Fairfax County Health Department
JoAnne Jorgenson Laboratory

Individualized Quality Control Plan (IQCP)

June 2016
Individualized Quality Control Program

WHAT

WHY

HOW

IQCP
Where to Begin

Cepheid® GeneXpert®
MTB/RIF Assay
• CDC/CMS IQCP guidance
  • *IQCP Developing an IQCP, A Step-By-Step Guide*

• Manufacturer’s IQCP guidance
  • *Developing an Individualized Quality Control Plan (IQCP)* for Cepheid’s GeneXpert® Diagnostic Systems

• COLA
  • *Individualized Quality Control Plan (IQCP) Implementation Guide*
• 76 Questions
  • **Pre-analytic** - 30
  • **Analytic** – 29
  • **Post-Analytic** – 9
  • **Final Review** - 8
<table>
<thead>
<tr>
<th>Phase of Testing</th>
<th>Element</th>
<th>Potential Error</th>
<th>Is there a potential source of error in your laboratory</th>
<th>Is there a system check in place to detect this potential error</th>
<th>Your Individualized Quality Control Plan (IQCP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre analytical</td>
<td>Specimen</td>
<td>Patient Prep</td>
<td>YES</td>
<td>NO</td>
<td>Staff are trained in the proper collection, handling, and transportation of specimens. FCHDL protocol for MTB/RIF testing states that staff must include on the test requisition, documentation of any drug therapy including the duration. Requests received without this information would require follow-up to determine if the sample meets criteria for this test. Staff are trained in the proper positioning of patients for specimen collection per PHN Procedural Memoranda.</td>
</tr>
<tr>
<td></td>
<td>Specimen</td>
<td>Patient &amp; Specimen ID</td>
<td>YES</td>
<td></td>
<td>Two identifiers are required for patient identification and labeling. Patients are routinely asked to state their name and date of birth.</td>
</tr>
</tbody>
</table>
## Pre-Analytic

<table>
<thead>
<tr>
<th>Question</th>
<th>YES/NO</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Analytic 7: Is the internal or electronic QC, or the test system itself, capable of detecting inadequate patient preparation? If YES, describe how internal QC or test system will detect this potential source of error. If NO, describe your laboratory process for ensuring patient preparation is consistently followed.</td>
<td>NO</td>
<td>Staff are trained in the proper collection, handling, and transportation of specimens. FCHDL protocol for MTB/RIF testing states that staff must include on the test requisition, documentation of any drug therapy including the duration. Requests received without this information would require follow-up to determine if the sample meets criteria for this test. Staff are trained in the proper positioning of patients for specimen collection per PHN Procedural Memoranda.</td>
</tr>
<tr>
<td>Pre-Analytic 8: Does your laboratory have a written procedure for patient identification and labeling of specimens? If yes, describe your laboratory’s procedure for patient identification and specimen labeling? If no, develop and describe your laboratory’s procedure for patient identification and specimen labeling.</td>
<td>YES</td>
<td>Two identifiers are required for patient identification and labeling. Patients are routinely asked to state their name and date of birth. Specimens have bar code labels that include two identifiers. See Patient Identification Procedural Memorandum.</td>
</tr>
</tbody>
</table>

## Analytic

<table>
<thead>
<tr>
<th>Question</th>
<th>YES/NO</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analytic 2: Does your laboratory have a process to ensure all components for the test are storage under conditions required by the manufacturer? If YES, describe your process for monitoring conditions. If NO, develop and implement a process and describe below.</td>
<td>YES</td>
<td>All storage temperatures are monitored and recorded daily and corrective action taken if out of range.</td>
</tr>
<tr>
<td>Analytic 3: Are the reagents and supplies shipped under conditions that are consistent with the manufacturer’s requirements? If yes, describe your process for receiving supplies and the conditions under which the supplies are delivered from your supplier. If no, develop a process for evaluating conditions of reagents upon receipt.</td>
<td>YES</td>
<td>All applicable supplies are delivered to the laboratory upon receipt and stored according to manufacturer’s requirements. All applicable supplies are shipped as per Manufacturer’s requirements.</td>
</tr>
</tbody>
</table>
Risk Assessment

**Post Analytic**

<table>
<thead>
<tr>
<th>Question</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post Analytic 7: Has your laboratory verified the accuracy of the test calculation? If yes, describe how the calculation is verified. If No, develop and implement a method for verifying calculated results.</td>
<td>NA</td>
</tr>
</tbody>
</table>

**Comment**

Results are compared to AFB smear, culture, and susceptibility testing results.

**Final Review**

<table>
<thead>
<tr>
<th>Question</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Final Review 1: Have you previously performed an EQC study for this test? If yes, confirm control values used for the EQC study fell within the expected range. If no, proceed to Review 2.</td>
<td>NO</td>
</tr>
<tr>
<td>Final Review 2: Does your external QC data demonstrate that the test system is consistently stable? If yes, describe the general QC performance over time for this test. If No, describe any repeated QC failures and the corrective action taken.</td>
<td>YES</td>
</tr>
</tbody>
</table>

**Comment**

External QC results over the past seven months have been consistently acceptable.
Individualized Quality Control Plan Summary Report

Fairfax County Health Department Laboratory   CLIA ID: 49D0670586
10310 Layton Hall Drive
Fairfax, VA 22030
Deborah K. Severson
MTB/RIF
10/20/15

Overall weighted risk score: 11

Key

0-40 = LOW risk
41-80 = MODERATE risk
>= 81 = HIGH risk

Low risk: Based upon the information you have provided during the risk assessment process, your potential risk for this test in your lab is relatively low. You have implemented procedures to reduce the risk to a manageable level. With the Lab Director’s approval, the manufacturer’s QC requirements may be sufficient for your laboratory, along with the procedures you routinely perform, as indicated in this risk assessment, to reduce risk in all phases of testing.

Monitor and review QC results per your normal procedure, and review your IQCP for effectiveness as required by your regulatory agency. Re-evaluate your IQCP and revise if performance failures have been identified.
Summary of Risk Assessment Mitigation

**Pre-analytic phase:** Based upon your laboratory’s risk assessment, the following are risk mitigation procedures performed by your laboratory to reduce the incidence of pre-analytic errors:

- Staff are trained in the proper collection, handling, and transportation of specimens.

FCHDL protocol for MTB/RIF testing states that staff must include on the test requisition, documentation of any drug therapy including the duration. Requests received without this information would require follow-up to determine if the sample meets criteria for this test.

**Analytic phase:** Based upon your laboratory’s risk assessment, the following are risk mitigation procedures performed by your laboratory to reduce the incidence of analytic errors:

- All storage temperatures are monitored and recorded daily and corrective action taken if out of range.

- All applicable supplies are delivered to the laboratory upon receipt and stored according to manufacturer’s requirements.
The fishbone diagram illustrates potential sources of error in the laboratory process. It categorizes errors into Specimen, Personnel, Reagents, Lab Environment, Test System, and Result Interpretation & Reporting. Each category is further divided into subcategories that detail specific error sources. This diagram is a tool to identify potential sources of error and is not intended to be a complete IQCP.
This IQCP for Fairfax County Health Department Laboratory has been reviewed and approved. This IQCP will be reviewed on a regular basis and if quality failures occur with this test, if necessary, the IQCP will be re-evaluated and revised.

Lab Director ____________________________ Date ____________________________

Fairfax County Health Department Laboratory  CLIA ID: 49D00670586
10310 Layton Hall Drive
Fairfax, VA 22030
Subsequent review of IQCP Name of test: MTB/RIF

Date of review ____________________________

Have there been QC failures, PT failures, or other quality failures identified for this test since the IQCP was developed? ___Yes ___No (skip to 8 or C below)

If yes, describe below and provide any necessary revisions to your IQCP in A below.

A ___ The IQCP for this test will be modified, as described below, based upon test performance since the IQCP was first developed.

B ___ The IQCP for this test continues to be sufficient to mitigate risk in my laboratory.

C ___ The Lab Director recommends the following modification to the IQCP, even though there have been no performance failures.

Laboratory Director ____________________________ Date ____________________________

Fairfax County Health Department Laboratory  CLIA ID: 49D00670586
10310 Layton Hall Drive
Fairfax, VA 22030
Manufacturer’s IQCP Guidance

APPENDIX A: Sample Fishbone Diagram for Xpert Testing Process

[Diagram showing the Xpert Testing Process with categories for Specimens, Testing Personnel, Environment, Reagents, and Test Systems with potential hazards and incorrect test result.]
## Manufacturer’s IQCP Guidance

### APPENDIX B: Sample Risk Assessment for Cepheid GeneXpert Tests

#### Risk Matrix - ISO 14971

<table>
<thead>
<tr>
<th>Probability of Harm</th>
<th>Severity of Harm</th>
<th>Legend</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Maggifiable</td>
<td>Unacceptable (1, 2, 3)</td>
</tr>
<tr>
<td></td>
<td>Minor</td>
<td>Acceptable (4, 5, 6)</td>
</tr>
</tbody>
</table>

#### Possible Source of Error

<table>
<thead>
<tr>
<th>Possible Source of Error</th>
<th>Potential Failure</th>
<th>Phase</th>
<th>Severity</th>
<th>Probability</th>
<th>Risk Index Before</th>
<th>Manufacturer Features to Minimize Risks</th>
<th>Possible Laboratory Solutions to Minimize Risk</th>
<th>Risk Index After</th>
<th>Documentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. SPECIMEN</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.1</td>
<td>Test is performed</td>
<td>Inaccurate</td>
<td>Pre-analytical</td>
<td></td>
<td>Package insert and training</td>
<td>Establish training for specimen collectors</td>
<td>Establish sample rejection criteria</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>in incorrect patient population</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.2</td>
<td>Wrong specimen type collected</td>
<td>No result</td>
<td>Pre-analytical</td>
<td></td>
<td>Package insert and training</td>
<td>Establish training for specimen collectors</td>
<td>Establish sample rejection criteria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.3</td>
<td>Wrong collection device used</td>
<td>No result</td>
<td>Pre-analytical</td>
<td></td>
<td>Package insert and training; Manufacturer recommends appropriate collection device</td>
<td>Establish sample rejection criteria</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.4</td>
<td>Specimen not collected correctly</td>
<td>No result</td>
<td>Pre-analytical</td>
<td></td>
<td>Package insert and specimen collection guidelines (available for some tests)</td>
<td>Establish training for specimen collectors</td>
<td>Follow manufacturer’s instructions</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* May not be applicable to all tests. Refer to package insert.
Our Risk Assessment has reviewed all relevant potential errors in the pre-analytic, analytic and post-analytic phases of testing. See attached IQCP Summary Report. FCHDL has the following processes in place for the detection of errors in each phase of testing:

- **Before Testing:**
  - Evaluation of specimen acceptance/rejection criteria for identifying specimens not suitable for testing.
  - Checking of the cartridge lot#/expiration date and reviewing the last QC results for that lot # prior to using the kit.

- **During Testing:**
  - Each cartridge has Sample Processing Control (SPC) and a Probe Check Control (PCC) to indicate whether or not the sample was processed correctly and to monitor bead rehydration, reaction-tube filling, probe integrity and dye stability. The instrument will not issue a result if the instrument QC and the SPC and PCC do not pass criteria for acceptability.

- **After Testing:**
  - All instrument printouts and worksheets are reviewed by a laboratory supervisor prior to releasing results.
The manufacturer’s instruction/package insert recommends performing QC in accordance with local, state, and federal accrediting organizations’ requirements as applicable. It does not specify frequency. In order to determine an acceptable frequency of QC for this method, the TB Lab tested three levels of QC on all new lot #s and shipments of MTB/RIF cartridges as well as three levels monthly over a 14 month period.

<table>
<thead>
<tr>
<th>YEAR</th>
<th>TBNEG MTB/RIF (NEG/NEG)</th>
<th>TBWT MTB/RIF (POS/NEG)</th>
<th>TBMDR MTB/RIF (POS/POS)</th>
<th>% DISCREPANT RESULTS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PASS</td>
<td>FAIL</td>
<td>PASS</td>
<td>FAIL</td>
</tr>
<tr>
<td>2014</td>
<td>37</td>
<td>0</td>
<td>37</td>
<td>0</td>
</tr>
<tr>
<td>2015</td>
<td>11</td>
<td>0</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td>TOTAL</td>
<td>48</td>
<td>0</td>
<td>48</td>
<td>0</td>
</tr>
</tbody>
</table>

After reviewing the resulting QC data, it was determined that the external negative and positive controls are reliably reproducible across a moderate period of testing and the following QC guidance was developed.
Quality Control Plan

Control Types/Levels:
The following controls, purchased from Maine Molecular Quality Control Inc. (MMQCI), will be run in order to monitor assay performance:
1. INTROL TBNEG (Neg/Neg)
2. INTROL TBWT-04 (Pos/Neg)
3. INTROL TBMDR-04 (Pos/Pos)

Criteria for acceptability:
1. The INTROL TBNEG must give results of “MTB Not Detected”
2. The INTROL TBWT-04 must give results of “MTB Detected; Rif Resistance Not Detected”
3. The INTROL TBMDR-04 must give results “MTB detected; if Resistance Detected”
4. All of the instrument and cartridge controls must pass
5. External controls are compared to the manufacturers expected ranges to verify that they are acceptable.

Frequency:
All three levels of controls will be run:
- For a newly trained operator, prior to testing specimens.
- With each new lot# or shipment
- Monthly for lot# in use
- If the storage temperature of the kit falls outside of 2°-28°C, test prior to use with all three controls.
- When review of QA indicates a deviation from expected results. Test using all three control strains.
**IQCP Components**

- **Risk Assessment**
  - Identifies potential failures and sources of error.
  - Must document that potential errors and sources of errors have been reviewed by the laboratory.

- **Quality Control Plan**
  - At a minimum, define type, number, and frequency of quality control methods to be utilized.

- **Quality Assessment**
  - Evaluates the overall IQCP implemented and must address pre-analytic, analytic, and post-analytic.

- **Signature Page**
  - Statement of approval signed by lab director.
Risk Assessment

- Performed by in-house personnel
- Covers all three phases of testing:
  - Pre-analytic
  - Analytic
  - Post-analytic
- Covers all 5 components:
  - Specimen
  - Reagent
  - Environment
  - Testing personnel
  - Test system
- Includes in-house data:
  - Previous QC records
  - Environmental monitoring records
  - Instrument/equipment performance records
- Review manufacturer’s instructions and recommendations to identify potential risks processes to mitigate risk
Quality Control Plan

- QC Plan must be signed and dated by the laboratory director prior to implementation
- Approved annually
- Must be followed as approved
- Specifies number, type (internal/external), and frequency of quality control
- QC performed at least as frequently as required in manufacturer’s instructions
- If ongoing assessments identify failures in one or more components of the QC Plan, the laboratory must investigate the cause and consider if modifications are needed to the plan to mitigate potential risk.
Quality Assessment

- Must include how the entire method will be assessed for failures and corrective actions.
- Monthly review of QC, instrument maintenance
- Evaluation of errors in all phases
- Evaluation of corrective actions taken if errors are identified
- Reevaluation of risk assessment when failures are identified
- Annual re-approval of QC Plan
Potential Deficiencies

- Incomplete risk assessments
  - All 5 requirements
  - All phases
  - No mitigation identified
  - Multiple instruments, multiple sites

- Inadequate quality control plans
  - QC cannot be performed less than stated in manufacturer’s package insert

- Insufficient monitoring
  - Annual review of each IQCP
  - Ongoing assessment of errors, QC failures,

- Individual laboratories not performing their own risk assessment, relying on manufacturer’s risk assessment
Questions