Essential Quality Assurance and Quality Control

for Microbiological Methods to meet Federal Water Program Requirements

Patsy Root

Chair, AOAC Water & Wastewater Community

Agenda

- Authors and backgrounds
- Definitions
- QA/QC for Micro
  - US EPA requirements at 40 CFR 136.7
  - What this mean for Micro consensus methods
- The **10** Micro QA/QC Points
- Summary
- Questions / Contact Information

Authors

- Patsy Root
  - Senior Regulatory Affairs Specialist, IDEXX Labs, Inc.; Environmental Laboratory Advisory Board, Chair; TNI Board Member
- Margo Hunt
  - US EPA, retired; *Standard Methods for the Examination of Water and Wastewater* Part 9000 coordinator;
- Laurie Kundrat; Microbiologics
- Karla Fjeld; Microbiologics
- Paper Citation: Root *et al*, *Journal of AOAC International* Vol. 97, 567 – 572, No. 2, 2014

Definitions

- **Quality Management System (QMS)**
  - A QMS describes the organizational structure, procedures, processes and resources needed to manage production of defensible and usable data that is of value to a customer or meets regulatory requirements
  - A QMS is a cycle that provides continuous feedback for improvement
  - Some of the items in a QMS program are: definition of personnel roles/duties, defining what to do, who does it & how, how errors are identified, communicated & corrected, how data and personnel are assessed and how data is evaluated and documented

Definitions

- **Quality Assurance**
  - Defining what is to be measured; implies a valid and reliable program for the systematic monitoring and evaluation of the various aspects of lab work/testing to ensure that standards of quality are being met
- **Quality Control**
  - Operational and personnel checks to verify that 'good' data is being consistently produced according to protocol or Standard Operating Procedures (SOPs)


Quality Management System
Quality Assurance
Quality Control

QA/QC for Micro

- US EPA outlined **12** basic QA/QC steps in the Federal Register at 40 CFR 136.7, but they were for Chemistry methods
  - Many of the 12 points also apply to Micro methods
  - Not all consensus Micro methods contain sufficient or detailed QA/QC
  - AOAC methods include specific QA/QC, but these are considered the *minimum controls* to perform the method effectively
- QA/QC measures are required in order to produce data of known and documented quality
- **Accredited labs** must demonstrate they are performing a method consistently using defensible QA/QC

QA/QC for Micro

- EPA requirements for **Chemistry*** QA/QC at **40 CFR 136.7**
- EPA is added requirements at 136.7 to specify 12 essential quality control elements that *must be in the laboratory's documented quality system*
- **(i)** Demonstration of Capability (DOC);
- **(ii)** Method Detection Limit (MDL);
- **(iii)** Laboratory reagent blank (LRB),also referred to as method blank (MB);
- **(iv)** Laboratory fortified blank (LFB),also referred to as a spiked blank, or laboratory control sample (LCS);
- **(v)** Matrix spike (MS) and matrix spike duplicate (MSD), or laboratory fortified matrix (LFM) and LFM duplicate, may be used for suspected matrix interference problems to assess precision;
- **(vi)** Internal standards (for GC/MS analyses), surrogate standards (for organic analysis) or tracers (for radiochemistry);
- **(vii)** Calibration (initial and continuing), also referred to as initial calibration verification (ICV) and continuing calibration verification (CCV);
- **(viii)** Control charts (or other trend analyses of quality control results);
- **(ix)** Corrective action (root cause analysis);
- **(x)** QC acceptance criteria;
- **(xi)** Definitions of preparation and analytical batches that may drive QC frequencies; and
- **(xii)** Minimum frequency for conducting all QC elements.

Top 10 Micro QA/QC Points

1. Demonstration of Capability
2. Method Blanks and Sterility Checks
3. QC Samples / Laboratory Fortified Blank (LFB)
4. Matrix Spike and Matrix Spike Duplicate
5. Calibration of Equipment, Performance Qualification (PQ)
6. Control Charts and Trend Analysis
7. Corrective Action / Root Cause Analysis
8. QC Acceptance Criteria
9. Definition of a Batch (prep and analytical)
10. Minimum Frequency QC Checks – Lab Equipment

Demonstration of Capability

- Each analyst must demonstrate initial and ongoing capability for each analysis performed. These results must be documented.
- Any potential problems must be identified, corrected, and documented. The intent is to prove both the reliability and integrity of the laboratory's test results.
- There are two types of DOC: initial and ongoing.

Method Blanks and Sterility Checks

- Sterility testing and the use of method blanks ensure that unknown samples have not been compromised, contaminated, or invalidated due to improper handling or preparation, inadequate sterilization, or environmental exposure.
- **Sterility checks** ensure that the processes used for sterilization are valid, and are done before running the method.
- **Method blanks** demonstrate that equipment, media, reagents, and sample containers were properly sterilized and *were not contaminated* while in storage or during the testing process.

QC Samples / Laboratory Fortified Blank (LFB)

- LFBs may also be referred to as QC samples, or negative and positive controls.
- They are used to ensure that growth media or other method reagents/materials are capable of supporting proper growth and/or analytical results.
- LFB samples may be used to establish intralaboratory or analyst-specific precision and bias, or to assess the performance of all or a portion of the measurement system.
- They may also be used for initial DOC and ongoing DOC.

Matrix Spike and Matrix Spike Duplicate

- The matrix being tested can have a profound and often unknown effect on resulting data.
- To mitigate unusable data, suspected difficult matrixes should be spiked with known concentrations of organisms to determine recoverability.
- Some methods may routinely require a matrix spike and matrix spike duplicate

Calibration of Equipment, Performance Qualification (PQ)

- The laboratory must demonstrate that it has sufficient equipment and instrumentation of appropriate quality for each analytical method it conducts.
- Test equipment and instrumentation before initial use and during continual usage in the laboratory to demonstrate that they perform consistently

Control Charts and Trend Analysis

- The laboratory must demonstrate equipment, instrumentation, or analytical changes over time.
- These trends in process control are best demonstrated in tabular form, graphs, or charts and show that the laboratory is operating under control and with the expected variations of the analyses.
- If trends exceed control limits, corrective action must be initiated.

Corrective Action / Root Cause Analysis

- Despite proper implementation of QSM and associated activities, event that result in incorrect or questionable data can still occur
- When this happens, it is important to have an established, methodical process to under and correct the cause of the issue
- RCA is a structured problem-solving process that involves identification of a specific procedural step or process that led to a faulty or unexpected outcome.
- Corrective actions are directed corrective measures aimed at preventing specific issues uncovered during
- RCA. It is likely that recurrence can be prevented if specific, measurable, corrective actions are put in place after a root cause is identified

QC Acceptance Criteria

- QC acceptance criteria are used to determine if test results are acceptable, and must be established to monitor the daily operation during laboratory testing processes
- *Establish acceptance criteria – examples*
  - tests for clean glassware
  - tests for reagent water quality
  - sterility checks of sterile reagent or dilution water
  - sample integrity and holding conditions

Definition of a Batch (prep and analytical)

- A batch is typically an uninterrupted series of analyses on a single matrix type using a single method
- For QC purposes, the maximum number of samples in a preparation batch is generally 20/matrix.
- Each analytical batch may contain more than the 20 samples prepared in one preparation batch.
  - Samples must be accompanied at least by a positive and negative control resulting in a minimum of three analyses.
  - The negative control may be a method blank.

Minimum Frequency QC Checks – Lab Equipment

- To ensure precise and consistent results, laboratory equipment must be installed, maintained, and calibrated properly.
- Critical equipment requires a higher frequency of testing; some examples are:

Autoclaves	Microscopes
Balances	Pipettes
Incubators/Thermometers	Membrane Filter Units
Biosafety Cabinets	Multi-well Sealers
Freezers/Refrigerators	pH meter

Summary

- QA and QC are part of a Quality System Management approach to meet objectives of management, customers and data users and to insure reliable data is produced
- QA /QC measures in current EPA-approved methods may not be sufficient to meet the above objectives
- Adding the 10 recommended QA/QC listed here will help ensure labs produce quality Micro data that is reproducible and defensible

Discussion & Questions

Thank you!

Patsy Root
IDEXX Labs Inc.
patsy-root@idexx.com

207-556-8947