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

To: THE FILE RE: DOCUMENT NUMBER K091949

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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.
   MicroScan MICroSTREP *plus*® Panel Penicillin (0.015 -16mcg/ml) - K062773 (WalkAway)
   MicroScan MICroSTREP *plus*® Panel Penicillin (0.015 -16mcg/ml) - K020626 (Manual)

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, package labeling, and, if available, advertisements or promotional materials (labeling changes are permitted as long as they do not affect the intended use).

   The Indication/Intended Use Statement has not changed.

3. A description of the device **MODIFICATION(S),** including clearly labeled diagrams, engineering drawings, photographs, user's and/or service manuals in sufficient detail to demonstrate that the **FUNDAMENTAL SCIENTIFIC TECHNOLOGY** of the modified device **has not changed**.

   **The modifications were:**

   In January 2008 the Clinical Laboratory Standards Institute (CLSI) modified the MIC breakpoint interpretive criteria for Penicillin, specific for *S. pneumoniae*. These modified criteria were approved by the FDA for the drug manufacturer, Baxter Healthcare, Inc., in February 2008. The previous and current drug interpretive criteria are illustrated in Table 1.

| **Table 1** | **Penicillin Drug Interpretive Criteria (pre-Feb.2008 Approval)** | | |
|---|---|---|---|
| | **S** | **I** | **R** |
| ***Streptococcus pneumoniae*** | **≤ 0.06** | **0.12-1** | **≥2** |
| **Beta-hemolytic Streptococci** | **≤0.12** | **-** | **-** |
| **Viridans Streptococci** | **≤0.12** | **0.25-2** | **≥4** |
| | | | |

| | Current Penicillin Drug Interpretive Criteria (post-Feb.2008 Approval) | | |
|---|---|---|---|
| | **S** | **I** | **R** |
| ***Streptococcus pneumoniae (non-meningiditis)*** | **≤2** | **4** | **≥8** |
| ***Streptococcus pneumoniae (meningiditis)*** | **≤0.06** | **-** | **≥0.12** |
| **Beta-hemolytic Streptococci** | **≤0.12** | **-** | **-** |
| **Viridans Streptococci** | **≤0.12** | **0.25-2** | **≥4** |

Subsequently, Siemens Healthcare Diagnostics, Inc. made the following device modifications:

- Change in the device Penicillin drug interpretive criteria for *S. pneumoniae* such that the criteria are consistent with the modifications approved by the FDA in February 2008. More specifically, the pre-approval drug interpretive criteria for *S. pneumoniae* of S≤0.06, I=0.12, R≥2 was changed to the post-approval drug interpretive criteria for *S. pneumoniae* (non-meningiditis) of S≤2, I=4, R≥8, and *S. pneumoniae* (meningiditis) of S≤2, R≥0.12.

- Change in device labeling to update the Penicillin drug interpretive criteria for *S. pneumoniae* to reflect the modifications as a result of the February 2008 FDA (CDER) approval.

4. **Comparison Information** (similarities and differences) to applicant's legally marketed predicate device including, labeling, intended use, physical characteristics, and

| **Item** | **Device: MicroScan MICroSTREP *plus*® Panel - Penicillin** | **Predicate: MicroScan MICroSTREP *plus*® Panel-Penicillin (K062773)** |
|---|---|---|
| **Similarities** | | |
| **Intended Use** | Determination of susceptibility to Penicillin with aerobic streptococci including *Streptococcus pneumoniae* | Same |
| **Indications for Use** | For use with aerobic streptococci including *Streptococcus pneumoniae* | Same |
| **Technology** | Overnight Microdilution MIC Susceptibility Testing | Same |
| **Components** | Dried Penicillin 0.015-16µg/ml | Same |
| **Inoculum** | Saline suspension of organism | Same |
| **Differences** | | |
| Penicillin Breakpoint Interpretive Criteria for *S. pneumoniae* | Non-meningiditis - S≤2, I=4, R≥8<br>Meningiditis – S≤0.06, R≥0.12 | S≤0.06, I=0.12-1, R≥2 |

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
   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
   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 design control activities summary:

   A risk analysis study was conducted to evaluate the performance of the MICroSTREP plus Panel – Penicillin in conjunction with the new Penicillin breakpoint interpretive criteria for *S. pneumoniae*. Performance data specific for the isolates of *S.pneumoniae* from the original 510(k) submissions (K020626 – Manual Read Method; K062773 – WalkAway® Instrument Read), have been reevaluated using the new drug interpretive criteria.

A total of 53 challenge and 243 clinical *S.pneumoniae* isolates were reevaluated for the Manual Read Method. A total of 53 challenge *S.pneumoniae* isolates were reevaluated for the Walkaway® Instrument Read method. The results were compared to that of the reference method.

Tables 1-3 below demonstrate the performance based on essential agreement and category agreement for clinical and challenge isolates in combination with the turbidity method of inoculation for the Manual Read method. Table 4 below demonstrates the performance based on essential and category agreement for challenge isolates in combination with the turbidity method of inoculation for the Walkaway® Instrument Read method.

**Table 1. Overnight Manual Read Method – Challenge Data**

**† Due to lack of Intermediate interpretive criteria, calculation of minor discrepancy is not possible.**

| No. | Read Method | Organism | Interpretive Criteria | No. Isolates Tested | Essential Agreement | Category Agreement | Minor Discrepancy (min) | Major Discrepancy (maj) | Very Major Discrepancy (vmj) |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Overnight Manual (K020626) | *S.pneumoniae* | Meningitidis S≤0.06; R≥0.12 | 53 | 53/53 (100%) | 50/53 (94.3%) | NA† | 3 (30%) | 0 |
| 2 | Overnight Manual (k020626) | *S.pneumoniae* | Non-Meningitidis S≤2; I=4; R≥8 | 53 | 53/53 (100%) | 50/53 (94.3%) | 3 (5.7%) | 0 | 0 |

**Table 2. Overnight Manual Read Method – Efficacy Data**

**† Due to lack of Intermediate interpretive criteria, calculation of minor discrepancy is not possible.**

| No. | Read Method | Organism | Interpretive Criteria | No. Isolates Tested | Essential Agreement | Category Agreement | Minor Discrepancy (min) | Major Discrepancy (maj) | Very Major Discrepancy (vmj) |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Overnight Manual (K020626) | *S.pneumoniae* | Meningitidis S≤0.06; R≥0.12 | 243 | 243/255 (92.6%) | 240/243 (98.8%) | NA† | 3 (2.1%) | 0 |
| 2 | Overnight Manual (k020626) | *S.pneumoniae* | Non-Meningitidis S≤2; I=4; R≥8 | 243 | 225/243 (92.6%) | 233/243 (95.9%) | 10 (4.1%) | 0 | 0 |

**Table 3. Overnight Manual Read Method – Combined Challenge and Efficacy Data**

**† Due to lack of Intermediate interpretive criteria, calculation of minor discrepancy is not possible.**

| No. | Read Method | Organism | Interpretive Criteria | No. Isolates Tested | Essential Agreement | Category Agreement | Minor Discrepancy (min) | Major Discrepancy (maj) | Very Major Discrepancy (vmj) |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Overnight Manual (K020626) | *S.pneumoniae* | Meningitidis S≤0.06; R≥0.12 | 296 | 278/296 (93.9%) | 290/296 (98.0%) | NA† | 6 (3.9%) | 0 |
| 2 | Overnight Manual (k020626) | *S.pneumoniae* | Non-Meningitidis S≤2; I=4; R≥8 | 296 | 278/296 (93.9%) | 283/296 (95.6%) | 13 (4.4%) | 0 | 0 |

**Table 4. Walkaway® Instrument Read Method – Challenge Data**

**† Due to lack of Intermediate interpretive criteria, calculation of minor discrepancy is not possible.**

| No. | Read Method | Organism | Interpretive Criteria | No. Isolates Tested | Essential Agreement | Category Agreement | Minor Discrepancy (min) | Major Discrepancy (maj) | Very Major Discrepancy (vmj) |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Overnight Walkway (K062773) | *S.pneumoniae* | Meningitidis S≤0.06; R≥0.12 | 53 | 53/53 (100%) | 52/53 (98.1%) | NA† | 0 | 1 (2.3%) |
| 2 | Overnight Walkaway (K062773) | *S.pneumoniae* | Non-Meningitidis S≤2; I=4; R≥8 | 53 | 53/53 (100%) | 45/53 (84.9%) | 8 (15.1%) | 0 | 0 |

EA = Essential Agreement
CA= Category Agreement
R= Resistant Isolates
min= minor discrepancies
maj = major discrepancies
vmj = very major discrepancies

Specifically related to the data of the challenge isolates tested in Table 4, it is noted that the percent category agreement falls below the acceptance criteria of greater than or equal to 90%, as outlined in the Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems Guidance. This is due to the low number of challenge isolates tested in conjunction with the occurrence of 8 minor discrepancies. Further evaluation revealed that the 8 minor discrepancies are due to the change in the SIR categories with the new Penicillin breakpoint interpretive criteria, and all fall within essential agreement.

Tables 1-4 reveal the occurrence of major discrepancies and one instance of a very major discrepancy which exceeds the acceptance criteria as outline in the Class II Special Control Guidance Document:: Antimicrobial Susceptibility Test (AST) Systems Guidance. This is

due to a lack of an *Intermediate* category for the new Penicillin breakpoint interpretive criteria for *S.pneumoniae*, meningiditis. Because there was only one occurrence of a very major error out of all the data which underwent reevaluation, it can be attributed to random error. The potential increased occurrence of major discrepancies (i.e. the device yielding a result of resistant (R) when the reference method result is susceptible (S)) specific to the Penicillin meningiditis interpretive criteria with *S.pneumoniae,* is addressed in the form of a limitation in the device labeling.

**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).**

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 device.

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(Reviewer's Signature) (Date)

Comments

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