April 25, 2019

Cepheid
Sudhakar Marla
Senior Director, Regulatory Affairs
904 Caribbean Drive
Sunnyvale, California 94089

Re: K190771
Trade/Device Name: Xpert MRSA/SA Blood Culture, GeneXpert Dx System, GeneXpert Infinity-48s System, GeneXpert Infinity-80 System
Regulation Number: 21 CFR 866.1640
Regulation Name: Antimicrobial Susceptibility Test Powder
Regulatory Class: Class II
Product Code: NQX, OOI
Dated: March 25, 2019
Received: March 26, 2019

Dear Sudhakar Marla:

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 (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 located 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.

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 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). 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 (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Steven R. Gitterman -S for

Uwe Scherf, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics
and Radiological Health
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: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*

K190771

Device Name

Xpert MRSA/SA Blood Culture

Indications for Use *(Describe)*

The Cepheid® Xpert® MRSA/SA Blood Culture test, performed on the GeneXpert® Instrument Systems, is a qualitative *in vitro* diagnostic test intended for the detection of *Staphylococcus aureus* (SA) and methicillin-resistant *Staphylococcus aureus* (MRSA) DNA directly from positive blood cultures. The assay utilizes automated real-time polymerase chain reaction (PCR) for the amplification of MRSA/SA specific DNA targets and fluorogenic target-specific hybridization probes for the real-time detection of the amplified DNA. The assay is performed directly on positive blood culture samples from BD BACTEC™ Plus Aerobic/F, BacT/ALERT® SA (Standard Aerobic) or VersaTREK REDOX 1® (aerobic) blood culture bottles that are determined by Gram Stain as Gram Positive Cocci in Clusters (GPCC) or as Gram Positive Cocci in singles (GPC). The Xpert MRSA/SA Blood Culture test is indicated for use in conjunction with other laboratory tests, such as culture, and clinical data available to the clinician as an aid in the detection of MRSA/SA from positive blood cultures. Subculturing of positive blood cultures is necessary to recover organisms for susceptibility testing or for epidemiological typing. The Cepheid Xpert MRSA/SA Blood Culture test is not intended to monitor treatment for MRSA/SA infections.

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.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

510(k) Summary

As required by 21 CFR Section 807.92(c). The purpose of this submission is to submit documentation to support a change to the assay definition file (ADF) for use with the Xpert MRSA/SA Blood Culture test.

Submitted by:	Cepheid 904 Caribbean Drive Sunnyvale, CA 90489 Phone number: (847) 228-3299 Fax number: (847) 890-6589
Contact:	Sudhakar Marla, Ph.D.
Date of Preparation:	April 25, 2019
Proprietary/Trade name:	Xpert® MRSA/SA Blood Culture
Common name:	Xpert MRSA/SA Blood Culture
Type of Test:	Nucleic Acid Amplification Test, DNA, Methicillin-resistant *Staphylococcus aureus* (MRSA) and *Staphylococcus aureus* (SA), qualitative
Regulation number:	21 CFR 866.1640
Classification name:	Antimicrobial susceptibility test powder
Primary Product code:	NQX; Class II
Secondary Product code:	OOI; Class II
Classification Advisory Panel	Microbiology (83)
Prescription Use	Yes
Predicate Device Assay:	Cepheid Xpert MRSA/SA Blood Culture [510(k) #K130894]

DEVICE DESCRIPTION

The Cepheid Xpert® MRSA/SA Blood Culture test is a rapid, automated DNA test for the simultaneous qualitative detection of MRSA and SA DNA directly from blood culture bottle samples that are detected as positive for microbial growth and shown to contain Gram Positive Cocci by Gram stain. The primers and probes in the Xpert MRSA/SA Blood Culture test detect nucleic acid sequences of the staphylococcal protein A (*spa*), the gene for methicillin/oxacillin resistance (*mecA*), and staphylococcal cassette chromosome (SCC*mec*) inserted in the SA chromosomal *attB* site.

The test includes a Sample Processing Control (SPC) to control for adequate processing of the target bacteria and to monitor the presence of inhibitor(s) in the PCR assay. The Probe Check Control (PCC) verifies reagent rehydration, PCR tube filling in the cartridge, probe integrity, and dye stability.

The sample for testing with the Xpert MRSA/SA Blood Culture test consists of an aliquot taken from a positive blood culture bottle. Using one of the disposable fixed 50 µL volume transfer pipettes provided with the test kit, an aliquot of the positive blood culture is transferred into a single-use tube of Elution Reagent, also provided with the kit. The Elution Reagent is briefly vortexed and the entire content is transferred to the sample chamber of the disposable fluidic cartridge (the Xpert MRSA/SA Blood Culture cartridge), after which the cartridge is ready to place on the instrument.

The assay is performed on the Cepheid GeneXpert Instrument Systems, which automate and integrate sample purification, nucleic acid amplification and detection of the target sequences in simple or complex samples using real-time PCR. The systems consist of an instrument, personal computer, and preloaded software for running the tests and viewing the results. The GeneXpert Instrument Systems require the use of single-use disposable cartridges that hold the PCR reagents and host the PCR process. Because the cartridges are self-contained, cross-contamination between samples is minimized. In this platform, additional sample preparation, amplification, and real-time detection are all fully-automated and completely integrated. The Xpert MRSA/SA Blood Culture test performed on the GeneXpert Instrument Systems provides results in approximately 60 minutes.

The GeneXpert Instrument Systems, comprised of the GeneXpert Dx Systems and the GeneXpert Infinity Systems, have 1 to 80 randomly accessible modules, depending upon the instrument, that are each capable of performing separate sample preparation and real-time PCR tests. Each module 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 PCR and detection.

INTENDED USE

The Intended Use is identical to the predicate device with the exception of the device name changed from Xpert® MRSA/SA Blood Culture Assay to Xpert® MRSA/SA Blood Culture.

Device Intended Use

The Cepheid® Xpert® MRSA/SA Blood Culture test, performed on the GeneXpert® Instrument Systems, is a qualitative *in vitro* diagnostic test intended for the detection of

Staphylococcus aureus (SA) and methicillin-resistant *Staphylococcus aureus* (MRSA) DNA directly from positive blood cultures. The assay utilizes automated real-time polymerase chain reaction (PCR) for the amplification of MRSA/SA specific DNA targets and fluorogenic target-specific hybridization probes for the real-time detection of the amplified DNA. The assay is performed directly on positive blood culture samples using BD BACTEC™ Plus Aerobic/F, BacT/ALERT® SA (Standard Aerobic) or VersaTREK REDOX 1® (aerobic) blood culture bottles that are determined as Gram Positive Cocci in Clusters (GPCC) or as Gram Positive Cocci in singles (GPC) by Gram stain. The Xpert MRSA/SA Blood Culture test is indicated for use in conjunction with other laboratory tests, such as culture, and clinical data available to the clinician as an aid in the detection of MRSA/SA from positive blood cultures. Subculturing of positive blood cultures is necessary to recover organisms for susceptibility testing or for epidemiological typing. The Cepheid Xpert MRSA/SA Blood Culture test is not intended to monitor treatment for MRSA/SA infections.

TECHNOLOGICAL CHARACTERISTICS

The Xpert MRSA/SA Blood Culture test has the same intended use as the predicate device and the same technological characteristics as the predicate device.

DEVICE COMPARISON

The purpose of this Special 510(k) submission is to request a modification of the assay definition file (ADF) for use with the Xpert MRSA/SA Blood Culture test. The updated Assay Definition File with rules-based algorithms and release of new GeneXpert software to support this update have been validated by the re-analyses of the original clinical performance data and a subset of the original analytical performance data, including LoD, inclusivity, exclusivity, potential interfering substances, reproducibility, and precision. The re-analyses showed the devices were substantially equivalent.

Table 8-1 shows the similarities and differences between the Xpert MRSA/SA Blood Culture test and predicate assay. The differences between Xpert MRSA/SA Blood Culture test and the predicate device do not raise different questions of safety and effectiveness.

Table 8-1: Comparison of Similarities and Differences of Xpert MRSA/SA Blood Culture with the Predicate Device

Similarities		
Item	**New Device**	**Predicate**
	Xpert MRSA/SA Blood Culture	**Current Xpert MRSA/SA Blood Culture 510(k) #K130894**
Intended Use	The Cepheid® Xpert® MRSA/SA Blood Culture test, performed on the GeneXpert® Instrument Systems, is a qualitative *in vitro* diagnostic test intended for the detection of *Staphylococcus aureus* (SA) and methicillin-resistant *Staphylococcus aureus* (MRSA) DNA directly from positive blood cultures. The assay utilizes automated real-time polymerase chain reaction (PCR) for the amplification of MRSA/SA specific DNA targets and fluorogenic target-specific hybridization probes for the real-time detection of the amplified DNA. The assay is performed directly on positive blood culture samples using BD BACTEC™ Plus Aerobic/F, BacT/ALERT® SA (Standard Aerobic) or VersaTREK REDOX 1® (aerobic) blood culture bottles that are determined as Gram Positive Cocci in Clusters (GPCC) or as Gram Positive Cocci in singles (GPC) by Gram stain. The Xpert MRSA/SA Blood Culture test is indicated for use in conjunction with other laboratory tests, such as culture, and clinical data available to the clinician as an aid in the detection of MRSA/SA from positive blood cultures. Subculturing of positive blood cultures is necessary to recover organisms for susceptibility testing or for epidemiological typing. The Cepheid Xpert MRSA/SA Blood Culture test is not intended to monitor treatment for MRSA/SA infections.	Same

Similarities		
Item	**New Device**	**Predicate**
	Xpert MRSA/SA Blood Culture	**Current Xpert MRSA/SA Blood Culture 510(k) #K130894**
Specimen Type	Positive Blood Culture	Same
Technological Principles	Fully automated nucleic acid amplification (DNA); real-time PCR	Same
DNA Target Sequence	Sequence incorporating the insertion site (*attB*) of Staphylococcal Cassette Chromosome *mec* (SCC*mec*) for detection of MRSA.	Same
Test Cartridge	Disposable single-use, multi-chambered fluidic cartridge.	Same
Sample Preparation	Self-contained and automated after mixed specimen is added to cartridge. All other reagents are contained in the cartridge.	Same
Probes	TaqMan® Probes	Same
Internal Controls	Sample processing control (SPC) and probe check control (PCC).	Same
DNA Target Sequence	Sequence specific to methicillin/oxacillin resistance (*mecA* gene)	Same
DNA Target Sequence	Sequence specific to *Staphylococcus aureus* species (*spa* gene)	Same
Ability to identify correctly “Empty Cassette Variants”	Yes, sequence specific to *Staphylococcus aureus* species (*mecA* gene)	Same
Time to Results	Approximately 60 minutes to result.	Same

Differences		
Item	**New Device**	**Predicate**
	Xpert MRSA/SA Blood Culture	**Current Xpert MRSA/SA Blood Culture 510(k) # K130894**
Instrument System	Cepheid GeneXpert Dx Systems and GeneXpert Infinity-48s and Infinity-80 Systems	Cepheid GeneXpert Dx Systems, GeneXpert Infinity-48 System, and GeneXpert Infinity-48s and Infinity-80 Systems
Minimum software requirements	GeneXpert Dx software version 5.3 and higher, GeneXpert Infinity-48s and Infinity-80 Xpertise software version 6.8 and higher	GeneXpert Dx software version 4.3 and higher, GeneXpert Infinity-48 Xpertise 4.3 and higher, GeneXpert Infinity-48s and Infinity-80 Xpertise software version 6.0 and higher
Assay Definition File	Rules-based algorithms incorporating delta Ct values between targets within a valid Ct range and algorithms based on the Ct value for the targets falling within a valid Ct range	Algorithms based on the Ct value for the targets falling within a valid Ct range

Conclusion

The Xpert MRSA/SA Blood Culture test is substantially equivalent to the predicate device.