Training Module I – Management Systems

Asia Pacific Economic Cooperation (APEC)
Laboratory Capacity Building Workshop

Thailand – August 2011

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High Level Importance: ISO 17025 Chemical Compliance

Asia Pacific Economic Cooperation (APEC) Laboratory
Capacity Building Workshop
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Presentation Outline

- ISO Quality Manual Contents
- Scope of the ISO 17025 accreditation
- Standard Operating Procedures (SOPs)
- Quality Assurance program
- Test method selection
- Method validation
- Instrument qualification
- Quality Control program
- Proficiency testing requirements
- Customer feedback and corrective action programs

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Other Standards in Addition to ISO 17025

- U.S. FDA Good Laboratory Practices (GLP)
  - Used in U.S. Labs and others around the world
  - Very strict record keeping protocols
  - Complete data reconstruction is required
- U.S. FDA Good Manufacturing Practices (GMP)
  - Used in pharmaceutical and dietary supplement labs
  - Includes strict requirements for method validation
  - Very strict record keeping is required

The Quality Manual Contents

- The manual needs to be a compete as possible
- All aspects of ISO 17025 need to be covered
- This manual should compliment the SOP book
- Laboratory management must be clear
  - Responsible parties for action
  - Reporting structures for lab testing
- Scope of the accreditation needs to be covered
  - Test methods that are accredited
  - Record keeping and document control

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The Quality Manual Contents

- All policies and procedures must be presented
- Customer feedback must be captured
- Corrective action plans must be understood
- The organization and presentation of the Quality Manual is critical
- This manual must be easily accessible to all responsible parties in the lab

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Scope of the ISO 17025 accreditation

- It is important that the scope covers all related test methods in the lab
- Each laboratory location needs to be accredited
- Each appropriate test method in a lab needs to be qualified
- The chemistry labs ISO scope needs to include all of the required procedures
- Before using a testing lab, it is important that the scope of the accreditation is understood

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Standard Operating Procedures (SOPs)

- All laboratories activities need to be detailed in an Standard Operating Procedure
- This includes everything from sample receipt and sample preparation – to the actual test analysis
- These SOPs must be easily understood and easy to follow
- Critical control points need to be pointed out clearly in each SOP

Standard Operating Procedures (cont)

- ”If a laboratory activity is not covered by an SOP, and documented, it did not happen”
- All SOPs need to be readily accessible in the laboratory
- All chemists need to document that they have read and understand all of the SOPs
- This needs to happen on a defined schedule

The Quality Assurance Program (QA)

- Not to be confused with Quality Control
- The QA function assures compliance with SOPs as well as policies and procedures
- Some labs have a dedicated QA department
- This is required for compliance with FDA GLP and GMP regulations
- The QA group performs the “check and balance” role for a testing lab

The Quality Assurance Program (cont)

- The QA group will audit the laboratory for compliance with SOPs
- The QA group will audit the test data for completeness and accuracy
- The QA function may be handled by the laboratory operations staff

Test Method Selection

- Research and development
- Testing in support of food safety initiatives
- Development of NLEA or DSHEA Nutrition Facts
- Data for regulatory submission
  - FDA GLP
  - FDA cGMP
  - Other applicable regulations
- Data for potential litigation
  - FDA
  - Competitors
  - Consumers

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Test Method Selection (cont)

- AOAC INT. - *Official Methods of Analysis*
- ISO, EN, CODEX, BIS, GB – Official Methods
- AOAC INT. – SLV methods
- Other compendia methods
  - USP, FCC
  - AACC
  - AOCS
- Published methods
- In-house developed methods

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Method Validation

- All accredited test methods must be validated
- This validation needs to be documented
- Full validation is not required when the lab uses AOAC Official Methods or other compendia method procedures
- All other methods require some level of validation
- Validation procedures need to be detailed in a Standard Operating Procedure

AOAC and ISO Procedures

- Single Laboratory Validation (SLV)
  - Detailed protocol
  - AOAC and ISO guidelines

- AOAC Official Methods of Analysis
  - Policies from AOAC - *Official Methods*^{sm}
  - ERP helps select the Study Director
  - 12 laboratory study
  - At least five test materials

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Method Validation Parameters

- Precision
  - “Agreement among repeated measurements or trials”
  - Repeatability (within one lab)
  - Reproducibility (between labs)

- Accuracy
  - “The difference between the true value and the value obtained”
  - Fortified samples
  - Standard reference materials
  - Alternative methods

Method Validation – continued

- Specificity
  - Ability to measure only the desired compound
- Limit of Detection
  - Lowest concentration of analyte that can be measured
- Limit of Quantitation
  - Lowest concentration of analyte that can be precisely and accurately measured
- Linearity
  - Variance from a straight line

Method Validation – continued

- Range
  - Upper and lower limits at which the analyte can be precisely and accurately measured
- Ruggedness
  - Reproducibility of results under varying conditions (e.g., different analysts, different instruments, different labs)
- Robustness
  - Repeatability under deliberately varied and “stressed”` conditions
  - Forced degradation of analyte

Instrument Qualification

- All instruments used with accredited assays need to be qualified for use
- This activity will vary between labs, but needs to be done before an instrument is used
- Some instrument vendors will provide this qualification as part of the purchase

Instrument Qualification (cont)

- FDA GMPs have a great protocol for this:
  - IQ: Installation qualification
  - OQ: Operational qualification
  - PQ: Performance qualification
- This protocol is very detailed and is used by regulated test labs
- This is not an ISO requirement, but extremely valuable for the lab

The Quality Control Program (QC)

- This program must define all aspects of the lab's efforts to monitor and control data quality
- A good QC program will drive data quality
- This program should include the following:
  - Policies on replicate testing
  - Policies on performing retests
  - Procedures for handling "out of specification" results
  - Procedures for handling "out of tolerance" results
  - Policies for use of control and reference materials
  - Programs for monitoring QC performance

QC Policy for Replicate Testing

- How many replicates are measured for each sample analysis?
- A policy needs to be developed
- It may be dependant upon the type of test
- It may be different for problematic sample matrices

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QC Policy for Repeat Testing

- When should a test be repeated?
  - The test QC failed
  - A problem occurred during the analysis
  - Unusual results are found
- How many replicates are measured during a repeat analysis?
- What is the policy for “invalidating” a test result
- This requires clear documentation

Out of Specification Results (OOS)

- A separate policy is needed for samples that have a specification
- Some action maybe required when a product has a result that is OOS
- This policy may be customer specific
- Some actions are required if the product being tested is regulated
- These actions usually include an investigation and some re-analysis

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Out of Tolerance Results (OOT)

- Tolerances for test results may be monitored by the laboratory for analyte – matrix combinations
- Tolerances may also be customer specific
- Any test results deemed to be OOT requires some action to be taken
- These actions may include reanalysis

Use of Control and Reference Materials

- Controls and reference materials should be used to monitor the accuracy of a test method
- These materials may be purchased as Standard Reference Materials
- These materials may be developed “in house”
- The control matrix should be the same or very similar to the test samples
- These materials should be analyzed with every group of test samples
- Ranges should be developed for acceptability

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Monitoring Ongoing Performance

- Results from control and reference materials should be monitored for acceptability
- These data should also be “plotted” for any trends in data quality
- Any “drift” or change in the accuracy of a test method can be detected with this system
- These data should be documented

Proficiency Testing Programs

- In addition to the control and reference materials, external proficiency testing is required by ISO
- These are test sample submitted to the lab by an independent third party
- Analyte levels in the samples are “blind”
- Data are submitted and the third party issues scores to the lab based on performance
- These data need to be documented and monitored

Proficiency Testing Programs (cont)

- Some type of proficiency data is required for every accredited test method (ISO)
- These programs are very helpful in accessing the quality of a chemistry laboratory

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Customer Feedback

- ISO requires that the testing lab has a system for clients to provide input
- This is often accomplished through surveys
- The survey information needs to be captured and monitored for trends and changes
- A system for follow-up on customer complaints is also required

Customer Feedback (cont)

- Any customer complaint requires some level of corrective action from the lab
- That leads to other types of corrective action –

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Corrective Action Programs (CAPA)

- A well developed CAPA program is very important for the chemistry lab
- Corrective actions need to occur as a results of any testing errors that are detected
- Corrective actions are required as a result of any customer complaints

Corrective Action Programs (cont)

- CAPA plans must detail the actions that need to occur and the responsible parties
- These plans must include documented actions and what the outcomes were
- CAPA plans must also include control plans, to ensure against repeat errors or problems

Summary

- ISO 17025 is a great program for chemistry labs
- The program requires very detailed documentation across the lab
- Some additional programs are helpful for today's complex testing environment
- The more detailed laboratory quality programs offer a higher probability of data accuracy

Conclusion

- Thank you for your attention
- Questions?
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