Quality Control Requirements for Microbiology Identification Systems

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What are the appropriate CLIA quality control (QC) procedures for microbiology identification (ID) systems (bacterial and yeast) that utilize panels or cards containing multiple substrates/reagents to generate the organism identification?
Background
QC Requirements for Microbiology Identification (ID) Systems

• CLIA regulations require the laboratory to check each batch (in-house), lot number (commercial) and shipment of reagents, discs, stains, antisera and identification systems for positive and negative reactivity and graded reactivity, if applicable.

• CLIA defines ID systems as “systems using two or more substrates or reagents, or a combination”.
Varying numbers of control organisms need to be tested to check positive and negative reactivity for each substrate/reagent on ID systems that include multiple reactions per panel.
# Commercially Available Microbiology ID Systems

<table>
<thead>
<tr>
<th>Manufacturers</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test Systems</td>
<td>11 Manual</td>
</tr>
<tr>
<td></td>
<td>2 Semi-automated</td>
</tr>
<tr>
<td></td>
<td>7 Automated</td>
</tr>
<tr>
<td>Identification Panels</td>
<td>56</td>
</tr>
<tr>
<td>Substrates/Reagents per Panel</td>
<td>2-95</td>
</tr>
<tr>
<td>QC Organisms Required per Panel</td>
<td>4-8</td>
</tr>
<tr>
<td>Approximate Cost per Panel</td>
<td>$4-$16</td>
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</tbody>
</table>
FDA Process

- In 1998, FDA ceased 510(k) premarket performance evaluations of automated and manual microbiology ID systems

- FDA does not review QC protocols or labeling for microbiology ID systems to meet CLIA requirements
Current Considerations
Manufacturer Request

- Two letters have been submitted to CLIAC suggesting QC requirements for Vitek ID products are excessive.

- For Vitek products, the manufacturer recommends one QC microorganism to check each shipment/lot number of ID cards.

- Previously, the manufacturer recommended testing up to eight microorganisms per shipment of ID cards to check positive/negative reactions for each substrate/reagent.
Determine Appropriate QC

- For each panel/card, is it necessary to check each substrate/reagent for positive/negative reactivity with each shipment/lot number?

- Is there an alternative to testing each reagent/substrate?

- Should a minimum number of control organisms be specified?
Process for Consideration

Since CLIA QC requirements must be general and cannot be specific to a particular manufacturer or test system, how should appropriate QC be determined?
Previous Surveys
American Society for Microbiology (ASM) Proposal

• In 1995-1996 ASM asked CLIAC to consider the appropriateness of CLIA microbiology QC requirements

• ASM agreed to collect QC performance data and share the results with CLIAC

• Based on survey data reflecting low failure rates, ASM suggested a decrease in frequency for QC testing of reagents and stains
ASM conducted two surveys on QC testing failures for commercial microbiology reagents and stains.

8/30/95, 9/25/96 - Data were presented to CLIAC representing 304 clinical microbiology laboratories and 14,731 lots of 21 different tests.
ASM Survey Findings

- Failure rate data suggested CLIA QC testing frequencies for microbiology reagents/stains were excessive.

- Based on survey results, ASM proposed laboratories be required to test only new lot numbers of commercial reagents that had a 98 percent or greater success rate.
1/24/03 - Based on data provided by ASM, CLIA regulations were revised to decrease frequency of QC testing for commercial microbiology reagents/stains
## Changes in Microbiology QC Requirements

<table>
<thead>
<tr>
<th>Regulations Prior to 2003</th>
<th>Current Regulations</th>
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</thead>
<tbody>
<tr>
<td><strong>Bacteriology</strong></td>
<td></td>
</tr>
<tr>
<td>Check positive/negative reactivity –</td>
<td>Check positive/negative reactivity –</td>
</tr>
<tr>
<td>Daily: reagents and DNA probes</td>
<td>Each batch, lot number and shipment of reagents, disks, stains, antisera and identification systems. In addition, check antisera every six months after opening or preparation</td>
</tr>
<tr>
<td>Weekly: bacitracin, optochin, ONPG, X, and V discs or strips</td>
<td></td>
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<tr>
<td>Monthly: antisera</td>
<td></td>
</tr>
<tr>
<td><strong>Mycology</strong></td>
<td></td>
</tr>
<tr>
<td>Check positive/negative/intended reactivity -</td>
<td>Check positive/negative/intended reactivity -</td>
</tr>
<tr>
<td>Daily: lactophenol cotton blue</td>
<td>Each batch, lot number and shipment of reagents, disks, stains (lactophenol cotton blue), antisera, and identification systems</td>
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<tr>
<td>Weekly: fungal identification tests</td>
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</tbody>
</table>
Future Plans
Need for Data

- CDC is working with ASM to gather QC performance data for microbiology ID systems.

- Survey is being planned to include—
  - Cross section of microbiology laboratories
  - Instruments, semi-automated, and manual methods
  - QC performance data from all manufacturers of bacterial and yeast ID systems
Use of Data

- Data will be used to determine
  - Stability
  - Error rates
  - Whether it is necessary to check each reagent/substrate in ID panels for positive/negative reactivity to ensure the correct organism ID

- If data support changing the QC procedures, these revisions will be published in the CLIA interpretive guidelines and disseminated to laboratories