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5. 510(K) Summary

The Summary for this 510(k) submission is submitted in accordance with the requirements of SMDA 1900 and CFR 807.92. **Attachment A** contains the 510(k) screening checklist and **Attachment B** contains the complete 510(k) Summary.

510(k) Number:

K112424 Verigene® *Staphylococcus* Blood Culture Nucleic Acid Test (BC-S)

Summary Preparation Date:

August 19, 2011 (Revised December 13, 2011)

Submitted by:

Nanosphere, Inc.
4088 Commercial Avenue
Northbrook, IL 60062
Phone: 847-400-9000
Fax: 847-400-9199

Contact:

Mark Del Vecchio
VP, Regulatory Affairs and Quality Assurance

Proprietary Names:

For the instrument:

Verigene® System

For the assay:

Verigene® *Staphylococcus* Blood Culture Nucleic Acid Test (BC-S)

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Common Names:

For the instrument:

Bench-top molecular diagnostics workstation

For the assay:

Rapid gram-positive blood culture assay
Staphylococcus aureus-Staphylococcus epidermidis blood culture assay
Methicillin-resistant *Staphylococcus aureus* (MRSA) blood culture assay
Methicillin-resistant *Staphylococcus epidermidis* (MRSE) blood culture assay

Regulatory Information:
Regulation section:

866.1640 Antimicrobial susceptibility powder

Classification:

Class II

Panel:

Microbiology (83)

Product Code(s):

NQX System, nucleic acid amplification test, DNA, methicillin-resistant *Staphylococcus aureus*, direct specimen

Other:

NSU Instrumentation for clinical multiplex test systems

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Predicate Devices:

Xpert MRSA/SA Blood Culture Assay (Cepheid)

S. aureus/CNS PNA FISH Culture Identification Kit (AdvanDx)

Phoenix Gram Positive (GP) Panel – Phoenix Automated Microbiology System (Cefoxitin) (Becton-Dickinson)

Verigene RVNAT$_{SP}$ Test (Nanosphere)

Indications for Use:

The **Verigene® Staphylococcus Blood Culture (BC-S) Nucleic Acid Test** performed using the sample-to-result Verigene System is a qualitative, multiplexed in vitro diagnostic test for the simultaneous detection and identification of potentially pathogenic gram-positive bacterial species Staphylococcus aureus ("SA") and Staphylococcus epidermidis ("SE") which may cause bloodstream infection (BSI). In addition, the BC-S test detects the mecA resistance marker inferring mecA-mediated methicillin/oxacillin resistance. In mixed growth, the BC-S Test does not specifically attribute mecA-mediated methicillin/oxacillin resistance to either SA or SE.

The BC-S test is performed directly on positive blood culture using *BACTEC™ Plus Aerobic/F* and *BacT/ALERT FA FAN®* Aerobic blood culture bottles, which contain gram-positive cocci in clusters (GPCCL) observed on Gram stain. Sub-culturing of positive blood cultures is necessary to recover organisms for susceptibility testing, differentiation of mixed growth, association of the mecA gene to an organism, or for epidemiological typing.

The BC-S test is indicated for use in conjunction with other clinical and laboratory findings, such as culture, to aid in the diagnosis of bacterial bloodstream infections; however, it is not used to monitor bloodstream infections.

Technological Characteristics:

The Verigene *Staphylococcus* Blood Culture Nucleic Acid Test (BC-S) is a molecular assay which relies on detection of specific nucleic acid targets in a microarray format. For each of the bacterial nucleic acid sequences detected by the BC-S test, Capture and Mediator oligonucleotides are utilized for gold nanoparticle probe-based endpoint detection. The Capture oligonucleotides bind to a specific portion of the nucleic acid target and are themselves bound onto a substrate in the microarray. The Mediator oligonucleotides bind to a different portion of the same nucleic acid target and allow binding of a gold nanoparticle probe to a portion complementary to a gold nanoparticle probe. Specific silver enhancement of the bound gold nanoparticle probes at the capture sites results in gold-silver aggregates that scatter light with high efficiency.

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The BC-S test is performed on the Verigene System, a 'sample-to-result', fully automated, bench-top molecular diagnostics workstation. The Verigene System consists of two components: the Verigene Reader and the Verigene Processor *SP*. The BC-S test utilizes single-use disposable test consumables and a self-contained Verigene Test Cartridge for each sample tested. For the BC-S test, the Verigene System allows automated nucleic acid extraction from gram-positive bacteria-containing blood culture specimens and target detection of bacteria-specific DNA.

The Reader is the Verigene System's user interface, which serves as the central control unit for all aspects of test processing and results generation. The Reader's graphical user interface guides the user through test processing and test results using a barcode scanner.

The user inserts the Test Cartridge into the Verigene Processor *SP*, which executes the test procedure, automating the steps of (1) Sample Preparation – Cell lysis and magnetic bead-based bacterial DNA isolation from blood culture samples and (2) Verigene Hybridization Test – Detection and identification of bacterial-specific DNA in a microarray format by using gold nanoparticle probe-based technology.

After test processing is complete, to obtain the test results the user removes the Test Cartridge from the Processor *SP*, removes the reagent pack from the substrate holder, and inserts the substrate holder into the Reader for analysis. Light scatter from the capture spots is imaged by the Reader and intensities from the microarray spots are used to make decisions regarding the presence (Detected) or absence (Not Detected) of a bacterial nucleic acid sequence/analyte.

Performance Data - Analytical Testing

Analytical Sensitivity / Limit of Detection (LOD)

Analytical sensitivity (LODs) for detection of 13 strains tested ranged from 1.9×10^5 to 7.5×10^6 CFU/mL.

Analytical Reactivity (Inclusivity)

Demonstrated reactivity to strains included 99 MRSA strains (including 65 representative NARSA strains), 18 methicillin-sensitive *Staphylococcus aureus* (SA), eight (8) borderline oxacillin-resistant *Staphylococcus aureus* or BORSA strains, six (6) methicillin-resistant *Staphylococcus epidermidis* (MRSE), and seven (7) methicillin-sensitive *Staphylococcus epidermidis* (SE).

Analytical Specificity (Exclusivity)

No cross-reactivity observed for any of the strains tested, which included 157 bacterial (115 gram-positive and 40 gram-negative, 1 acid-fast positive and 1 mollicute) and 6 yeast strains.

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Interfering Substances

No inhibitory effects observed from interfering substances including hemoglobin, triglycerides, bilirubin, gamma-globulin, and SPS, introduced directly into blood and then cultured in the blood culture bottle. Multiple types of blood culture bottles were also tested.

Fresh vs. Frozen Samples

Test results for representative strains of MRSA/SA and MRSE/SE were unaffected by exposure to up to two freeze/thaw cycles.

Competitive Inhibition

Competitive inhibition representing mixed bacteremia with SA and SE was evaluated by testing SA/MRSA samples at a high titer in the presence of SE/MRSE at a low titer (at LOD) and vice versa. No evidence of competitive inhibition was observed.

Carry-over / Cross-contamination

No evidence of carryover and/or cross-contamination from the high positive samples, or any other internal or external sources, was observed during either the sample extraction and hybridization procedural steps, when alternately running high positive samples followed by true negative samples.

Performance Data - Clinical Testing

Precision and Reproducibility Studies

The Reproducibility Study was conducted at three external sites and the Precision Study took place internally at Nanosphere, Inc. The Precision and Reproducibility Study Panel comprised of twelve (12) specimens, consisting of pure isolates grown in blood culture bottles until bottle positivity and bottle positivity plus an additional 8 hours. The specimens included 2 levels of 2 different MRSA strains, 2 levels of a MRSE strain, 2 negative controls (1 media only and 1 bacterial), 2 levels of an SA strain, and 2 levels of an SE strain.

Each specimen was tested in duplicate twice daily by two operators for twelve days (precision) and five days (reproducibility). The study demonstrated excellent reproducibility across multiple reagent lots, days, operators, runs, instruments and replicates.

Precision	***Reproducibility***			*All Sites*
NS	*Site 1*	*Site 2*	*Site 3*	
100 % (576/576) 99.4 % - 100 %	100 % (240/240) 98.5 % - 100 %	100 % (240/240) 98.5 % - 100 %	100 % (240/240) 98.5 % - 100 %	100 % (1296 / 1296) 99.7 % - 100 %

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Method Comparison

The Method Comparison Study was conducted at five external clinical sites. Subjects included individuals receiving routine care requiring blood culture testing. Three-hundred and thirty (330) culture-positive, gram-positive (GPCCL) blood culture specimens from these patients were identified for BC-S testing. BC-S test results were compared with reference method results obtained from the standard biochemical bacterial detection and susceptibility techniques utilized in routine clinical practice.

S. aureus (n=330)

Sensitivity =100% (97.1%-100%)

Specificity=100% (98.2%-100%).

S. epidermidis (n=330)

Sensitivity = 97.0% (91.2%-99.4%)

Specificity= 99.6% (97.6%-99.9%)

*mec*A (n=221)

Sensitivity =98.6% (94.6%-99.8%)

Specificity= 98.8% (93.4%-99.9%)

Substantial Equivalence

The Verigene *Staphylococcus* Blood Culture Nucleic Acid Test (BC-S) is as safe and effective as the AdvanDx *S. aureus*/CNS PNA FISH Culture Identification Kit, Cepheid Xpert MRSA/SA Blood Culture Assay, BD Phoenix Gram Positive (GP) Panel – Phoenix Automated Microbiology System (Cefoxitin) and Nanosphere Verigene RVNAT$_{SP}$. The BC-S has similar intended use and indications, technological characteristics, performance characteristics and principles of operation as its predicate devices. The minor differences between the BC-S and its predicate devices raise no new issues of safety or effectiveness. Performance data demonstrate that the BC-S is as safe and effective as predicate devices. Thus, the BC-S is substantially equivalent.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

10903 New Hampshire Avenue
Silver Spring, MD 20993

Nanosphere, Inc.
c/o Mark A. Del Vecchio
Vice President, Regulatory Affairs
4088 Commercial Avenue
Northbrook, IL 60062

DEC 16 2011

Re: K112424
Trade/Device Name: Verigene® *Staphylococcus* Blood Culture Nucleic Acid Test (BC-S) on the Verigene® System
Regulation Number: 21 CFR 866.1640
Regulation Name: Antimicrobial susceptibility test powder
Regulatory Class: Class II
Product Code: NQX, NSU
Dated: December 13, 2011
Received: December 15, 2011

Dear Mr. Del Vecchio:

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. 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.

If your device is classified (see above) into class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

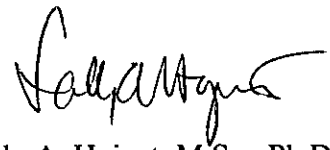
Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice

requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. 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 the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,



Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

4. Indications for Use Statement

510(k) Number (if known): K112424

Device Name: Verigene® *Staphylococcus* Blood Culture Nucleic Acid Test (BC-S) on the Verigene® System

The **Verigene® Staphylococcus Blood Culture (BC-S) Nucleic Acid Test** performed using the sample-to-result Verigene System is a qualitative, multiplexed in vitro diagnostic test for the simultaneous detection and identification of potentially pathogenic gram-positive bacterial species Staphylococcus aureus ("SA") and Staphylococcus epidermidis ("SE") which may cause bloodstream infection (BSI). In addition, the BC-S test detects the mecA resistance marker inferring mecA-mediated methicillin/oxacillin resistance. In mixed growth, the BC-S Test does not specifically attribute mecA-mediated methicillin/oxacillin resistance to either SA or SE.

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Prescription Use ✓ (Part 21 CFR 801 Subpart D) and/or Over-The-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K112424