SPECIAL 510(k): Device Modification
ODE Review Memorandum (Decision Making Document is Attached)

To: THE FILE RE: DOCUMENT NUMBER K101879

This 510(k) submission contains information/data on modifications made to the SUBMITTER'S own Class II, Class III or Class I devices requiring 510(k). The following items are present and acceptable (delete/add items as necessary):

1. The name and 510(k) number of the SUBMITTER'S previously cleared device:
Xpert® MRSA/SA Blood Culture Assay, K082140 (09/29/2009)

2. Submitter's statement that the **INDICATION/INTENDED USE** of the modified device as described in its labeling **HAS NOT CHANGED** along with the proposed labeling which includes instructions for use and package labeling.

   The labeling for this modified subject device has been reviewed to verify that the indication/intended use for the device is unaffected by the modification.

3. The modification to this device consist of the revision of the product labeling as a corrective action to Cepheid MRSA/SA Blood Culture Class I Recall (Z-1898-2010). **This modification has not had any effect or caused any changes to the FUNDAMENTAL SCIENTIFIC TECHNOLOGY of this device**.

   a) There were no changes made to the device (composition or technological characteristics).

   b) The product labeling has been revised to include the following modifications:

      i) Intended Use Section:
         (a) The indication/intended use statement remains the same. An additional sentence was added to the Indication/intended use statement for clarification and language consistency purposes.

         (b) The addition of a warning box with the following statement under the intended use statement.

> When a MRSA negative/*SA* positive result is obtained, the results should be interpreted as MRSA indeterminate/ *Staph*ylococcus aureus positive, antimicrobial susceptibility testing pending. Further testing should be performed using an FDA-cleared, phenotypic antimicrobial susceptibility testing method on isolated colonies recovered from the blood culture bottle. MRSA positive/SA positive results can still be reported as such.

      ii) Interpretation of Results section:
         (a) The addition of new instruction for interpretation of MRSA negative/SA positive results.
            - The results should be interpreted as MRSA indeterminate/ *Staph*ylococcus aureus positive, antimicrobial susceptibility testing pending. Further testing should be performed using an FDA-cleared, phenotypic antimicrobial susceptibility testing method on isolated colonies recovered from the blood culture bottle.

      iii) Limitation section:
         (a) The addition of the following statements:
            - The Xpert MRSA/SA Blood Culture Assay may generate false negative MRSA results when testing borderline oxacillin resistant *S. aureus* (BORSA). The mechanism of oxacillin resistance in BORSA strains is due to an increased production of B-lactamases, not the *mecA* gene. BORSA with oxacillin MICs of 4-8 µg/mL are considered borderline resistant but, would be reported as MRSA negative by the Xpert MRSA/SA Blood Culture Assay. BORSA strains are rare in the United States.

            - The Xpert MRSA/SA Blood Culture Assay may generate false negative MRSA results when testing modified *S. aureus* (MOD-SA). The mechanism of oxacillin resistance in

MOD-SA strains is due to changes in affinity of penicillin binding proteins for oxacillin, not the *mecA* gene. MOD-SA with oxacillin MICs of 4-8 µg/mL are considered borderline resistant but, would be reported as MRSA negative by the Xpert MRSA/SA Blood culture Assay. MOD-SA strains are rare in the United States.

- As with all PCR based *in vitro* diagnostic tests, extremely low levels of target below the LoD of the assay may be detected, but results may not be reproducible.

- Xpert MRSA/SA Blood Culture Assay results may sometimes be "INVALID" due to a failed SPC control, "ERROR" or "NO RESULT", and require retesting that can lead to a delay in obtaining final results.

4. **Comparison Information** (similarities and differences): The package insert was revised to add a clarification statement and a black warning box in the Intended Use section, new instruction for interpretation of the MRSA negative/SA positive results in the Interpretation of Results section and additional statements in the Limitation section.

Similarities and Differences		
	Predicate	**Device**
Item	**Xpert MRSA/SA Blood Culture K082140**	**Xpert MRSA/SA Blood Culture K101879**
Intended Use	The Cepheid Xpert™ MRSA/SA Blood Culture Assay performed on the GeneXpert® Dx System™ is a qualitative *in vitro* diagnostic test intended for the detection of *Staphylococcus aureus* (SA) and methicillin-resistant *Staphylococcus aureus* (MRSA) DNA directly from patient 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 specimens using BD BACTEC™ Plus Aerobic/F 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 Cepheid Xpert™ MRSA/SA Blood Culture Assay is not intended to monitor treatment for MRSA/SA infections. Subculturing of positive blood cultures is necessary to recover organisms for susceptibility testing or for epidemiological typing.	The Cepheid Xpert™ MRSA/SA Blood Culture Assay performed on the GeneXpert® Dx System™ is a qualitative *in vitro* diagnostic test intended for the detection of *Staphylococcus aureus* (SA) and methicillin-resistant *Staphylococcus aureus* (MRSA) DNA directly from patient 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 specimens using BD BACTEC™ Plus Aerobic/F 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 Assay 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 patient 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 Assay is not intended to monitor treatment for MRSA/SA infections. When a MRSA negative/*SA* positive result is obtained, the results should be interpreted as MRSA indeterminate/ *Staph*ylococcus aureus positive,

Similarities and Differences		
	Predicate	**Device**
Item	**Xpert MRSA/SA Blood Culture K082140**	**Xpert MRSA/SA Blood Culture K101879**
		antimicrobial susceptibility testing pending. Further testing should be performed using an FDA-cleared, phenotypic antimicrobial susceptibility testing method on isolated colonies recovered from the blood culture bottle. MRSA positive/SA positive results can still be reported as such.
Indication for Use	Identification of MRSA and SA colonization	Same
Specimen Type	Positive Blood Culture specimens using BD BACTEC™ Plus Aerobic/F blood culture bottles that are determined as Gram Positive Cocci in Clusters (GPCC) or Gram Positive Cocci in single (GPC), by Gram stain.	Same
Technological Principles	Fully-automated nucleic acid amplification (DNA); real-time PCR	Same
DNA Target Sequence	Sequence incorporating the insertion site (attBsse) of Staphylococcal mec (SCCmec) for detection of MRSA. Sequence specific to methicillin/Oxacillin resistance (mecA gene)	Same
Labeling	Package Insert	Same, with clarifications and addition of black box statement, limitations and instruction for interpretation of MRSA negative/SA positive results.
Users	Operators with no clinical lab experience to experienced clinical laboratory technologists.	Same

5. A **Design Control Activities Summary** which includes:
   a) Identification of Risk Analysis method(s) used to assess the impact of the modification on the device and its components, and the results of the analysis. – Risks were identified during the assessment of the product recall and mitigated by adding a recommendation to the product labeling.

   b) Based on the Risk Analysis, an identification of the verification and/or validation activities required, including methods or tests used and acceptance criteria to be applied. - The verification and/or validation activities were conducted under the firm's Design Control for Design Changes and Change Control procedures in accordance with 21 CFR Part 820.30.

   c) A declaration of conformity with design controls. The declaration of conformity should include:
      i) A statement signed by the individual responsible, that, as required by the risk analysis, all verification and validation activities were performed by the designated individual(s) and the results demonstrated that the predetermined acceptance criteria were met, and
      ii) A statement signed by the individual responsible, that the manufacturing facility is in conformance with design control procedure requirements as specified in 21 CFR 820.30 and the records are available for review.

   The signed statement for declaration of conformity with design controls was submitted.

6. A **Truthful and Accurate Statement**, a **510(k) Summary or Statement** and the **Indications for Use Enclosure (and Class III Summary for Class III devices).**

A signed Truthful and Accurate Statement, a 510(k) summary and Indications for Use Enclosure were provided.

The labeling for this modified subject device has been reviewed to verify that the indication/intended use for the device is unaffected by the modification. In addition, the submitter's description of the particular modification(s) and the comparative information between the modified and unmodified devices demonstrate that the fundamental scientific technology has not changed. The submitter has provided the design control information as specified in The New 510(k) Paradigm and on this basis, I recommend the device be determined substantially equivalent to the previously cleared (or their preamendment) device.