Development of an Individualized Quality Control Plan (IQCP) for MGIT Pyrazinamide (PZA) Drug Susceptibility Testing (DST)

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Background

IQCP is a 3-step process to identify the specific quality control requirements for a particular test.

1. Risk Assessment (RA)
2. Quality Control (QC) plan
3. Quality Assessment (Assurance) (QA) monitoring

Our laboratory developed an IQCP for MGIT PZA DST based on manufacturer’s instructions—weekly QC (vs. each run) and only one control (susceptible to PZA)
Methods – How We Looked for Possible Risks

CMS requires that all 3 phases of testing be included in RA:
- Pre-analytical
- Analytical
- Post-analytical

CMS requires that these 5 test components be included in RA:
- Specimen
- Test System
- Reagents
- Environment
- Testing Personnel
Methods – Where We Looked for Possible Risks
(or: What could possibly go wrong today - or tomorrow?!)

Where we looked for risks:

- PZA testing Process Map
- Procedures (both PZA & PZA QC procedures)
- Any associated forms and documents
- The MGIT 960 System User’s Manual
- Manufacturer’s package inserts
- Personal experiences
Methods – Evaluating Possible Risks by Determining Probability of Occurrence

<table>
<thead>
<tr>
<th>Probability of Occurrence</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improbable</td>
<td>Once in the life of the system</td>
</tr>
<tr>
<td>Remote</td>
<td>&lt; 1% of testing</td>
</tr>
<tr>
<td>Occasional</td>
<td>Between 1% - 10%</td>
</tr>
<tr>
<td>Probable</td>
<td>Between 10% - 50%</td>
</tr>
<tr>
<td>Frequent</td>
<td>&gt; 50% of testing</td>
</tr>
</tbody>
</table>
## Methods – Evaluating Possible Risks by Determining Severity of Harm

Definitions for Severity of Harm Used In Our Laboratory Were Based On:

- Potential for Material Cost
- Scope of Impact (Team, Branch, Outside Branch, Outside CDC)
- Potential for Injury or Impairment to Patient or Personnel
## Methods – Our Laboratory’s Risk Acceptability Matrix

<table>
<thead>
<tr>
<th>Probability of Occurrence</th>
<th>Severity of Harm</th>
<th>Negligible</th>
<th>Minor</th>
<th>Serious</th>
<th>Critical</th>
<th>Catastrophic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequent</td>
<td></td>
<td>Unacceptable</td>
<td>Unacceptable</td>
<td>Unacceptable</td>
<td>Unacceptable</td>
<td>Unacceptable</td>
</tr>
<tr>
<td>Probable</td>
<td>Acceptable</td>
<td>Acceptable</td>
<td>Unacceptable</td>
<td>Unacceptable</td>
<td>Unacceptable</td>
<td>Unacceptable</td>
</tr>
<tr>
<td>Occasional</td>
<td>Acceptable</td>
<td>Acceptable</td>
<td>Unacceptable</td>
<td>Unacceptable</td>
<td>Unacceptable</td>
<td>Unacceptable</td>
</tr>
<tr>
<td>Remote</td>
<td>Acceptable</td>
<td>Acceptable</td>
<td>Acceptable</td>
<td>Unacceptable</td>
<td>Unacceptable</td>
<td>Unacceptable</td>
</tr>
<tr>
<td>Improbable</td>
<td>Acceptable</td>
<td>Acceptable</td>
<td>Acceptable</td>
<td>Acceptable</td>
<td>Acceptable</td>
<td>Unacceptable</td>
</tr>
</tbody>
</table>
On our spreadsheet we had columns filled in for each risk, its control(s), the phase of testing and the test component affected, and supporting documentation.

We then estimated each risk’s Probability of Occurrence and Severity of Harm using our laboratory’s definitions.

The acceptability of each risk was then determined using our laboratory’s Risk Acceptability Matrix.

If any risks were found to be unacceptable, additional controls were identified to reduce the probability of occurrence or severity of harm.

If additional controls are identified, existing procedures may need to be modified.
# Results – Examples from our Laboratory’s Risk Assessment Table*

*Probability, Severity, and Acceptability Determined After Thorough Documentation of Controls

<table>
<thead>
<tr>
<th>Risk</th>
<th>Testing Phase</th>
<th>Probability (with controls in place)</th>
<th>Severity</th>
<th>Risk Acceptable?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incorrect or incomplete information for specimen entered on submission form</td>
<td>Pre-analytic</td>
<td>Occasional</td>
<td>Minor</td>
<td>Yes</td>
</tr>
<tr>
<td>Use of expired calibrator tubes resulting in erroneous results</td>
<td>Pre-analytic</td>
<td>Improbable</td>
<td>Serious</td>
<td>Yes</td>
</tr>
<tr>
<td>Contamination introduced during set up of MGIT seed tubes / MGIT PZA media tubes</td>
<td>Analytic</td>
<td>Remote</td>
<td>Minor</td>
<td>Yes</td>
</tr>
<tr>
<td>MGIT drawer fails to maintain correct temperature range</td>
<td>Analytic</td>
<td>Improbable</td>
<td>Serious</td>
<td>Yes</td>
</tr>
<tr>
<td>Improper seating of inoculated MGIT tube in instrument resulting in spill</td>
<td>Analytic</td>
<td>Improbable</td>
<td>Critical</td>
<td>Yes</td>
</tr>
<tr>
<td>Printer malfunctions while printing reports</td>
<td>Post-analytic</td>
<td>Occasional</td>
<td>Minor</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*Probability, Severity, and Acceptability Determined After Thorough Documentation of Controls
Results – Examples of Control Documentation:
Incorrect or Incomplete Information Entered on Submission Form

Controls (established or proposed)

✓ CDC’s new submission forms w/ 2D barcode technology and new ELIMS software will reduce errors in transcription. The barcodes created by the submitter’s input will be scanned into CDC’s new ELIMS software when received at CDC.

✓ Procedures will be established to check patient demographics, specimen, transport medium, and submitter information against the submission form to prevent mismatched or missing information.

✓ An accessioning sticker will be placed on the submission form to indicate if the identifiers on the specimen and submission form agree.

✓ The submitting lab will be called to clarify conflicting information or to obtain missing information.

Known Limitations (Residual Risk)

✓ Transcription errors may still occur when data is entered manually

✓ Error could occur at submitting lab and not be apparent on form or sample
Results

- Our Risk Assessment identified >25 risks.
- Controls were already in place for the majority.
- No unacceptable residual risk was identified.
- A QC Plan has been developed, along with QA Monitoring to periodically review the QC Plan for effectiveness.
- Actively refining our IQCP
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