February 20, 2026

Cepheid
Katy Reilly
Regulatory Affairs Principal, New Product Development
904 Caribbean Dr.
Sunnyvale, California 94089

Re: K253653
Trade/Device Name: Xpert Hemorrhagic Fever
Regulation Number: 21 CFR 866.4000
Regulation Name: Device To Detect And Identify Biothreat Microbial Agents In Human Clinical Specimens
Regulatory Class: Class II
Product Code: QVR, OOI
Dated: November 20, 2025
Received: November 20, 2025

Dear Katy Reilly:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device"

(https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality Management System Regulation (QMSR) (21 CFR Part 820), which includes, but is not limited to, ISO 13485 clause 7.3 (Design controls), ISO 13484 clause 8.3 (Nonconforming product), and ISO 13485 clause 8.5 (Corrective and preventative action). Please note that regardless of whether a change requires premarket review, the QMSR requires device manufacturers to review and approve changes to device design and production (ISO 13485 clause 7.3 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the Quality Management System Regulation (QMSR) (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

BRYAN M. GRABIAS -S
2026.02.20 12:26:37
-05'00'

Bryan Grabias
Acting Branch Chief
Bacterial Respiratory and Medical Countermeasures Branch
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K253653

Device Name
Xpert Hemorrhagic Fever

Indications for Use *(Describe)*
The Xpert Hemorrhagic Fever test, performed on the GeneXpert Edge X 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 test uses EDTA-treated whole blood specimens collected by capillary or 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 test 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 in accordance with the guidelines provided by the Centers for Disease Control and Prevention (CDC) and United States Department of Defense (DoD).
The Xpert Hemorrhagic Fever test 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 test. 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.

The Xpert Hemorrhagic Fever test is for use only by United States Department of Defense 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 Department of Defense and public health authorities.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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Attachment 14-3

510(k) Summary
for
Xpert Hemorrhagic Fever

TABLE OF CONTENTS

1. 510(k) Summary

As required by 21 CFR Section 807.92(c).

Submitted by:	Cepheid 904 Caribbean Drive Sunnyvale, CA 94089 Phone Number: 856-723-5005
Contact:	Katy Reilly
Date of Preparation:	11/20/2025
Device:	
Trade name	Xpert® Hemorrhagic Fever
Common name	Hemorrhagic Fever
Type of Test	Multiplex real-time reverse transcription polymerase chain reaction (RT-qPCR) test intended for the qualitative *in vitro* detection and identification of RNA from multiple biothreat agents.
Regulation Number	21 CFR 866.4000
Classification Name	Device to detect and identify biothreat microbial agents in human clinical specimens.
Primary Product Code	QVR
Secondary Product Code	OOI
Classification Advisory Panel	Microbiology (83)
Prescription Use	Yes
Predicate Device Assay	BioFire® Global Fever Special Pathogens Panel (K213362)

1.1. Device Description

Xpert Hemorrhagic Fever ("Xpert HF") is an automated *in vitro* diagnostic test for the qualitative detection and identification of RNA from Ebola virus (including Zaire, Sudan, Taï Forest, and Bundibugyo, not differentiated), Crimean-Congo hemorrhagic fever (CCHF) virus, Marburg virus, and Lassa virus in EDTA-treated whole blood specimens collected by capillary or 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 HF test is performed on the GeneXpert Edge X system, which consists of an instrument and a mobile tablet with preloaded software for performing the test and viewing the results. The GeneXpert Edge X system automates and integrates sample extraction, nucleic acid purification and amplification, and detection of target sequences from EDTA-treated whole blood specimens by using reverse transcription (conversion of RNA templates into DNA) followed by real-time PCR. The GeneXpert Edge X instrument is equipped with one GeneXpert module which contains a syringe drive for dispensing fluids (i.e., the syringe drive activates the plunger that works in concert with the rotary valve in the cartridge to move fluids between chambers), an ultrasonic horn for lysing cells or spores, and a proprietary I-CORE® thermocycler for performing real-time RT-PCR and PCR as well as detection. The GeneXpert Edge X system 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.

The Xpert HF test includes reagents for the detection of RNA from Ebola virus (including Zaire, Sudan, Taï Forest, and Bundibugyo, not differentiated), Crimean-Congo hemorrhagic fever (CCHF) virus, Marburg virus, and Lassa virus in EDTA-treated capillary or venous whole blood specimens. The primers and probes in the Xpert HF test are designed to amplify and detect unique sequences in the genes that encode the following protein: Ebola nucleoprotein (NP), Lassa glycoprotein precursor (GPC), CCHF polymerase (L), and Marburg nucleoprotein (NP). 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 adequate extraction and processing of the target sequences and to monitor for the presence of inhibitors in the PCR reaction. The SAC ensures that sufficient human cells have been added in test cartridge. The PCC verifies reagent rehydration, PCR tube filling in the cartridge, probe integrity, and dye stability.

Venous and capillary whole blood specimens collected into EDTA anticoagulant tubes are added to an off-board sample reagent (SR) vial in which the sample is inactivated. The inactivated sample is then added to the Xpert HF cartridge before being loaded onto the GeneXpert Edge X instrument, which performs hands-off, automated sample processing, and real-time RT-PCR for the detection of these viral RNAs.

The results are interpreted by the Cepheid OS X software from measured fluorescent signals and embedded calculation algorithms and are clearly shown in the "Result Summary Page". The Xpert HF test provides test results for Ebola, CCHF, Marburg and Lassa. If encountered, NO

RESULT-REPEAT TEST and INSTRUMENT ERROR test results are also reported and the user is instructed to repeat the test.

The Xpert HF test is designed for use with fingerstick K_2-EDTA whole blood (CWB) or EDTA-treated whole blood obtained from venous draw (VWB). The ancillary EDTA anticoagulant whole blood collection tubes verified and/or validated for use with the Xpert HF test included:

- BD Microtainer® Contact-Activated Lancet (P/N 366594 or P/N 366578)
- BD Microtainer® Blood Collection Tubes (P/N 3665974) for capillary whole blood collection
- BD Vacutainer® Blood Collection Tubes for venous whole blood collection
    - P/N 367841 (2 mL)
    - P/N 366643 (10 mL)
    - P/N 367899 (6 mL)

These ancillary collection tubes allow VWB and CWB specimens from patients to be collected, preserved and transported to the laboratory prior to analysis with the Xpert HF test.

1.2. Device Intended Use

The Xpert® Hemorrhagic Fever test, performed on the GeneXpert® Edge X 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 test uses EDTA-treated whole blood specimens collected by capillary or 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 test 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 in accordance with the guidelines provided by the Centers for Disease Control and Prevention (CDC) and United States Department of Defense (DoD).

The Xpert Hemorrhagic Fever test 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 test. 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.

The Xpert Hemorrhagic Fever test is for use only by United States Department of Defense 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 Department of Defense and public health authorities.

1.3. Substantial Equivalence

Table 1 shows the similarities and differences between the subject device to the previously cleared predicate device (K213362).

Table 1. Comparison of Similarities and Differences Between Subject Device and the Predicate Device

Attribute	Subject Device	Predicate Device
	Cepheid Xpert® Hemorrhagic Fever	**BioFire Defence, LLC BIOFIRE® Global Fever Special Pathogens Panel (K213362)**
Regulation	**21 CFR 866.4000** Device to detect and identify biothreat microbial agents in human clinical specimens.	**21 CFR 866.4000** Device to detect and identify biothreat microbial agents in human clinical specimens. **21 CFR 866.3966** Device to detect and identify selected microbial agents that cause acute febrile illness
Product Code	QVR, OOI	QVR, QMV, OOI
Device Class	Same	Class II
Technology/ Detection	Multiplex real-time reverse transcription polymerase chain reaction (RT-qPCR).	Multiplexed nested nucleic acid amplification test with melt analysis
Intended Use	The Xpert® Hemorrhagic Fever test, performed on the GeneXpert® Edge X 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 test uses EDTA-treated whole blood specimens collected by capillary or venous draw from	The BioFire® Global Fever Special Pathogens Panel is a qualitative, multiplexed, nucleic acid-based test intended for use with BioFire® FilmArray® 2.0 and BioFire® FilmArray® Torch Systems. The BioFire Global Fever Special Pathogens Panel is for the simultaneous qualitative detection and identification of multiple bacterial, viral, and protozoan nucleic acids directly from EDTA whole blood collected from individuals with signs and/or symptoms of acute febrile illness or recent acute febrile illness and known or suspected exposure to the target pathogens described below. **Pathogens identified:** Chikungunya virus Dengue virus (serotypes 1, 2, 3 and 4)

Attribute	Subject Device	Predicate Device
	Cepheid Xpert® Hemorrhagic Fever	**BioFire Defence, LLC BIOFIRE® Global Fever Special Pathogens Panel (K213362)**
	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 test 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 in accordance with the guidelines provided by the Centers for Disease Control and Prevention (CDC) and United States Department of Defense (DoD). The Xpert Hemorrhagic Fever test 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 test. 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. The Xpert Hemorrhagic Fever test is for use only by United States Department of Defense 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 Department of Defense and public health authorities.	*Leishmania* spp. that cause visceral leishmaniasis (e.g., *L. donovani* and *L. infantum*) *Leptospira* spp. *Plasmodium* spp. (including species differentiation of *Plasmodium falciparum* and *Plasmodium vivax/ovale*) West Nile virus **Pathogens presumptively identified:** *Bacillus anthracis* Crimean-Congo hemorrhagic fever virus *Ebolavirus* spp. *Francisella tularensis* Lassa virus *Marburgvirus* Yellow fever virus *Yersinia pestis* Pathogens for which the panel provides presumptive identification results require 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-infections with pathogens not included on the BioFire Global Fever Special Pathogens Panel. Not all pathogens that cause acute febrile illness are detected by this test, and negative results do not preclude infection with the pathogens targeted by the device and should not be used as the sole basis for diagnosis, treatment, or other patient management decisions. Evaluation for more common causes of acute febrile illness (e.g., infections of the upper and lower respiratory tract or gastroenteritis, as well as non-infectious causes) should be considered prior to evaluation with this panel. In the United States, patient travel history, exposure risk, and consultation of the CDC Yellow Book should be considered prior to use of the BioFire Global Fever Special

Attribute	Subject Device	Predicate Device
	Cepheid Xpert® Hemorrhagic Fever	**BioFire Defence, LLC BIOFIRE® Global Fever Special Pathogens Panel (K213362)**
		Pathogens Panel as some pathogens are more common in certain geographical locations. Results are meant to be used in conjunction with other clinical, epidemiologic, and laboratory data, in accordance with the guidelines provided by the relevant public health authorities. The BioFire Global Fever Special Pathogens Panel is indicated for use in laboratories having appropriate biosafety equipment, personal protective equipment (PPE), containment facilities and personnel trained in the safe handling of diagnostic clinical specimens potentially containing any of the pathogens detected by this panel. The BioFire Global Fever Special Pathogens Panel is indicated for use in laboratories that follow public health guidelines that address appropriate biosafety conditions, interpretation of test results, and coordination of findings with public health authorities. **For *In Vitro* Diagnostic Use.**
Assay Targets	• Ebola virus (including Zaire, Sudan, Taï Forest, and Bundibugyo, not differentiated) • Crimean-Congo hemorrhagic fever (CCHF) virus • Marburg virus • Lassa virus	• *Bacillus anthracis* • Crimean-Congo hemorrhagic fever virus • *Ebolavirus* spp. • *Francisella tularensis* • Lassa virus • *Leishmania* spp. (*L. donovani* and *L. infantum*) • *Leptospira* spp. • *Marburgvirus* • Chikungunya virus • Dengue virus (serotypes 1, 2, 3 and 4) • *Plasmodium* spp. (including species differentiation of *Plasmodium falciparum* and *Plasmodium vivax/ovale*) • West Nile virus • Yellow fever virus • *Yersinia pestis*

Attribute	Subject Device	Predicate Device
	Cepheid Xpert® Hemorrhagic Fever	**BioFire Defence, LLC BIOFIRE® Global Fever Special Pathogens Panel (K213362)**
Specimen Type	Venous Whole Blood (VWB) and Capillary Whole Blood (CWB) collected in EDTA tube	Whole blood (collected in EDTA tube)
Test Format	Same	Single Use
Automation	Automated Nucleic Acid Extraction, Detection and Results Interpretation	Automated Nucleic Acid Extraction, Melt Curve Analysis, Detection and Results Interpretation
Assay Results	Same	Qualitative
Non-Determinate Results Text	INSTRUMENT ERROR NO RESULT-REPEAT TEST	INVALID
Internal Control	Sample Processing Control (SPC) Sample Adequacy Control (SAC) Probe Check Control (PCC)	RNA Process Control PCR2 Control Melt Analysis Control
Instrument Systems	Cepheid GeneXpert® Edge X system	BioFire FilmArray 2.0 or BioFire FilmArray Torch systems
GeneXpert Software	Cepheid OS X 1.0 or higher	BIOFIRE® FILMARRAY® Software
Time to Result	Same	About 1 hour

The following performance data (analytical and clinical) were provided in support of the substantial equivalence determination.

1.4. Performance Studies

1.4.1. Analytical Performance

Analytical Sensitivity / Limit of Detection (LoD)

Studies were performed to determine the analytical limit of detection (LoD) of the Xpert Hemorrhagic Fever test. The LoD of the Xpert Hemorrhagic Fever 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 Xpert Hemorrhagic Fever. The verified LoD in VWB was subsequently verified in clinical capillary whole blood (CWB) matrix for a subset of the strains.

The LoD of the Xpert Hemorrhagic Fever 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 and CWB matrices are presented in **Table 2** and for live viruses in **Table 3.**

Table 2. Verified LoD in VWB and CWB Matrices

Analyte	Virus Strain	LoD	
		VWB	CWB
Ebola	Ebola Zaire Inactivated Virus (copies/mL)	926.1	1852.2
	Ebola Zaire AccuPlex (copies/mL)	1065	2130
	WHO Ebola Reference Reagent (units/mL)	550.6	NA
	Ebola Sudan Inactivated Virus (copies/mL)	1830.3	NA
	Ebola Sudan AccuPlex (copies/mL)	132.3	NA
	Ebola Tai Forest Inactivated Virus (copies/mL)	4383.2	NA
	Ebola BDBV Inactivated Virus (copies/mL)	4420.5	NA
Lassa	Lassa Inactivated Virus (copies/mL)	1094.3	1094.3
	Lassa AccuPlex (copies/mL)	1892	1892
CCHF	CCHF Inactivated Virus (copies/mL)	377.4	377.4
	CCHF AccuPlex (copies/mL)	203.1	406.2
Marburg	Marburg Inactivated Virus (copies/mL)	665.6	665.6
	Marburg AccuPlex (copies/mL)	435	435

Table 3. Estimated LoD of Live Viruses in VWB Matrix

Virus	Strain (Lineage/Clade)	Estimated LoD	
		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
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

Virus	Strain (Lineage/Clade)	Estimated LoD	
		PFU/mL	copies/mL[a]

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

Analytical Reactivity (Inclusivity)

The analytical reactivity/inclusivity of the Xpert Hemorrhagic Fever test was evaluated by bench testing against multiple strains of Ebola, Lassa, CCHF, and Marburg viruses at near LoD or challenging concentrations in venous whole blood. 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 4.**

Table 4. Analytical Reactivity (Inclusivity) of the Xpert Hemorrhagic Fever Test

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	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
	Chinese HY13	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

Virus	Strain (Lineage/Clade)	Concentration Tested		Results	Multiples of LoD
		PFU/mL	Copies/mL		
	Inactivated	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 intead 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 5**.

Table 5. Predicted Inclusivity of the Xpert Hemorrhagic Fever Test

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

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 factors, including genetic similarity to Xpert Hemorrhagic Fever 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 6**.

Table 6. Analytical Specificity of the Xpert Hemorrhagic Fever 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
		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

Organism	Strain	Concentration Tested	Test Results Reported for 3/3 Replicates			
			Ebola	Lassa	CCHF	Marburg
	Rubella virus[a]	5.00E+02 $TCID_{50}$/mL	Not Detected	Not Detected	Not Detected	Not Detected
	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[g]	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

Organism	Strain	Concentration Tested	Test Results Reported for 3/3 Replicates			
			Ebola	Lassa	CCHF	Marburg
	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
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 6**).

No cross-reactivity was observed for each of the 4 on-panel organism (Ebola, Lassa, CCHF and Marburg inactivated viruses) tested individually at > 10^5 copies/mL as shown in **Table 7**.

Table 7. Analytical Specificity of the Xpert Hemorrhagic Fever 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.

Microbial Interference

Microbial interference of the Xpert Hemorrhagic Fever test was evaluated by testing a six 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.

Competitive Interference

Competitive interference of the Xpert Hemorrhagic Fever test caused by co-infections were evaluated by testing contrived samples of individual Ebola, Lassa, CCHF or Marburg AccuPlex at 3x LoD in the presence of different on-panel target organism at a higher concentration in VWB matrix. The concentration at 3x LoD was 3195 copies/mL for Ebola AccuPlex, 5676 copies/mL for Lassa AccuPlex, 603.3 copies/mL for CCHF and 1305 copies/mL for Marburg. 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 competitive interference study are presented in **Tables 8 – 11** for Ebola, Lassa, CCHF, Marburg, respectively.

Table 8. Assessment of Competitive Interference on Xpert HF 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 9. Assessment of Competitive Interference on Xpert HF 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 10. Assessment of Competitive Interference on Xpert HF 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 11. Assessment of Competitive Interference on Xpert HF 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

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 test. Positive and negative samples were prepared in venous whole blood 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 performance, are listed in **Table 12.**

Table 12. Potentially Interfering Substances in the Xpert Hemorrhagic Fever Test

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	1 µg/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

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 Edge X 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 Edge X module immediately by another negative sample. This was repeated on 5 GeneXpert Edge X modules and this testing scheme was repeated 8 times for a total of 17 runs resulting in 8 positive and 9 negative specimens per GeneXpert Edge X 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.

Reproducibility-Precision

The reproducibility of the Xpert Hemorrhagic Fever test was established at 3 external sites representative of a CLIA-waived environment 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 untrained 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) using the GeneXpert Edge X Instrument.

The percent agreement between the Xpert Hemorrhagic Fever test result and the expected result analyzed across each of the nine (9) operators across each of the three (3) sites is shown in **Table 13**. 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 13. Percent Agreement of 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 ND results on both initial and repeat testing.
b. Of the 18 samples tested, one yielded ND results 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 ND results on both initial and repeat testing

1.4.2. 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 test. Due to the low prevalence of the Xpert Hemorrhagic Fever test analytes, the study was conducted using samples contrived with live Crimean-Congo Hemorrhagic Fever (CCHF) virus, Ebola virus, Lassa Virus and Marburg virus in paired capillary whole blood (CWB) and 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 14**.

Table 14. 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 either the CWB or VWB specimen with live cultures consisting of representative strains of CCHF virus, Ebola virus, Lassa virus and Marburg virus. For each analyte, 408 CWB and 408 VWB specimens were contrived at 1-2x limit of detection (LoD) to clinically relevant concentrations. 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 eligible CWB specimens evaluated, 9 (1.1%; 9/816) specimens yielded a non-determinate result on the initial test. After retest, 0 (0.0%; 0/816) specimens yielded a non-determinate result.

Out of the 816 VWB specimens evaluated, 10 (1.2%; 10/816) specimens yielded non-determinate results 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 test were calculated relative to the expected results in CWB and VWB and presented in **Table 15** and **Table 16**, respectively.

Table 15. Performance of Xpert Hemorrhagic Fever by Concentration in CWB

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	52/53	98.1	90.1-99.7	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	75.5-100.0	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	101/102	99.0	94.7-99.8	408/408	100.0	99.1-100.0
Lassa	1-2x	48/52	92.3	81.8-97.0	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	98/102	96.1	90.3-98.5	408/408	100.0	99.1-100.0
Marburg	1-2x	50/52	96.2	87.0-98.9	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	100/102	98.0	93.1-99.5	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

Table 16. Performance of Xpert Hemorrhagic Fever 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

Analyte	Level	PPA			NPA		
		TP/(TP+FN)	PPA (%)	95% CI	TN/(FP+TN)	NPA (%)	95% CI
	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	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 test stratified by strain were calculated relative to the expected results in CWB and VWB and presented in **Table 17** and **Table 18**, respectively.

Table 17. Performance of Xpert Hemorrhagic Fever by Strain in CWB

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**	26/27	96.3	81.7-99.3
	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**	47/51	92.2	81-5-96.9
	Pinneo	51/51	100.0	93.0-100.0
Marburg	**Angola**	51/52	98.0	89.7-99.7
	Musoke	51/52	98.0	89.7-99.7

Abbreviations: TP, True Positive; FN: False Negative; PPA, Positive Percent Agreement; CI, Confidence Interval

Table 18. Performance of Xpert Hemorrhagic Fever 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
	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

1.5. Conclusions

The results of the analytical and clinical performance studies summarized above demonstrate that the Xpert Hemorrhagic Fever test is substantially equivalent to the predicate device.