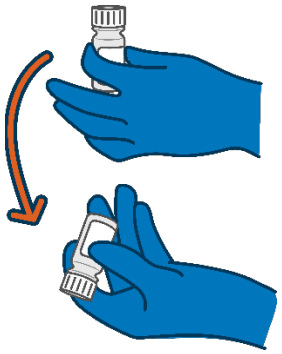


Figure 7. 1 Flip Down + 1 Flip Up = 1 Full Invert

Warning Failing to wait 10 minutes may result in incorrect results and/or increased safety risk due to incomplete inactivation of the sample.

31. Wait **10 minutes** to inactivate the sample.
32. Discard both pairs of gloves.
33. Put on a clean pair of gloves.
34. Open the wrapper of the **1.1 mL** pipette wrapper, leaving the pipette inside the wrapper.
35. Open the test cartridge lid (Figure 8).

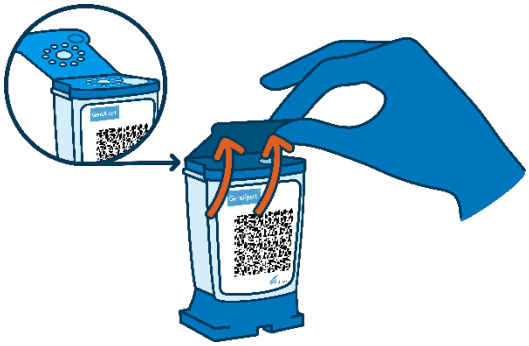


Figure 8. Open the Xpert Hemorrhagic Fever Cartridge Lid

Warning	Failing to invert 3 times may result in incorrect results.

36. After waiting 10 minutes, invert the sample reagent vial **3 times** (Figure 9).

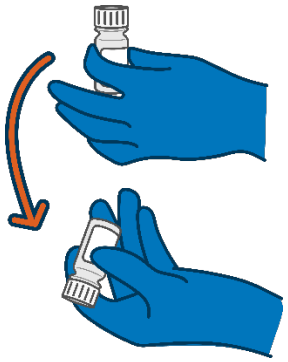


Figure 9. 1 Flip Down + 1 Flip Up = 1 Full Invert

37. Twist to open the sample reagent vial.
38. Remove and place the cap upside down on the absorbent pad, if available.

Warning	Failing to use the correct pipette may result in incorrect or invalid results.

39. Remove the **1.1 mL** pipette from the wrapper.
40. Squeeze the bulb of the pipette until completely flat.
41. While squeezing the bulb of the pipette, place the tip of the pipette in the sample reagent vial (Figure 10).

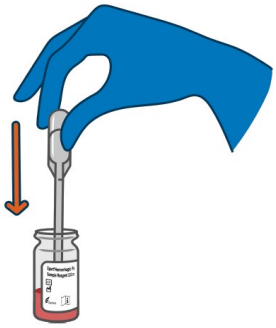


Figure 10. Tip of Pipette into Sample Reagent Vial

42. Check that the tip of the pipette is **close** to the bottom of the sample reagent vial (Figure 11).

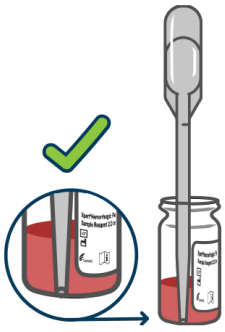


Figure 11. Tip of Pipette Close to Bottom of Sample Reagent Vial

43. **Slowly** release pressure from the pipette until the liquid reaches the **fill line** (Figure 12).

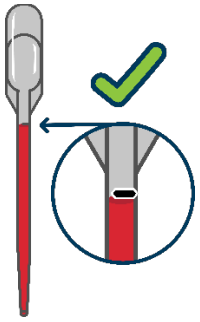


Figure 12. Fill Until the Liquid Reaches Fill Line

Warning	Failing to fill the pipette up to the fill line may result in incorrect or invalid results.

44. Check that there is **liquid up to the fill line**.
45. Remove the pipette from the sample reagent vial.
46. Place the pipette into the sample chamber (**largest opening**) of the cartridge (Figure 13).

Figure 13. Xpert Hemorrhagic Fever Cartridge (Top View)

47. Squeeze the bulb of the pipette completely flat to dispense all the liquid into the bottom of the sample chamber **(largest opening)**.
48. While still squeezing the bulb of the pipette, remove the pipette from the cartridge.

Note	If there is still liquid inside the pipette, squeeze the top bulb of the pipette into the **largest opening of the cartridge** until the pipette is empty.

49. Check that no liquid has **accidentally been drawn back into the pipette.**
50. Discard the pipette in a biohazard container.
51. Close the cartridge lid.
52. Twist the cap back on the sample reagent vial. Refer to Section 13.2 for how to handle the leftover sample in Sample Reagent.

Note	Save the sample reagent with sample for re-test if necessary.

53. The cartridge is now ready for testing.
54. Decontaminate work surfaces and properly dispose of biohazard waste according to your institution regulations.
55. Change gloves and prepare to load the cartridge into the instrument.

14.2. Starting the Test

Important	Before you start the test, make sure the GeneXpert Dx system is running GeneXpert Dx software version 6.5 or higher and that the Xpert Hemorrhagic Fever Panel Assay Definition File (ADF) is imported into the software.
Note	The steps you follow can be different if the system administrator changes the default workflow of the system.

1. Turn on the GeneXpert instrument and then turn on the computer. The GeneXpert Dx software will launch automatically or may require double-clicking the GeneXpert Dx software.
2. Log on to the GeneXpert Dx System software using your user name and password.
3. In the GeneXpert System window, click **Create Test** (GeneXpert Dx). The Create Test window opens.
4. Scan in the Patient ID (optional). If typing the Patient ID, make sure the Patient ID is typed correctly. The Patient ID is shown on the left side of the View Results window and is associated with the test results.
5. Scan in Sample ID or type the Sample ID. If typing the Sample ID, make sure the Sample ID is typed correctly. The Sample ID is shown on the left side of the View Results window and is associated with the test results.
6. Scan the barcode on the Xpert Hemorrhagic Fever cartridge. Using the barcode information, the software automatically fills in the boxes for the following fields: Reagent Lot ID, Cartridge SN, and Expiration Date.

Note	If the barcode on the Xpert Hemorrhagic Fever cartridge does not scan, then repeat the test with a new cartridge.

7. Click **Start Test**. In the dialog box that displays, type your password, if required.
8. Open the instrument module door with the blinking green light and load the cartridge
9. Close the door. The test starts and the green light stops blinking. When the test is finished, the light turns off.
10. Wait until the system releases the door lock before opening the module door and removing the cartridge.
11. Dispose of used cartridges in the appropriate specimen waste container according to your institution's standard practices.

Note	Do not open or attempt to alter any part of the used cartridge for disposal. Do not turn off or unplug the instrument while a test is in progress. Turning off or unplugging the instrument or computer will stop the test

14.3. Viewing Result and Printing Results

This section lists the basic steps for viewing and printing results. For more detailed instructions on how to view and print the results, see the *GeneXpert Dx System Operator Manual*.

1. Click the **View Results** icon to view results.
2. Upon completion of the test, click the **Report** button of the View Results window to view and/or generate a PDF report file.

15. Quality Control

15.1. Internal Controls

Each Xpert Hemorrhagic Fever cartridge includes three internal controls: A Sample Adequacy Control (SAC), a Sample Processing Control (SPC), and a Probe Check Control (PCC).

- **Sample Adequacy Control (SAC):** Ensures that the sample was correctly added to the cartridge. The SAC verifies that the correct sample has been added to the sample chamber. The SAC should be positive in a negative sample and can be negative or positive in a positive sample. The SAC passes if it meets the validated acceptance criteria.
- **Sample Processing Control (SPC)**: Ensures the sample was processed correctly. The SPC verifies that release of RNA from the viruses has occurred if the organism is present and verifies that the sample processing is adequate. Additionally, this control detects sample-associated inhibition of the RT-PCR and PCR reactions. The SPC should be positive in a negative sample and

can be negative or positive in a positive sample. The SPC passes if it meets the validated acceptance criteria.

- **Probe Check Control (PCC):** Before the start of the PCR reaction, the GeneXpert system measures the fluorescence signal from the PCC performed after the reverse transcription step and before PCR begins. The PCC monitors bead rehydration, reaction tube filling, probe integrity, and dye stability. The PCC passes if it meets the validated acceptance criteria.

15.2 External Controls

- External controls may be used by customers to fulfill various needs including, but not limited to, verification of new assays, verification of new assay kit lots, standard quality control (QC) processes, or for training of new operators. External quality controls are not required but may be purchased from outside vendors or may be prepared from the leftover samples or by following institutional procedures.
- The external quality control materials provided by the specified vendor in Section 10 are an optional source. All external controls must be used in accordance with local, state, and/or federal regulations or accreditation requirements, as applicable.

16. Interpretation of Results

The results are interpreted automatically by the GeneXpert Dx system from measured fluorescent signals and embedded calculation algorithms and are clearly shown in the View Results Window. Possible results are summarized in Table 3.

Table 3. Xpert Hemorrhagic Fever Panel Possible Results and Interpretation

Result	Interpretation
Ebola DETECTED; Lassa DETECTED; CCHF DETECTED; Marburg DETECTED (See Figure 14)	Ebola (including Zaire, Sudan, Taï Forest and Bundibugyo, not differentiated) target RNA is DETECTED; Lassa target RNA is DETECTED; CCHF target RNA is DETECTED; Marburg target RNA is DETECTED. • The Ebola, Lassa, CCHF, and Marburg: targets have Ct values within the valid range and endpoints above the threshold setting • SAC – NA (not applicable); SAC is ignored because the Ebola / Lassa / CCHF / Marburg target amplification may compete with this control. • SPC – NA (not applicable); SPC is ignored because the Ebola / Lassa / CCHF / Marburg target amplification may compete with this control. • Probe Check - PASS; all probe check results pass.
Ebola DETECTED; Lassa NOT DETECTED; CCHF NOT DETECTED; Marburg NOT DETECTED	Ebola (including Zaire, Sudan, Taï Forest and Bundibugyo, not differentiated) target RNA is DETECTED; Lassa target RNA is NOT DETECTED; CCHF target RNA is NOT DETECTED; Marburg target RNA is NOT DETECTED. • The Ebola target has Ct values within the valid range and endpoints above the threshold setting • SAC – NA (not applicable); SAC is ignored because the Ebola target amplification may compete with this control. • SPC – NA (not applicable); SPC is ignored because the Ebola target amplification may compete with this control. • Probe Check – PASS; all probe check results pass.
Ebola NOT DETECTED; Lassa DETECTED; CCHF NOT DETECTED; Marburg NOT DETECTED	Ebola (including Zaire, Sudan, Taï Forest and Bundibugyo, not differentiated) target RNA is NOT DETECTED; Lassa target RNA is DETECTED; CCHF target RNA is NOT DETECTED; Marburg target RNA is NOT DETECTED. • The Lassa target has Ct values within the valid range and endpoints above the threshold setting • SAC – NA (not applicable); SAC is ignored because the Lassa target amplification may compete with this control.

Result	Interpretation
	• SPC – NA (not applicable); SPC is ignored because the Lassa target amplification may compete with this control. • Probe Check - PASS; all probe check results pass.
Ebola NOT DETECTED; Lassa NOT DETECTED; CCHF DETECTED; Marburg NOT DETECTED	Ebola (including Zaire, Sudan, Taï Forest and Bundibugyo, not differentiated) target RNA is NOT DETECTED; Lassa target RNA is NOT DETECTED; CCHF target RNA is DETECTED; Marburg target RNA is NOT DETECTED. • The CCHF target has Ct values within the valid range and endpoints above the threshold setting • SAC – NA (not applicable); SAC is ignored because the CCHF target amplification may compete with this control. • SPC – NA (not applicable); SPC is ignored because the CCHF target amplification may compete with this control. • Probe Check - PASS; all probe check results pass.
Ebola NOT DETECTED; Lassa NOT DETECTED; CCHF NOT DETECTED; Marburg DETECTED	Ebola (including Zaire, Sudan, Taï Forest and Bundibugyo, not differentiated) target RNA is NOT DETECTED; Lassa target RNA is NOT DETECTED; CCHF target RNA is NOT DETECTED; Marburg target RNA is DETECTED. • The Marburg target has Ct values within the valid range and endpoints above the threshold setting. • SAC – NA (not applicable); SAC is ignored because the Marburg target amplification may compete with this control. • SPC – NA (not applicable); SPC is ignored because the Marburg target amplification may compete with this control. • Probe Check - PASS; all probe check results pass.
Ebola NOT DETECTED; Lassa NOT DETECTED; CCHF NOT DETECTED; Marburg NOT DETECTED (See Figure 15)	Ebola (including Zaire, Sudan, Taï Forest and Bundibugyo, not differentiated) target RNA is NOT DETECTED; Lassa target RNA is NOT DETECTED; CCHF target RNA is NOT DETECTED; Marburg target RNA is NOT DETECTED. • SAC – PASS; Adequate sample input (SAC) is detected. SAC has a Ct within the valid range and endpoint above the threshold setting. • SPC – PASS; SPC has a Ct within the valid range and endpoint above the threshold setting. • Probe Check - PASS; all probe check results pass.
INVALID (See Figure 16)	Presence or absence of Ebola (including Zaire, Sudan, Taï Forest and Bundibugyo, not differentiated), Lassa, CCHF and Marburg target RNA cannot be determined. • Ebola / Lassa / CCHF / Marburg target – INVALID • SAC and/or SPC – FAIL; SAC or SPC does not meet acceptance criteria. • Probe Check – PASS; all probe check results pass. Repeat test according to the Retest Procedure in Section 17.2.
ERROR (See Figure 17)	Presence or absence of Ebola (including Zaire, Sudan, Taï Forest and Bundibugyo, not differentiated), Lassa, CCHF, and Marburg target RNA cannot be determined. • Ebola/ Lassa/ CCHF/ Marburg target – NO RESULT • SAC – NO RESULT • SPC – NO RESULT

Result	Interpretation
	• Probe Check – FAIL*; all or one of the probe check results fail * If the probe check passed or shows NA, the error is caused by the maximum pressure limit exceeding the acceptable range or by a system component failure. Repeat test according to the Retest Procedure in Section 17.2.
NO RESULT (See Figure 18)	Presence or absence of Ebola (including Zaire, Sudan, Taï Forest and Bundibugyo, not differentiated), Lassa, CCHF and Marburg target RNA cannot be determined. A NO RESULT indicates that insufficient data were collected. For example, cartridge integrity test failed, the operator stopped a test that was in progress or a power failure occurred. • Ebola/ Lassa/ CCHF/ Marburg target – NO RESULT • SAC – NO RESULT • SPC – NO RESULT • Probe Check – NA (not applicable) Repeat test according to the Retest Procedure in Section 17.2.

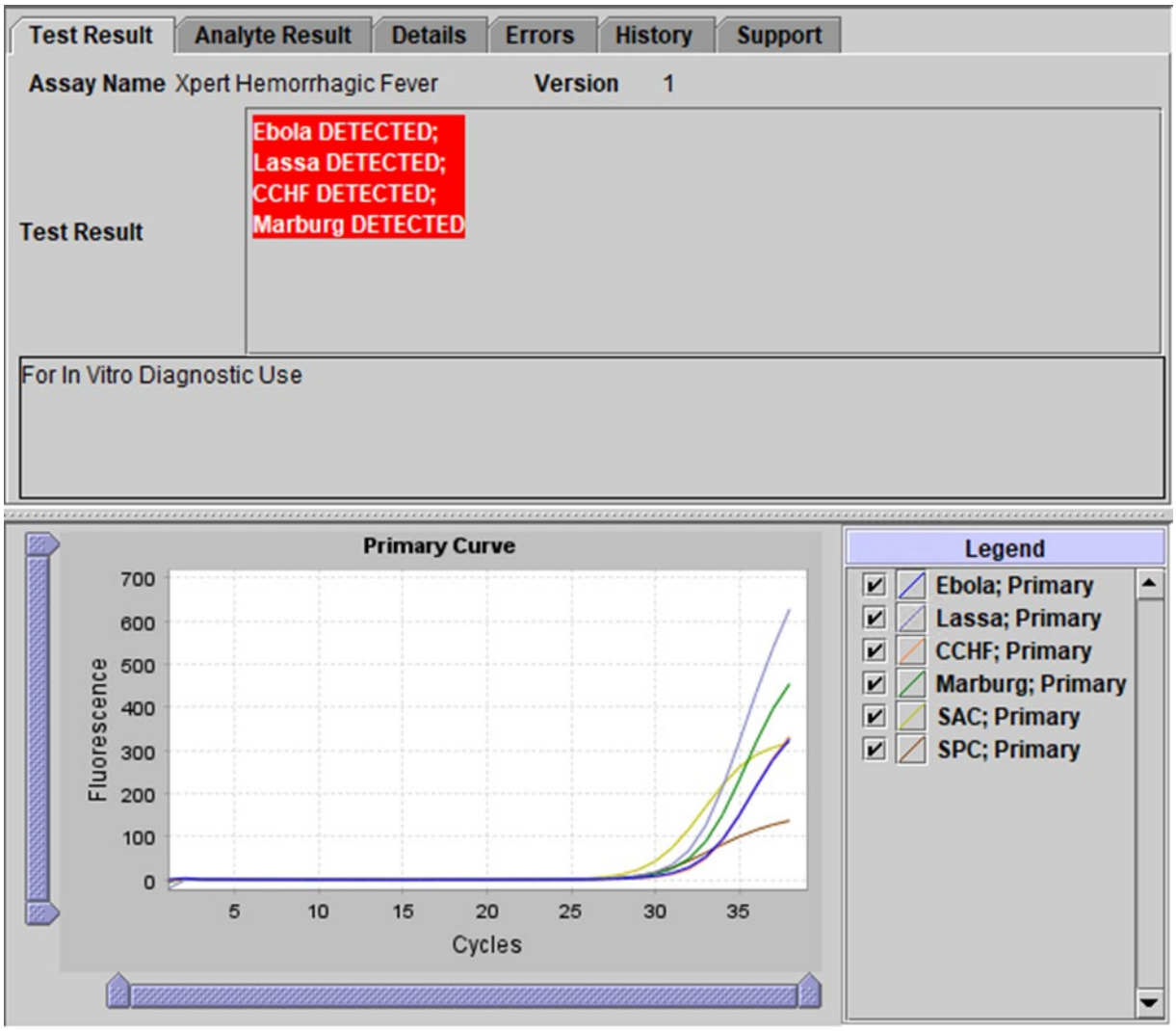


Figure 14. Example of Xpert Hemorrhagic Fever Test Result for Positive Specimen

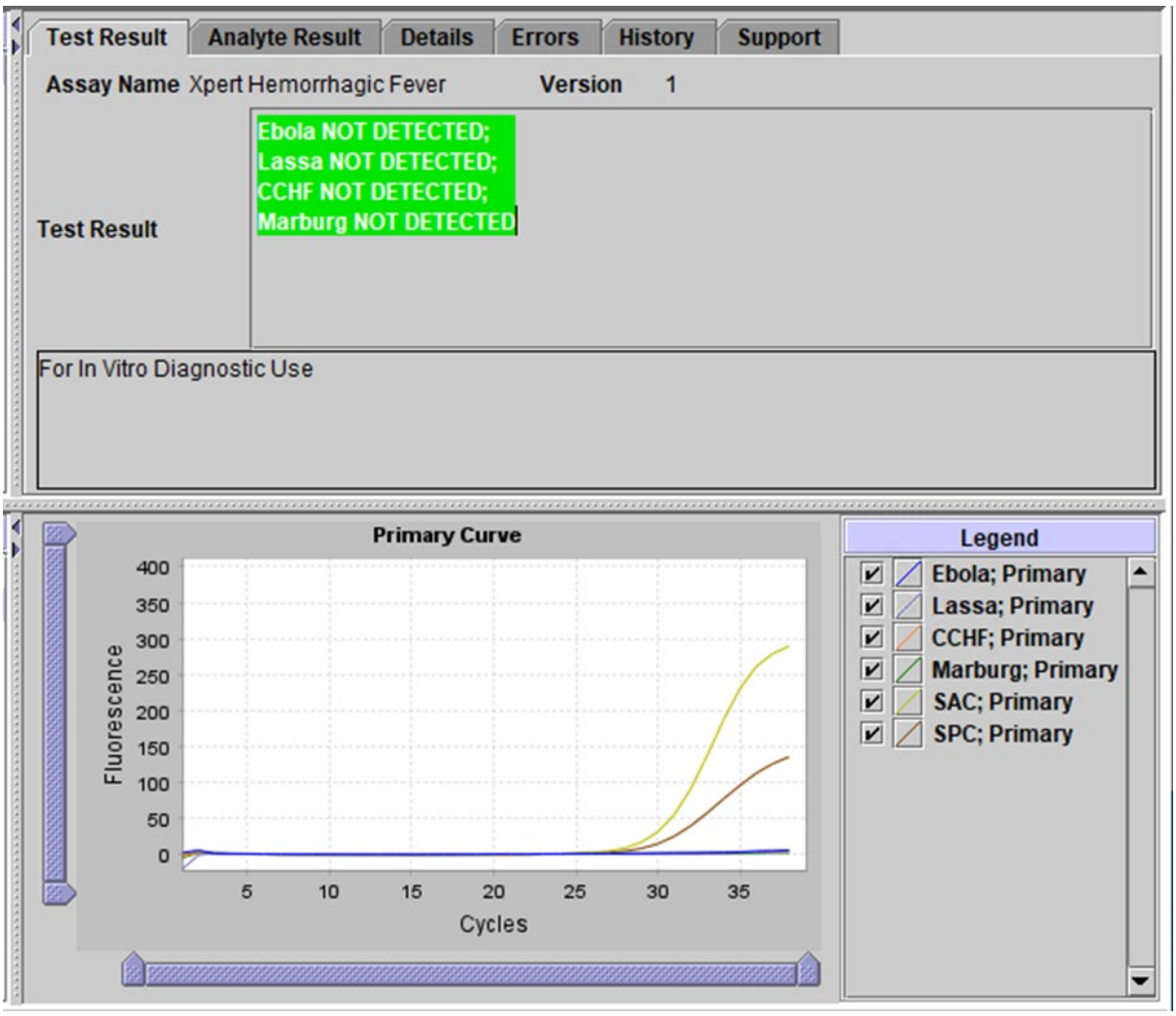


Figure 15. Example of Xpert Hemorrhagic Fever Test Result for Negative Specimen

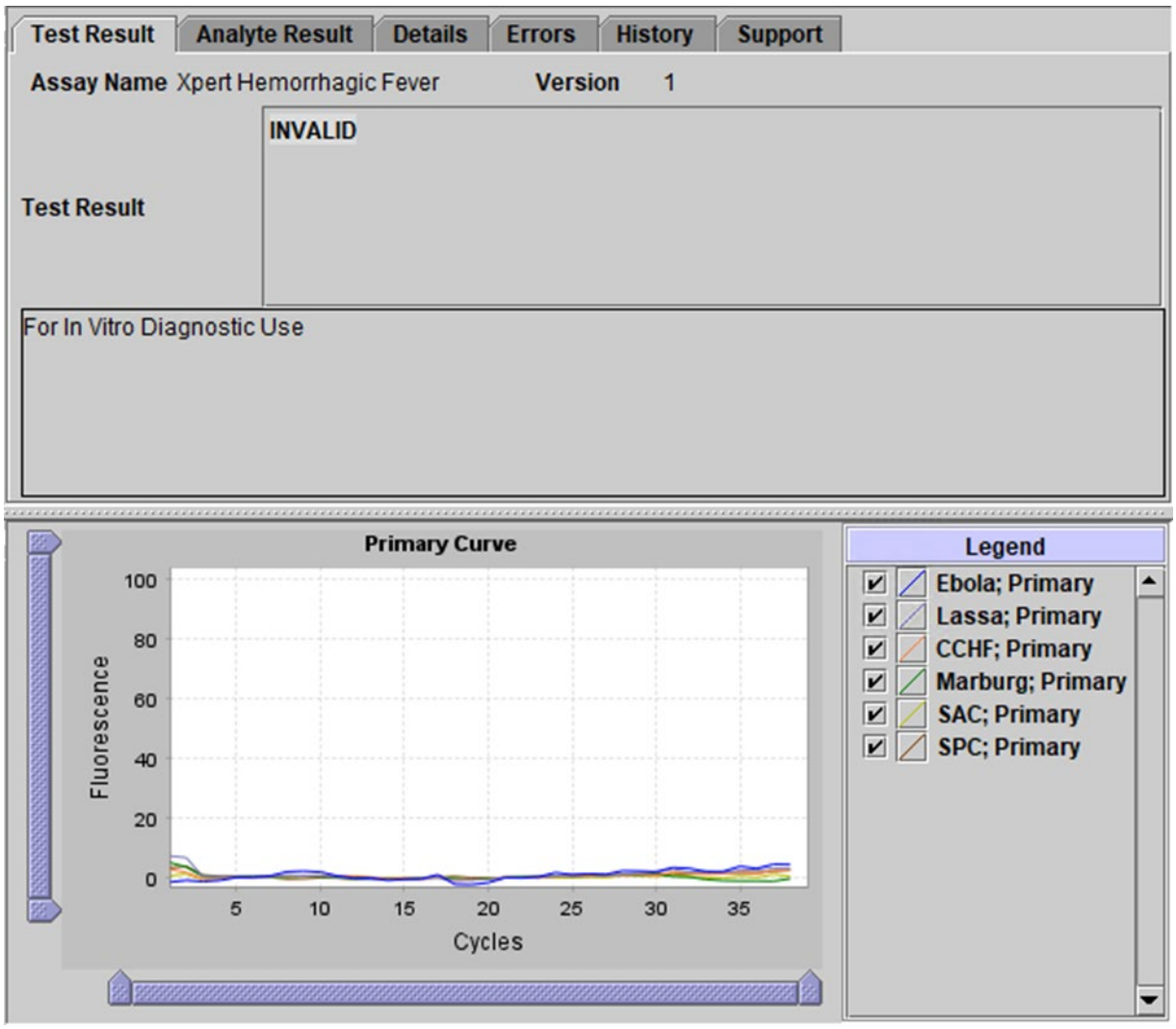


Figure 16. Example of "INVALID" Test Result

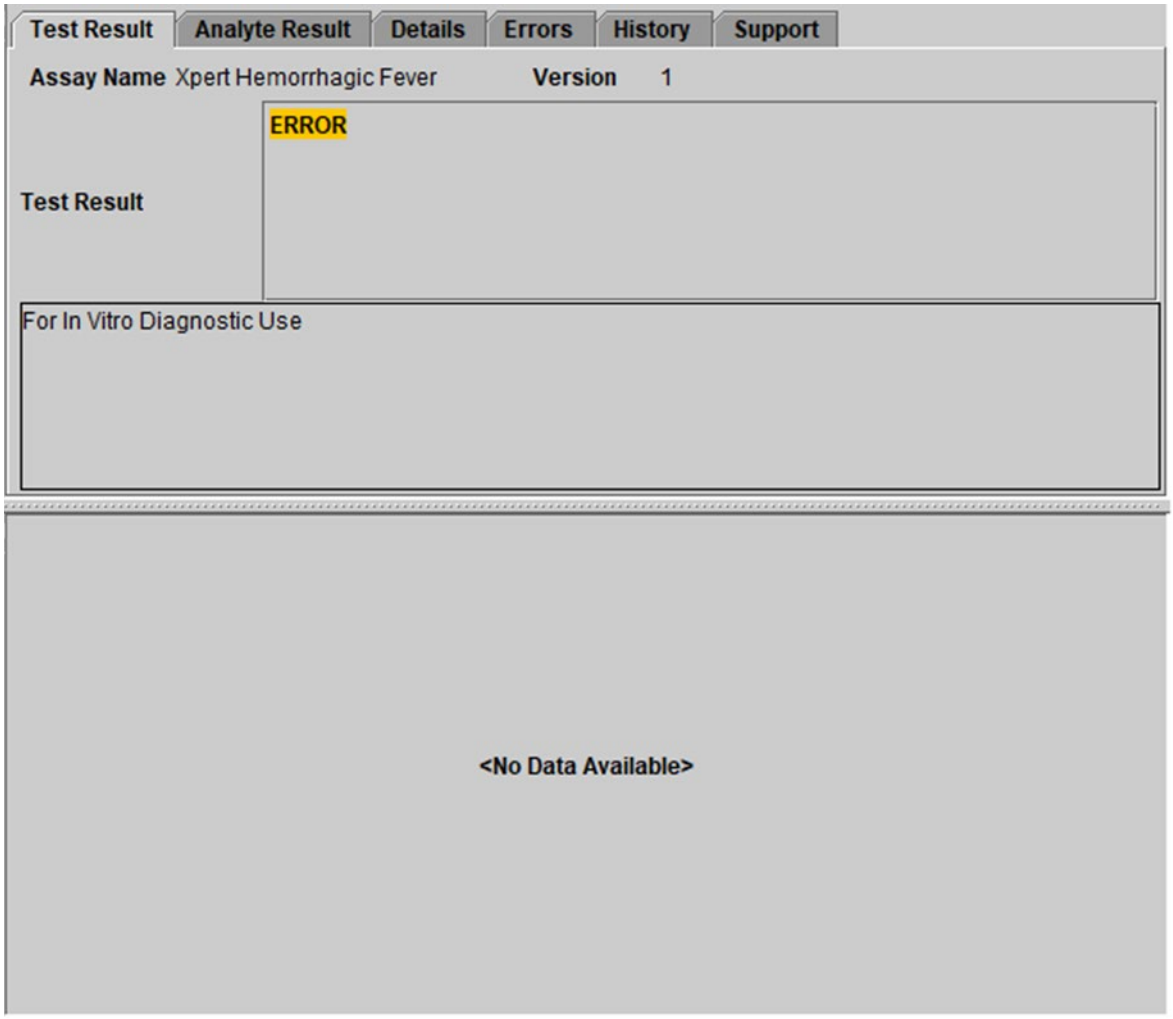


Figure 17. Example of "ERROR" Test Result

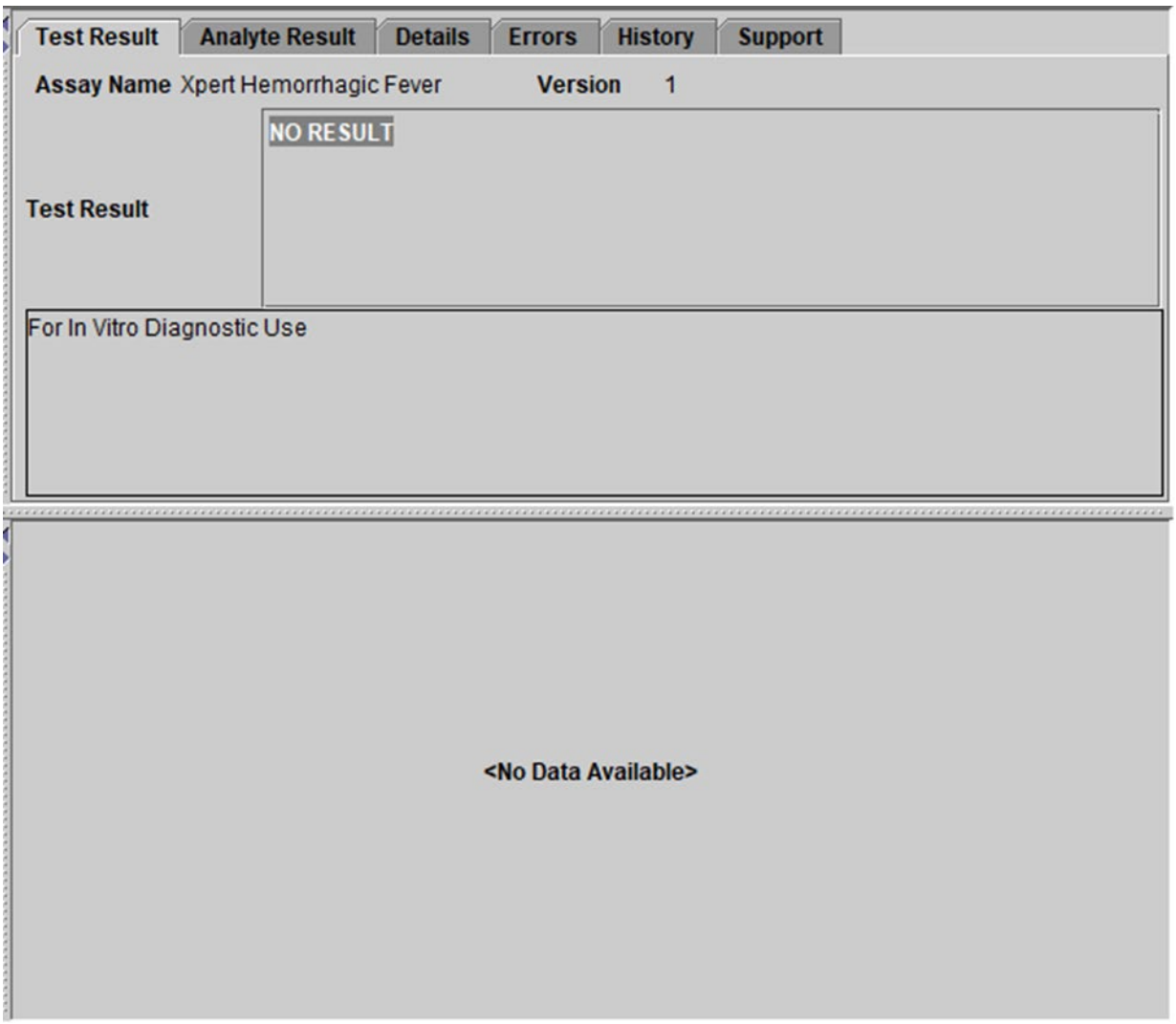


Figure 18. Example of "NO RESULT" Test Result

17. Retests

17.1. Reasons to Repeat the Test

If any of the test results mentioned below occur, repeat the test according to the instructions in the Retest Procedure section (Section 17.2).

- An **INVALID** result indicates that the SAC and/or SPC failed. The sample was not properly processed, or PCR was inhibited.
- An **ERROR** result indicates that the Probe Check Control failed and the test was aborted possibly due to the reaction tube being filled improperly, a reagent probe integrity problem was detected, or because the maximum pressure limits were exceeded.
- A **NO RESULT** indicates that insufficient data were collected. For example, cartridge failed integrity test, the operator stopped a test that was in progress , or a power failure occurred.

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17.2. Retest Procedure

For retest of a non-determinate result (e.g., "**INVALID**" or "**ERROR**" or "**NO RESULT**"), use a new cartridge (do not re-use the cartridge). Use the leftover sample from the original Sample Reagent vial. Follow the procedure in Section 14.1, Preparing the Specimen and Cartridge, and follow Steps 33-55. Once the new cartridge is prepared, follow the procedure in Section 14.2, Starting the Test.

If venous blood sample (in Sample Reagent) does not reach the fill line of 1.1 mL transfer pipette, use 200 µL blood from the original EDTA blood collection tube to make new sample into a new Sample Reagent vial (follow steps in Section 14.1).

18. Limitations

- For prescription use only.
- The performance of the Xpert Hemorrhagic Fever Panel test was validated using the procedures provided in these Instructions for Use only. Modifications to these procedures may alter the performance of the test.
- Erroneous test results might occur from improper specimen collection; failure to follow the recommended sample collection, handling, and storage procedures; technical error; sample mix-up; or because the number of organisms in the specimen is too low to be detected by the test. Careful compliance with the instructions in these Instructions for Use is necessary to avoid erroneous results.
- False negative results may occur if virus is present at levels below the analytical limit of detection.
- Not all pathogens that cause febrile illness are detected by this test, and negative results do not rule out the presence of other infections.
- Evaluation of more common causes of acute febrile illness should be considered prior to evaluation with this test.
- Test results are to be interpreted in conjunction with other clinical, epidemiologic, and laboratory data available to the clinician.
- When using this test, consider patient travel history and exposure risk, as some pathogens are more common in certain geographical locations.
- Nine strains of Lassa evaluated in the Inclusivity study (Section 19.3) were detected by the Xpert Hemorrhagic Fever Panel test. Wet testing demonstrated two of the strains had weaker detection. (Lassa G2405 strain (lineage IV) was detected at 7.4x LoD and Lassa Sauerwald strain (lineage II) was detected at 38.1x LoD). *In silico* analysis of Lassa Togo strain predicted decreased Xpert Hemorrhagic Fever Panel sensitivity. Additional testing of negative results may be warranted if Lassa virus infection is suspected.
- Aigai virus (formerly known as CCHF AP92) was detected at 7.49×10^4 copies/mL in the Exclusivity study (Section 19.4).
- This test is a qualitative test and does not provide a quantitative value for the analyte(s) in the sample.

- Performance of this test has not been established for monitoring treatment of infection with any of the panel analytes.
- This test is not intended for widespread screening of asymptomatic individuals who are not at risk for exposure.
- Due to the rarity of Ebola virus, Crimean-Congo Hemorrhagic Fever Virus, Marburg virus, and Lassa virus clinical specimens, performance characteristics were established using contrived clinical specimens. The sensitivity of the Xpert Hemorrhagic Fever Panel using venous whole blood from patients infected with viruses detected by this assay is unknown.
- *Plasmodium ovale* (*curtis*i) and *Borrelia recurrentis* were identified as having ≥80% homology with different BDBV oligonucleotides. While microbial interference on BDBV detection is not predicted, the absence of microbial interference has not been confirmed by wet-testing.

19. Performance Characteristics

19.1. Clinical Performance

One (1) multi-center clinical study was conducted at two (2) locations in the United States to assess the clinical performance of the Xpert Hemorrhagic Fever Panel test. Due to the low prevalence of the Xpert Hemorrhagic Fever Panel test analytes, the study was conducted using samples contrived with live Crimean-Congo Hemorrhagic Fever (CCHF) virus, Ebola virus, Lassa Virus and Marburg virus venous whole blood (VWB) specimens that were prospectively collected from 408 blood donors (≥14 years old) symptomatic and asymptomatic of fever between January 2025 and April 2025. Available demographic data from the blood donors from whom the specimens were collected is presented in **Table 4**.

Table 4. Demographic Information for Eligible Donor

Subpopulation	Category	N (%)
Age	14-21	7/408 (1.7%)
	22-59	319/408 (78.2%)
	≥60	82/408 (20.1%)
Sex	Male	310/408 (76.0%)
	Female	98/408 (24.0%)
Race	Black or African American	246/408 (60.3%)
	White	162/408 (39.7%)
Ethnicity	Hispanic or Latino	65/408 (15.9%)
	Not Hispanic or Latino	343/408 (84.1%)
Symptoms	Febrile	318/408 (77.9%)
	Non-Febrile	90/408 (22.1%)

The contrived samples were prepared by spiking VWB specimens with live cultures consisting of representative strains of CCHF virus, Ebola virus, Lassa virus and Marburg virus. For each analyte, 408 VWB specimens were contrived at 1-2x limit of detection (LoD) to clinically relevant concentrations. An additional 408 specimens were tested as negatives. Specimens were randomized as such that the analyte status of each contrived sample and negative specimen was blinded to the users performing the testing.

Out of the 816 VWB specimens evaluated, 10 (1.2%; 10/816) specimens yielded a non-determinate result on the initial test. After retest, 0 (0.0%; 0/816) specimens yielded a non-determinate result.

The positive percent agreement (PPA) and negative percent agreement (NPA) of the Xpert Hemorrhagic Fever Panel test were calculated relative to the expected result and are presented in **Table 5.**

Table 5. Performance of Xpert Hemorrhagic Fever Panel by Concentration in VWB

Analyte	Level	PPA			NPA		
		TP/(TP+FN)	PPA (%)	95% CI	TN/(FP+TN)	NPA (%)	95% CI
CCHF	1-2x	51/52	98.1	89.9-99.7	N/A	N/A	N/A
	1000x	12/12	100.0	75.8-100.0	N/A	N/A	N/A
	4000x	12/12	100.0	75.8-100.0	N/A	N/A	N/A
	5000x	12/12	100.0	75.8-100.0	N/A	N/A	N/A
	10000x	14/14	100.0	78.5-100.0	N/A	N/A	N/A
	Overall	101/102	99.0	94.7-99.8	408/408	100.0	99.1-100.0
Ebola	1-2x	53/53	100.0	93.2-100.0	N/A	N/A	N/A
	1000x	14/14	100.0	78.5-100.0	N/A	N/A	N/A
	4000x	14/14	100.0	78.5-100.0	N/A	N/A	N/A
	5000x	9/9	100.0	70.1-100.0	N/A	N/A	N/A
	10000x	12/12	100.0	75.8-100.0	N/A	N/A	N/A
	Overall	102/102	100.0	96.4-100.0	408/408	100.0	99.1-100.0
Lassa	1-2x	52/52	100.0	93.1-100.0	N/A	N/A	N/A
	1000x	12/12	100.0	75.8-100.0	N/A	N/A	N/A
	4000x	12/12	100.0	75.8-100.0	N/A	N/A	N/A
	5000x	12/12	100.0	75.8-100.0	N/A	N/A	N/A
	10000x	14/14	100.0	78.5-100.0	N/A	N/A	N/A
	Overall	102/102	100.0	96.4-100.0	408/408	100.0	99.1-100.0
Marburg	1-2x	51/52	98.1	89.9-99.7	N/A	N/A	N/A
	1000x	12/12	100.0	75.8-100.0	N/A	N/A	N/A
	4000x	12/12	100.0	75.8-100.0	N/A	N/A	N/A
	5000x	12/12	100.0	75.8-100.0	N/A	N/A	N/A
	10000x	14/14	100.0	78.5-100.0	N/A	N/A	N/A
	Overall	101/102	99.0	94.7-99.8	408/408	100.0	99.1-100.0

Abbreviations: TP, True Positive; FN: False Negative; TN, True Negative; FP, False Positive; PPA, Positive Percent Agreement; NPA, Negative Percent Agreement; CI, Confidence Interval, N/A = Not Applicable

The positive percent agreement (PPA) of the Xpert Hemorrhagic Fever Panel test stratified by strain was calculated relative to the expected result and is presented in **Table 6.**

Table 6. Performance of Xpert Hemorrhagic Fever Panel by Strain in VWB

Analyte	Strain	PPA		
		TP/(TP+FN)	PPA (%)	95% CI
CCHF	Afg09-2990	51/51	100.0	93.0-100.0
	DAK8194	50/51	98.0	89.7-99.7
Ebola	Bundibugyo Uganda	27/27	100.0	87.5-100.0
	Sudan Boniface	27/27	100.0	87.5-100.0
	Tai Forest	21/21	100.0	84.5-100.0
	Zaire Makona	27/27	100.0	87.5-100.0
Lassa	Josiah 1976	51/51	100.0	93.0-100.0

Analyte	Strain	PPA		
		TP/(TP+FN)	PPA (%)	95% CI
	Pinneo	51/51	100.0	93.0-100.0
Marburg	**Angola**	50/51	98.0	89.7-99.7
	Musoke	51/51	100.0	93.0-100.0
Abbreviations: TP, True Positive; FN: False Negative; PPA, Positive Percent Agreement; CI, Confidence Interval				

19.2. Analytical Sensitivity (Limit of Detection)

Studies were performed to determine the analytical limit of detection (LoD) of the Xpert Hemorrhagic Fever Panel test. The LoD of the Xpert Hemorrhagic Fever Panel test was first estimated using 2 reagent lots and testing limiting dilution of AccuPlex and inactivated Ebola, Lassa, CCHF and Marburg viruses, including the WHO Ebola Reference Reagent, in clinical venous whole blood (VWB) matrix following the Clinical and Laboratory Standards Institute (CLSI) document EP17-A2. The LoD is defined as the lowest concentration for each strain at which 95% (19/20) of replicates yield a positive result. The higher of the two estimated LoD value for each strain as determined Probit regression analysis was verified in VWB using one lot of the Xpert Hemorrhagic Fever Panel test.

The LoD of the Xpert Hemorrhagic Fever Panel test was also estimated by testing venous whole blood contrived with serial dilutions of live viruses (Ebola, Lassa, CCHF and Marburg) using one reagent lot. The estimated LoD was determined as the lowest concentration in a serial 5-fold dilution with four out of four replicates reporting positive results.

The verified LoD values for AccuPlex and inactivated viruses (Ebola, Lassa, CCHF and Marburg) in clinical VWB matrices are presented in **Table 7** and for live viruses in **Table 8**.

Table 7. Verified LoD in VWB – AccuPlex and Inactivated Viruses

Analyte	Virus Strain	Verified LoD in VWB
Ebola	Ebola Zaire Inactivated Virus (copies/mL)	926.1
	Ebola Zaire AccuPlex (copies/mL)	1065
	WHO Ebola Reference Reagent (units/mL)	550.6
	Ebola Sudan Inactivated Virus (copies/mL)	1830.3
	Ebola Sudan AccuPlex (copies/mL)	132.3
	Ebola Tai Forest Inactivated Virus (copies/mL)	4383.2
	Ebola BDBV Inactivated Virus (copies/mL)	4420.5
Lassa	Lassa Inactivated Virus (copies/mL)	1094.3
	Lassa AccuPlex (copies/mL)	1892
CCHF	CCHF Inactivated Virus (copies/mL)	377.4
	CCHF AccuPlex (copies/mL)	203.1
Marburg	Marburg Inactivated Virus (copies/mL)	665.6
	Marburg AccuPlex (copies/mL)	435

Table 8. Estimated LoD in VWB – Live Viruses

Virus	Strain (Lineage/Clade)	Estimated LoD in VWB	
		PFU/mL	copies/mL[a]
Ebola	Zaire Makona[b]	2	6.80E+02
	Zaire Mayinga	2	2.28E+02
	Sudan Boniface[b]	10	9.07E+02
	Bundibugyo[b]	1	2.27E+03
	Tai Forest[b]	25	1.35E+03

Virus	Strain (Lineage/Clade)	Estimated LoD in VWB	
		PFU/mL	copies/mL[a]
Lassa	Pinneo (I) [b]	100	2.40E+03
	Weller (III)	200	1.51E+03
	Josiah (IV) [b]	100	4.65E+02
CCHF	DAK8194 (I) [b]	2	3.29E+02
	UG3010 (II)	50	5.55E+03
	IbAr10200 (III)	10	1.67E+02
	Afg09-2990 (IV)[b]	50	3.28E+02
	Drozdov (V)	0.4	1.92E+02
Marburg	Angola[b]	10	3.00E+02
	Ci67	10	2.70E+02
	Musoke[b]	10	2.44E+02
	Ravn	2	3.92E+02

a. Concentration determined by qPCR
b. Strains used in contrived clinical study

19.3. Analytical Reactivity (Inclusivity)

The analytical reactivity/inclusivity of the Xpert Hemorrhagic Fever Panel test was evaluated by bench testing against multiple strains of Ebola, Lassa, CCHF, and Marburg virus at near LoD or challenging concentration in VWB. Testing was performed with either inactivated or live organisms in replicates of 3 per strain. All strains were detected in all 3 valid replicates. The results of the inclusivity wet-testing are shown in **Table 9**.

Table 9. Analytical Reactivity (Inclusivity) of Xpert Hemorrhagic Fever Panel

Virus	Strain (Lineage/Clade)	Concentration Tested		Results	Multiples of LoD
		PFU/mL	Copies/mL		
Ebola	Zaire Makona	6	2.04E+03	Ebola DETECTED	3x
	Zaire Mayinga	6	6.83E+02		3x
	Inactivated Zaire Guéckédou	409.5	2.78E+03		3x
	Sudan Boniface	30	2.72E+03		3x
	Sudan Gulu	10	3.60E+03		4x
	Bundibugyo Uganda	3	6.80E+03		3x
	Tai Forest	75	4.04E+03		3x
Lassa	Pinneo (I)	300	7.21E+03	Lassa DETECTED	3x
	Sauerwald (II)	4000	9.16E+04		38.1x
	Weller (III)	600	4.53E+03		3x
	G2405 (IV)	200	3.46E+03		7.4x
	Josiah (IV)	300	1.39E+03		3x
	Macenta (IV)	1	1.21E+03		2.6x
	Benin (VII)	150	8.49E+03		3.5x
Crimean-Congo Hemorrhagic Fever	DAK 8194 (I)	6	9.87E+02	CCHF DETECTED	3x
	UG3010 (II)	150	1.66E+04		3x
	IbAr10200 (III)	30	5.00E+02		3x
	SPU128/81/7 (III)	90	5.68E+02		3.4x
	Afg09-2990 (IV)[a]	150	9.84E+02		3x

Virus	Strain (Lineage/Clade)	Concentration Tested		Results	Multiples of LoD
		PFU/mL	Copies/mL		
	Chinese HY13 (IV)	12	9.52E+02		2.9x
	Pak JD-206 (IV)	6	9.17E+02		2.8x
	Drozdov (V)	1.2	5.76E+02		3x
Marburg	Angola	30	9.00E+02	Marburg DETECTED	3x
	Ci67	30	8.10E+02		3x
	Musoke	30	7.32E+02		3x
	Inactivated Musoke	NA	3.99E+03		6x
	Ravn	6	1.18E+03		3x
	Inactivated Ravn	NA	3.99E+03		6x
	Inactivated Voege	6.93	2.00E+03		3x

a. Four replicates instead of 3 were tested for this strain. All 4 valid replicates reported CCHF Detected.

In silico analysis of sequence data were used to predict analytical inclusivity for strains that were not available for wet-testing, such as those listed in **Table 10**.

Table 10. Predicted Inclusivity of Xpert Hemorrhagic Fever Panel

Virus	Strain
Ebola	Zaire Booue 1996
	Zaire Ebola virus/H.sapiens-wt/COD/2018/Tumba
	Zaire Ebolavirus/H.sapiens-wt/COD/2020/Ituri
	Zaire Gabon 2002
	Sudan Uganda 2022
Lassa	Soromba
	Togo 2016/7082
Marburg	Ozolin

19.4. Analytical Specificity (Exclusivity)

The analytical specificity/exclusivity of the Xpert Hemorrhagic Fever test was evaluated by wet-testing 4 on-panel organisms (Ebola, Lassa, CCHF and Marburg) and a panel of 63 off-panel microorganisms (39 viruses, 20 bacteria and 4 protozoa) based on a combination of factors, including genetic similarity to Xpert Hemorrhagic Fever Panel analytes, clinical relevance, and probability of their presence in blood.

Each strain was tested individually with 3 replicates at high concentrations of $\geq 10^5$ units/mL (copies/mL, PFU/mL, $TCID_{50}$/mL, IU/mL, $CEID_{50}$/mL, parasites/mL, or cells/mL) for viruses and protozoa, $\geq 10^6$ units/mL (CFU/mL or copies/mL for bacteria), or the highest possible titer available and/or clinically relevant if high concentration virus/bacteria stocks were not available. A sample was considered negative if all 3 replicates reported NOT DETECTED. The analytical specificity results for off-panel microorganisms are shown in **Table 11**.

Table 11. Analytical Specificity of Xpert Hemorrhagic Fever Panel Against Off-Panel Organisms

Organism	Strain	Concentration Tested	Test Results Reported for 3/3 Replicates			
			Ebola	Lassa	CCHF	Marburg
Virus	Adenovirus[a]	1.60E+07 $TCID_{50}$/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Aigai virus[a] (formerly CCHF AP92)	7.49E+05 copies/mL	Not Detected	Not Detected	**Detected**	Not Detected
		7.49E+04 copies/mL	Not Detected	Not Detected	**Detected**	Not Detected

Organism	Strain	Concentration Tested	Test Results Reported for 3/3 Replicates			
			Ebola	Lassa	CCHF	Marburg
		2.50E+04 copies/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Chikungunya virus[a]	2.80E+05 $TCID_{50}$/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Cytomegalovirus (CMV)[a]	8.89E+03 $TCID_{50}$/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Dengue virus (DENV-1)[a]	2.80E+05 $TCID_{50}$/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Dengue virus (DENV-2)[a]	1.00E+05 $TCID_{50}$/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Dengue virus (DENV-3)[a]	8.90E+05 $TCID_{50}$/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Dengue virus (DENV-4)[a]	2.32E+04 $TCID_{50}$/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Enterovirus (EV71)[a]	1.60E+06 $TCID_{50}$/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Epstein Barr virus (EBV) B95-8[a]	1.21E+05 copies/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Hendra virus[b]	2.47E+07 copies/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Hepatitis A virus[a]	2.80E+06 $TCID_{50}$/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Hepatitis B virus[a]	1.64E+06 IU/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Hepatitis C virus[a]	6.26E+05 IU/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Hepatitis E virus[c]	3.70E+06 copies/mL	Not Detected	Not Detected	Not Detected	Not Detected
	HIV1[a]	1.01E+05 $TCID_{50}$/mL	Not Detected	Not Detected	Not Detected	Not Detected
	HIV2[a]	1.01E+05 $TCID_{50}$/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Influenza A virus[a]	9.60E+06 $CEID_{50}$/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Influenza B virus[a]	8.89E+05 $CEID_{50}$/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Japanese encephalitis virus[b]	1.08E+05 copies/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Lujo virus[a]	1.56E+05 PFU/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Machupo virus[a]	1.77E+05 PFU/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Mayaro virus (Alphavirus sp.)[a]	1.60E+06 $TCID_{50}$/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Measles virus[a]	1.60E+04 $TCID_{50}$/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Mobala virus Acar3080[a]	1.33E+05 PFU/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Mopeia virus[a]	1.34E+05 PFU/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Parvovirus B19[d]	4.20E+06 copies/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Reston virus[a]	1.00E+06 copies/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Rift Valley Fever virus MP-12[a]	1.60E+05 PFU/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Rubella virus[a]	5.00E+02 $TCID_{50}$/mL	Not Detected	Not Detected	Not Detected	Not Detected

Organism	Strain	Concentration Tested	Test Results Reported for 3/3 Replicates			
			Ebola	Lassa	CCHF	Marburg
	Sindbis virus[b]	2.50E+07 copies/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Spondweni virus[a]	1.02E+05 PFU/mL	Not Detected	Not Detected	Not Detected	Not Detected
	St. Louis encephalitis virus[a]	2.80E+05 $TCID_{50}$/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Usutu virus[a]	1.60E+06 $TCID_{50}$/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Varicella-zoster virus[a]	1.00E+03 copies/mL	Not Detected	Not Detected	Not Detected	Not Detected
	West Nile virus[e]	6.80E+08 copies/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Yellow Fever vaccine strain 17D[a]	1.60E+05 $TCID_{50}$/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Yellow Fever virus[a]	1.26E+05 PFU/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Zika virus[a]	1.60E+05 copies/mL	Not Detected	Not Detected	Not Detected	Not Detected
Bacteria	*Bacillus anthracis*[f]	2.30E+08 copies/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Borrelia burgdorferi	N/A (1:10 dilution of stock)	Not Detected	Not Detected	Not Detected	Not Detected
	Clastridium botulinum[f]	4.58E+06 copies/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Enterococcus faecalis	3.28E+06 CFU/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Escherichia coli	3.12E+07 CFU/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Francisella tularensis	N/A (1:10 dilution of stock)	Not Detected	Not Detected	Not Detected	Not Detected
	Haemophilus influenzae	6.33E+04 CFU/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Klebsiella pneumoniae	1.02E+06 CFU/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Leptospira interrogans	2.29E+06 cells/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Listeria monocytogenes	1.70E+06 CFU/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Neisseria meningitidis	1.33E+05 CFU/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Pseudomonas aeruginosa	1.00E+07 CFU/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Rickettsia monacensis	9.00E+04 $TCID_{50}$/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Salmonella enterica	3.49E+07 CFU/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Staphylococcus aureus	1.00E+06 CFU/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Staphylococcus epidermidis	2.98E+07 CFU/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Streptococcus pneumoniae	1.00E+06 CFU/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Streptococcus pyogenes	1.87E+06 CFU/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Vibrio cholerae	1.01E+06 Unit/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Yersinia pestis[f]	2.30E+08 copies/mL	Not Detected	Not Detected	Not Detected	Not Detected

Organism	Strain	Concentration Tested	Test Results Reported for 3/3 Replicates			
			Ebola	Lassa	CCHF	Marburg
Protozoa	*Leishmania braziliensis*	2.05E+06 cells/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Plasmodium falciparum	1.05E+05 parasites/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Plasmodium vivax	2.70E+05 parasites/mL	Not Detected	Not Detected	Not Detected	Not Detected
	Toxoplasma gondii	1.01E+06 cells/mL	Not Detected	Not Detected	Not Detected	Not Detected

a. Virus (Live or Inactivated)
b. Genomic RNA
c. Synthetic RNA
d. Synthetic DNA
e. Plasmid
f. Genomic DNA

Aigai virus (formerly known as CCHF AP92) produced CCHF DETECTED results at ≥ 7.49E+04 copies/mL. No cross-reactivity was observed when Aigai virus was evaluated at 2.50E+04 copies/mL (**Table 11).**

No cross-reactivity was observed for each of the 4 on-panel organisms (Ebola, Lassa, CCHF and Marburg inactivated viruses) tested individually at > 10^5 copies/mL as shown in **Table 12.**

Table 12. Analytical Specificity of Xpert Hemorrhagic Fever Panel Against On-Panel Organisms

Strain	Concentration Tested	Test Results Reported for 3/3 Replicates			
		Ebola	Lassa	CCHF	Marburg
Zaire Ebola virus	8.87E+06 copies/mL	DETECTED	NOT DETECTED	NOT DETECTED	NOT DETECTED
Lassa virus	1.45E+07 copies/mL	NOT DETECTED	DETECTED	NOT DETECTED	NOT DETECTED
CCHF virus	3.31E+09 copies/mL	NOT DETECTED	NOT DETECTED	DETECTED	NOT DETECTED
Marburg virus	3.18E+07 copies/mL	NOT DETECTED	NOT DETECTED	NOT DETECTED	DETECTED

In addition to the experimental testing, *in silico* analyses directed toward the potential to cross-react with specific pathogens that were unavailable for wet testing was also performed. This included Andes virus, Bas-Congo virus, Lloviu virus, Lymphocytic chorimeningitis virus, Batai virus, Bombali virus, Chapare virus, Dugbe virus, Guanarito virus, Hantaan virus, Ilesha virus, Junin virus, La Crosse virus, Murray Valley encephalitis virus, Ngari virus, Nipah virus, Puumala virus, Sabia virus, Seoul virus, Severe fever with thrombocytopenia syndrome virus, Tacaribe virus, Thogoto virus, and Tick-borne encephalitis virus. No expected cross-reactivity with off-panel pathogens was predicted by *in silico* analysis.

19.5. Microbial Interference

Microbial interference of the Xpert Hemorrhagic Fever test was evaluated by testing 6 potentially interfering off-panel microorganisms consisting of 3 viruses and 3 bacteria strains. Samples consisted of Ebola, Lassa, CCHF and Marburg AccuPlex seeded at 3x LoD into VWB matrix in the presence of Hepatitis B virus (HBV), Human Immunodeficiency virus (HIV) 1, West Nile Virus (each seeded at 1x10^5 PFU/mL), *Escherichia coli, Staphylococcus aureus*, and *Streptococcus pyogenes* (each seeded at 1x10^6 CFU/mL). Replicates of 8 were tested for each potentially interfering microbial strain combination. For each analyte, all 8 of 8 valid replicates of the positive samples were correctly identified by the Xpert Hemorrhagic Fever test. No microbial interference was reported.

19.6. Competitive Interference

Competitive interference of the Xpert Hemorrhagic Fever Panel test caused by co-infections was evaluated by testing contrived samples of individual Ebola, Lassa, CCHF or Marburg AccuPlex at 3x LoD in the presence of different on-panel target organisms at a higher concentration in VWB matrix. The concentration at 3x LoD was 3195 copies/mL for Ebola AccuPlex and 5676 copies/mL for Lassa AccuPlex, 603.3 copies/mL for CCHF AccuPlex and 1305 copies/mL for Marburg AccuPlex. The competitive strains were evaluated at > 10^5 RNA (copies/mL).

Replicates of 8 were tested for each on-panel target organism and each competitive strain combination. The virus at high

concentration shows no competitive inhibitory effects if 8 of 8 replicates for the on-panel target strain report the correct test result. The results for the competitive interference study are presented in **Tables 13 – 16** for Ebola, Lassa, CCHF, and Marburg, respectively.

Table 13. Assessment of Competitive Interference for Xpert Hemorrhagic Fever Detection of Ebola

Ebola Accuplex at 3x LoD	On-Panel Competitive Microorganism	Competitive Strain High Titer	# of Correct Test Results/ # of Valid Reps Tested
3195 copies/ mL	None (Control)		8/8
	Lassa	1.00E+05 copies/mL	8/8
	CCHF	1.00E+05 copies/mL	8/8
	Marburg	1.00E+05 copies/mL	8/8

Table 14. Assessment of Competitive Interference for Xpert Hemorrhagic Fever Panel Detection of Lassa

Lassa Accuplex at 3x LoD	On-Panel Competitive Microorganism	Competitive Strain High Titer	# of Correct Test Results/ # of Valid Reps Tested
5676 copies/ mL	None (Control)		8/8
	Ebola	1.00E+05 copies/mL	8/8
	CCHF	1.00E+05 copies/mL	8/8
	Marburg	1.00E+05 copies/mL	8/8

Table 15. Assessment of Competitive Interference for Xpert Hemorrhagic Fever Panel Detection of CCHF

CCHF Accuplex at 3x LoD	On-Panel Competitive Microorganism	Competitive Strain High Titer	# of Correct Test Results/ # of Valid Reps Tested
609.3 copies/ mL	None (Control)		8/8
	Ebola	1.00E+05 copies/mL	8/8
	Lassa	1.00E+05 copies/mL	8/8[a]
	Marburg	1.00E+05 copies/mL	8/8

a. One of 8 replicate tests was reported as ERROR. The run was successfully repeated to obtain 8 valid replicates.

Table 16. Assessment of Competitive Interference for Xpert Hemorrhagic Fever Panel Detection of Marburg

Marburg Accuplex at 3x LoD	On-Panel Competitive Microorganism	Competitive Strain High Titer	# of Correct Test Results/ # of Valid Reps Tested
1305 copies/ mL	None (Control)		8/8
	Ebola	1.00E+05 copies/mL	8/8
	Lassa	1.00E+05 copies/mL	8/8
	CCHF	1.00E+05 copies/mL	8/8

19.7. Potentially Interfering Substances

Substances that may be present in the whole blood or introduced during specimen collection were evaluated for the potential to interfere with accurate detection of Ebola, Lassa, CCHF and Marburg by directly testing on the Xpert Hemorrhagic Fever Panel test. Positive and negative samples were prepared in VWB matrix. Negative samples (n = 8) were tested in the presence of each substance to determine the effect on the performance of the sample processing control (SPC) and the sample adequacy control (SAC). Positive samples (n = 8) were tested per substance with Ebola, Lassa, CCHF and Marburg AccuPlex spiked at 3x the LoD determined for each strain. The exogeneous and endogenous substances, including their descriptions and concentrations that were evaluated and shown to not interfere with Xpert Hemorrhagic Fever Panel

performance, are listed in **Table 17**.

Table 17. Potentially Interfering Substances Showing No Interference with Xpert Hemorrhagic Fever Panel

Category	Substance	Description	Concentration Tested
Exogenous Substances	Acetaminophen	Painkiller	0.156 mg/mL
	Acetylsalicylic acid	Painkiller	0.03 mg/mL
	Artemether	Antimalarial	0.04 µg/mL
	Artesunate	Antimalarial	0.003 mg/mL
	Atovaquone	Antiprotozoal agents	0.005 mg/mL
	Azithromycin	Macrolide Antibiotics	0.0111 mg/mL
	Caffeine	Stimulant	0.108 mg/mL
	Cetirizine HCl	Antihistamines	0.00435 mg/mL
	Prednisone	Corticosteroids	0.099 µg/mL
	Dextromethorphan	Antitussives/ Cough Syrup	0.0156 µg/mL
	Doxycycline	Tetracycline Antibiotics	0.02 mg/mL
	Heparin	Anticoagulant	3.3 units/mL
	Ibuprofen	Nonsteroidal Anti-Inflammatory Drug	0.219 mg/mL
	Imipenem	Carbapenem Antibiotics	0.1 mg/mL
	Lumefantrine	Antimalarial	0.001 mg/mL
	Mefloquine	Antimalarial	0.0035 mg/mL
	Nicotine	Stimulant	0.0199 mg/mL
	Prednisolone	Corticosteroids	0.0012 mg/mL
	Proguanil	Antimalarial	0.001 mg/mL
	Quinidine	Class IA Antiarrhythmic Agent, Antimalarial	0.0105 mg/mL
	Quinine	Antimalarial	0.01 mg/mL
	Vancomycin	Glycopeptide Antibiotics	0.12 mg/mL
Endogenous Substances	Albumin	Protein in Blood	60 mg/mL
	Bilirubin, Conjugated	Metabolic Product in Blood	0.4 mg/mL
	Bilirubin, Un-conjugated	Metabolic Product in Blood	0.4 mg/mL
	Cholesterol	Lipid in Blood	4 mg/mL
	Human Genomic DNA	Nucleic Acid in Blood	1µg/mL
	Hemoglobin	Protein in Blood	10 mg/mL
	Immunoglobulin	Protein in Blood	20 mg/mL
	RF (Rheumatoid Factor)	Protein in Blood	40 IU/mL
	Triglycerides	Lipid in Blood	15 mg/mL
Exogenous Substances Related to Specimen Collection	Alcohol	Central Nervous System Depressant	0.5% v/v
	Hand Cream	Glycerin as Active Ingredient	1 mg/mL
	Hand Sanitizer	Ethanol as Active Ingredient	1 mg/mL
	Hand Soap	Sodium Dodecyl Sulfate as Active Ingredient	0.5% v/v

19.8. Carry-over Contamination

A study was conducted to demonstrate that the single-use, self-contained Xpert Hemorrhagic Fever cartridge prevents specimens and amplicon carryover by testing a negative sample immediately after testing a very high positive sample in the same GeneXpert module. The negative sample used in the study consisted of AccuPlex Ebola, Lassa, CCHF and Marburg spiked into venous whole blood at $1x10^6$ copies/mL. The negative sample was tested at the start of the study. Following the initial testing of the negative sample, the high positive sample was processed in the same GeneXpert module,

followed immediately by another negative sample. This was repeated using 5 GeneXpert modules and this testing scheme was repeated 8 times for a total of 17 runs resulting in 8 positive and 9 negative samples per GeneXpert module. All 40 positive samples were correctly reported as **Ebola DETECTED; Lassa DETECTED; CCHF DETECTED; Marburg DETECTED.** All 45 negative samples were correctly reported as Ebola NOT DETECTED; Lassa NOT DETECTED; CCHF NOT DETECTED; Marburg NOT DETECTED.

19.9. Reproducibility-Precision

The reproducibility and precision of the Xpert Hemorrhagic Fever Panel test was established at 3 external sites using three contrived panels. Panel 1 and 2 were 4-member panels including 1 negative sample and either low positive (~1.5x LoD) or moderate positive (~3.0x LoD) samples. Panel 3 included 3 panel members with a negative sample and two moderate positive (~3x LoD) samples. The negative samples consisted of pooled negative EDTA-treated VWB specimens without the target viral RNA. The positive panel members were prepared by diluting recombinant pseudoviral constructs containing target viral RNA for each of the four analytes (Ebola, CCHF, Lassa, and Marburg) into pooled negative EDTA-treated VWB specimens. Testing was conducted over 6 days using 3 lots of Xpert Hemorrhagic Fever cartridges at 3 participating sites, each with 3 users per site yielding a total of 162 observations per panel member (3 Sites x 3 Lots x 2 Days/Lot x 3 Users/Site x 1 Run x 3 Replicates = 162 observations).

The percent agreement between the Xpert Hemorrhagic Fever Panel test result and the expected result analyzed across each of the 9 operators across each of the 3 sites is shown in **Table 18**. In addition, the overall percent agreement for each sample (% total agreement) was calculated as well as the two-sided Wilson Score confidence intervals (CI) are presented in the last column.

Table 18. Percent Agreement for Qualitative Results

Panel Member	Site 1				Site 2				Site 3				% Agreement by Analyte
	PANEL 1												
	Op1	Op2	Op3	Site Total	Op1	Op2	Op3	Site Total	Op1	Op2	Op3	Site Total	(%; 95% CI)
Negative	100.0% (18/18)	100.0% (17/17)[a]	100.0% (18/18)	100.0% (53/53)	100.0% (18/18)	100.0% (18/18)	100.0% (18/18)	100.0% (54/54)	100.0% (18/18)	100.0% (18/18)	100.0% (18/18)	100.0% (54/54)	100.0% (97.7%-100.0%) (161/161)
Lassa Virus ~1.5x LoD	100.0% (18/18)	100.0% (18/18)	100.0% (18/18)	100.0% (54/54)	100.0% (18/18)	100.0% (18/18)	100.0% (18/18)	100.0% (54/54)	100.0% (18/18)	100.0% (18/18)	100.0% (18/18)	100.0% (54/54)	100.0% (97.7%-100.0%) (162/162)
CCHF Virus ~1.5x LoD	100.0% (17/17)[b]	100.0% (18/18)	100.0% (18/18)	100.0% (53/53)	100.0% (18/18)	100.0% (18/18)	100.0% (18/18)	100.0% (54/54)	100.0% (18/18)	100.0% (18/18)	94.4% (17/18)	98.1% (53/54)	99.4% (96.6%-99.9%) (160/161)
Ebola Virus ~1.5x LoD	100.0% (18/18)	100.0% (18/18)[c]	100.0% (18/18)	100.0% (54/54)	100.0% (18/18)	100.0% (18/18)	100.0% (18/18)	100.0% (54/54)	100.0% (18/18)	100.0% (18/18)	94.4% (17/18)	98.1% (53/54)	99.4% (96.6%-99.9%) (161/162)
Panel Member	**Site 1**				**Site 2**				**Site 3**				**% Agreement by Analyte**
	PANEL 2												
	Op1	**Op2**	**Op3**	**Site Total**	**Op1**	**Op2**	**Op3**	**Site Total**	**Op1**	**Op2**	**Op3**	**Site Total**	**(%; 95% CI)**
Negative	100.0% (18/18)	94.4% (17/18)	100.0% (18/18)	98.1% (53/54)	100.0% (18/18)	100.0% (18/18)	100.0% (18/18)	100.0% (54/54)	100.0% (18/18)	100.0% (18/18)	100.0% (18/18)	100.0% (54/54)	99.4% (96.6%-99.9%) (161/162)
Marburg Virus ~1.5x LoD	100.0% (18/18)	94.4% (17/18)	100.0% (18/18)	98.1% (53/54)	100.0% (18/18)	100.0% (18/18)	100.0% (18/18)	100.0% (54/54)	100.0% (18/18)	100.0% (18/18)	100.0% (18/18)	100.0% (54/54)	99.4% (96.6%-99.9%) (161/162)
Ebola Virus ~3.0x LoD	100.0% (18/18)	94.4% (17/18)	100.0% (18/18)	98.1% (53/54)	100.0% (18/18)	100.0% (18/18)	100.0% (18/18)	100.0% (54/54)	100.0% (18/18)	100.0% (18/18)	100.0% (18/18)	100.0% (54/54)	99.4% (96.6%-99.9%) (161/162)
Lassa Virus ~3.0x LoD	100.0% (18/18)	94.4% (17/18)	100.0% (18/18)	98.1% (53/54)	100.0% (18/18)	100.0% (18/18)	100.0% (18/18)	100.0% (54/54)	100.0% (18/18)	100.0% (18/18)	100.0% (18/18)	100.0% (54/54)	99.4% (96.6%-99.9%) (161/162)

Panel Member	Site 1				Site 2				Site 3				% Agreement by Analyte
	PANEL 3												
	Op1	Op2	Op3	Site Total	Op1	Op2	Op3	Site Total	Op1	Op2	Op3	Site Total	(%; 95% CI)
Negative	100.0% (18/18)	100.0% (18/18)	100.0% (18/18)	100.0% (54/54)	100.0% (18/18)	100.0% (18/18)	100.0% (18/18)	100.0% (54/54)	100.0% (18/18)	66.7% (12/18)	100.0% (18/18)	88.9% (48/54)	96.3% (92.2%-98.3%) (156/162)
Marburg Virus ~3.0x LoD	100.0% (18/18)	100.0% (18/18)	100.0% (18/18)	100.0% (54/54)	100.0% (18/18)	100.0% (18/18)	100.0% (18/18)	100.0% (54/54)	100.0% (18/18)	66.7% (12/18)	100.0% (18/18)	88.9% (48/54)	96.3% (92.2%-98.3%) (156/162)
CCHF Virus ~3.0x LoD	100.0% (18/18)	100.0% (18/18)	100.0% (18/18)	100.0% (54/54)	100.0% (17/17)[d]	100.0% (18/18)	100.0% (18/18)	100.0% (53/53)	100.0% (18/18)	100.0% (18/18)	100.0% (18/18)	100.0% (54/54)	100.0% (97.7%-100.0%) (161/161)

Abbreviation: CCHF = Crimean-Congo Hemorrhagic Fever, Op = Operator

a. Of the 18 samples tested, one yielded an ND result on both initial and repeat testing.
b. Of the 18 samples tested, one yielded an ND result on both initial and repeat testing.
c. One Ebola Virus panel member (~1.5× LoD), yielded the following test result: "Ebola DETECTED; Lassa NOT DETECTED; CCHF NOT DETECTED; Marburg DETECTED", the Marburg result was excluded from the agreement table.
d. Of the 18 samples tested, one yielded an ND result on both initial and repeat testing.

20. References

1. World Health Organization. Diagnostic Testing for Ebola Disease and Marburg Virus Disease: Interim Guidance. Geneva: WHO; 2026
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7. World Health Organization (WHO). Laboratory Biosafety Manual, Fourth Edition. Geneva, Switzerland: World Health Organization; 2020.
8. Occupational Safety and Health Standards, Hazard Communication, Toxic and Hazard Substances (March 26, 2012) (29 CFR, part 1910, subpart Z).
9. REGULATION (EC) No 1272/2008 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 December 2008 on the classification, labeling and packaging of substances and mixtures amending and repealing, List of Precautionary Statements, Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006 (2008).

21. Cepheid Headquarters Locations

Corporate Headquarters

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www.cepheid.com

22. Technical Assistance

Before contacting Cepheid Technical Support, collect the following information:

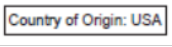
- Product name
- Lot number
- Serial number of the instrument
- Error messages (if any)
- Software version and, if applicable, Computer Service Tag number

United States Technical Support

Telephone: + 1 888 838 3222
Email: techsupport@cepheid.com

Contact information for all Cepheid Technical Support offices is available on our website: www.cepheid.com/en/support/contact-us.

23. Table of Symbols

Symbol	Meaning
	Catalog number
	*In vitro* diagnostic medical device
	Do not reuse
	Batch code
	Consult instructions for use
	Manufacturer
	Country of Manufacture
	Contains sufficient for <n> tests
	Control
	Expiration date
	Temperature limitation
	Biological risks
	Caution
	Warning
	Skin corrosion, eye damage and corrosive to metals
	For prescription use only
	Country of Origin: United States of America

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24. Revision History

Revision	Effective	Description of Changes
A	2026-09	Initial release (WHO EUL)