Improving the Defensibility of Your Data Using CRMs

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Agenda

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- ISO Guide 17025
- Uses of CRMs
- Basics of Quality Control
  - Method Validation
  - Staff Training
  - Ongoing Performance
  - Corrective Action
- Questions

Assuring the Quality of Test Results

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HOW CAN WE DEFEND OUR DATA?

BY ASSURING THE QUALITY OF OUR TEST RESULTS

Assuring the Quality of Test Results

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ISO Guide 17025

Section 5.9

Assuring the Quality of Test and Calibration Results

5.9.1 – The laboratory shall have quality control procedures for monitoring the validity of tests undertaken. The resulting data shall be recorded so trends are detectable. Statistical techniques shall be applied to the reviewing of the results.

Assuring the Quality of Test Results

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ISO Guide 17025

Section 5.9.1

The monitoring may include:

Regular use of Certified Reference Materials.

Assuring the Quality of Test Results

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All the elements required to assure quality defensible data

can be found in ISO Guide 17025

….And CRMs can be used to satisfy these elements

Requirements

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ISO 17025 requires laboratories to:

- Establish, operate, and maintain a quality system consistent with ISO 9001
- Be technically competent to operate the test systems for which they are accredited
- Be able to generate technically valid results for the test systems for which they are accredited

5.2 - Personnel

- 5.2.1 - Laboratory management shall ensure the competence of all who operate specific equipment, perform tests and/or calibrations, evaluate results, and sign test reports and calibration certificates.
- 5.2.2 – The management of the laboratory shall formulate the goals with respect to education, training, and skills of the laboratory personnel. The effectiveness of the training actions shall be evaluated.

5.4 - Methods and Method Validation

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- 5.4.1 – The laboratory shall use appropriate methods and procedures for all tests and/or calibrations within its scope. This includes, where appropriate, an estimation of the measurement uncertainty.
- 5.4.4 – Non standard methods shall be validated appropriately before use. Procedures for non-standard methods should include reference standards and reference materials required; checks that the equipment is working properly, calibration and adjustment of the equipment; uncertainty or procedure for estimating uncertainty.
- 5.4.5.2 – The techniques used for the determination of the performance of a method should be one or a combination of; calibration using reference standards, interlaboratory comparisons, assessment of the uncertainty of results.

5.4.6 - Estimation of Uncertainty of Measurement

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- 5.4.6.2 – Testing laboratories shall have and apply procedures for estimating uncertainty of measurement.
- 5.4.6.3 – When estimating the uncertainty of measurement, all uncertainty components which are of importance shall be taken into account.

5.5 - Equipment

- 5.5.2 – Equipment used for testing shall be capable of achieving the accuracy required. Before being placed into use equipment shall be calibrated and checked.
- 5.5.3 – Equipment shall be operated by authorized personnel.

5.6 - Measurement Traceability

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- 5.6.2.1.1 – Calibrations and measurements made by the laboratory must be traceable to SI Units.
- 5.6.2.1.2 – Certain calibrations/measurements cannot be strictly made in SI Units. Confidence in measurements in these cases can be made with the use of Certified Reference Materials provided by a competent supplier.

5.6.3 - Reference Standards and Reference Materials

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- 5.6.3.1 – Reference standards shall be calibrated by a body that can provide traceability as described in 5.6.2.1
- 5.6.3.2 – Reference materials shall, where possible, be traceable to SI units of measurement, or to Certified Reference Materials.

WHAT DOES ALL THIS MEAN TO ME

TRACEABILITY

QUALITY CONTROL

Traceability

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ISO 17025 Requires Traceability

Traceability is a property of the result of a measurement or the value of a standard where by it can be related to the stated references, usually national or international standards, through an unbroken chain of comparisons all having stated uncertainties.

Traceability/Quality Control

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ISO 17025 laboratories need to:

- Use traceable calibration standards whenever they are available.

- If traceable standards are not available, an ISO Guide 34 accredited producer of calibration materials should be selected to assure the best possible standards

- Verify calibrations against independent quality control standards from a ISO Guide 34 accredited supplier

Traceability/Quality Control

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- I do not have the capability or adequate resources to produce my own traceable quality control standards . What can I do?

Use Certified Reference Materials

Certified Reference Materials (CRMs)

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- A Certified Reference Material is defined in ISO Guide 34 as a reference material characterized by a metrologically valid procedure for one or more specified properties, accompanied by a certificate that provides the value of a specified property, its associated uncertainty, and a statement of metrological traceability.
- CRM producers go through rigorous quality control requirements per ISO Guide 34 in order to be accredited.

What are CRMs: Characteristics

- Characteristics of Certified Reference Materials:
  - A standard with known concentrations (assigned values) of specified analytes
  - The standard has a known uncertainty, homogeneity and stability
  - The assigned values are traceable to an independent reference
  - A certificate of analysis is included with the CRM
  - The certificate of analysis includes reference to the characteristics of the certified reference materials

Certificate of Analysis

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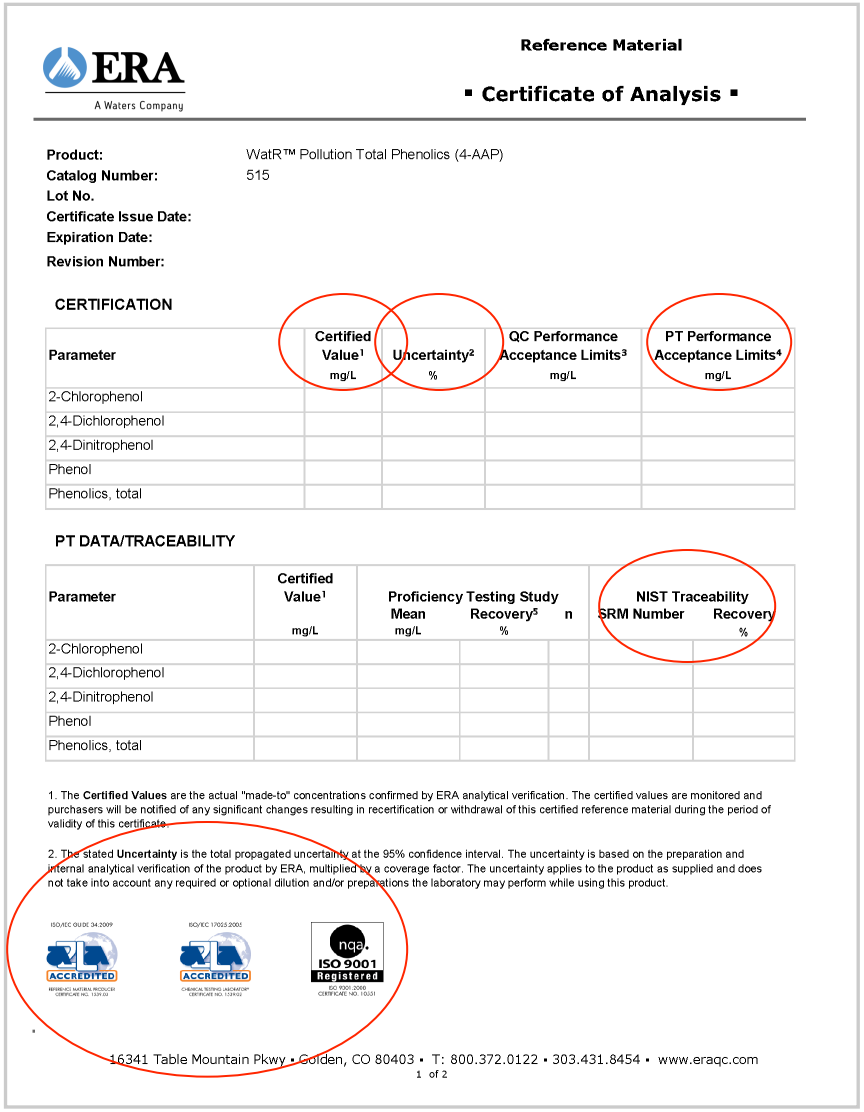

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Reference Material

▪ Certificate of Analysis ▪

Product: WatR™ Pollution Total Phenolics (4-AAP)
Catalog Number: 515
Lot No.
Certificate Issue Date:
Expiration Date:
Revision Number:

CERTIFICATION

Parameter	Certified Value[1] mg/L	Uncertainty[2] %	QC Performance Acceptance Limits[3] mg/L	PT Performance Acceptance Limits[4] mg/L
2-Chlorophenol				
2,4-Dichlorophenol				
2,4-Dinitrophenol				
Phenol				
Phenolics, total				

PT DATA/TRACEABILITY

Parameter	Certified Value[1] mg/L	Proficiency Testing Study Mean mg/L	Recovery[5] %	n	NIST Traceability SRM Number	Recovery %
2-Chlorophenol						
2,4-Dichlorophenol						
2,4-Dinitrophenol						
Phenol						
Phenolics, total						

1. The **Certified Values** are the actual "made-to" concentrations confirmed by ERA analytical verification. The certified values are monitored and purchasers will be notified of any significant changes resulting in recertification or withdrawal of this certified reference material during the period of validity of this certificate.

2. The stated **Uncertainty** is the total propagated uncertainty at the 95% confidence interval. The uncertainty is based on the preparation and internal analytical verification of the product by ERA, multiplied by a coverage factor. The uncertainty applies to the product as supplied and does not take into account any required or optional dilution and/or preparations the laboratory may perform while using this product.

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1 of 2

- Certified value
- Uncertainty
- Performance Acceptance Limits
- NIST Traceability
- Accreditations and Registration

Types of CRMs

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- Calibration Standards
  - Individual, high concentration solutions
  - Multi-analyte, high concentration mixtures
  - Low concentration, ready-to-use, solutions
- Calibration Check Standards
  - Simple matrix
  - Similar to calibration standards
- Matrix Quality Control Standards (Custom)
  - Real or synthetic matrix
  - Various analytes, various concentrations
  - May include interferences
  - Designed to mimic a real sample

Use of CRMs:
Basics of Quality Control

Basics of Quality Control

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- Quality control generally applies to four basic functions of the laboratory
  - Method development (ISO 17025 Section 5.4)
  - Staff training (ISO 17025 Section 5.2)
  - Ongoing performance (ISO 17025 Section 5.6)
  - Corrective action

Method Development

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- 4 Key areas of method development
  - Precision
  - Accuracy
  - Analysis range
  - Ruggedness

Method Development

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- Precision
  - "Degree of agreement between independent measurements under controlled conditions"
  - How close repeated measurements are to each other
    - "Repeatability"
  - Represented by standard deviation

- Accuracy
  - "Degree of agreement of a measured value with the true or expected value"
  - How close measurements are to the "true" value
  - Represented by the percent recovery
    - Use CRMs to determine the accuracy and precision of your method

Method Development

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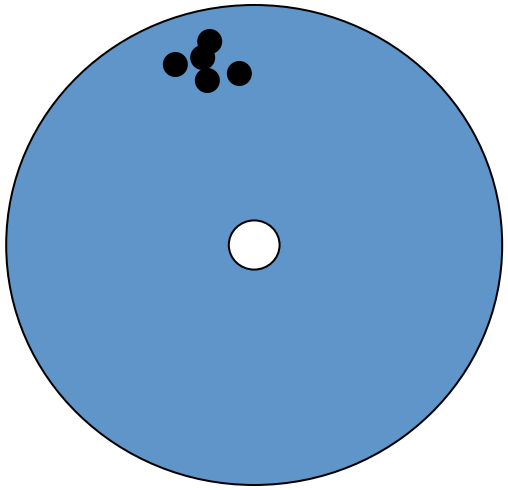
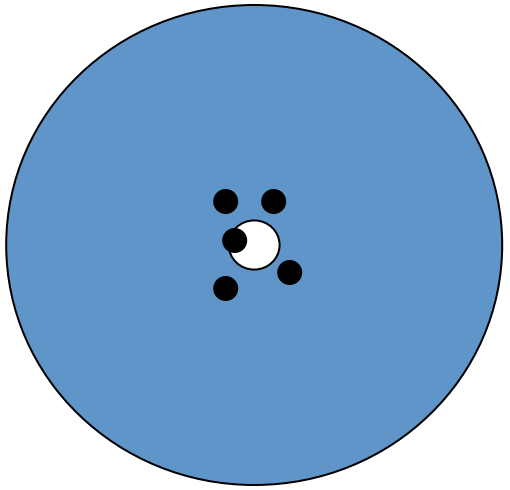
- Precision and accuracy



Precise but not accurate



Accurate but not precise

Method Development

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- Analysis Range
  - Establish an appropriate quantitation range
  - How low can I go? How low should I go?
  - Perform MDL studies and establish a Practical Quantitation Limit (PQL)

- Ruggedness
  - There will be a variety of matrices. Can my method handle these matrices
  - Routine maintenance of your equipment
    - CRMs can monitor the ongoing performance of your equipment

Basics of Quality Control

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Staff Training

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- When hiring new staff or giving them a new method to perform, it is important to train them and ensure training was effective.
  - Use CRMs as hands-on training samples
  - Document the analyst's performance versus the assigned value
  - Proof of competency to perform the analysis

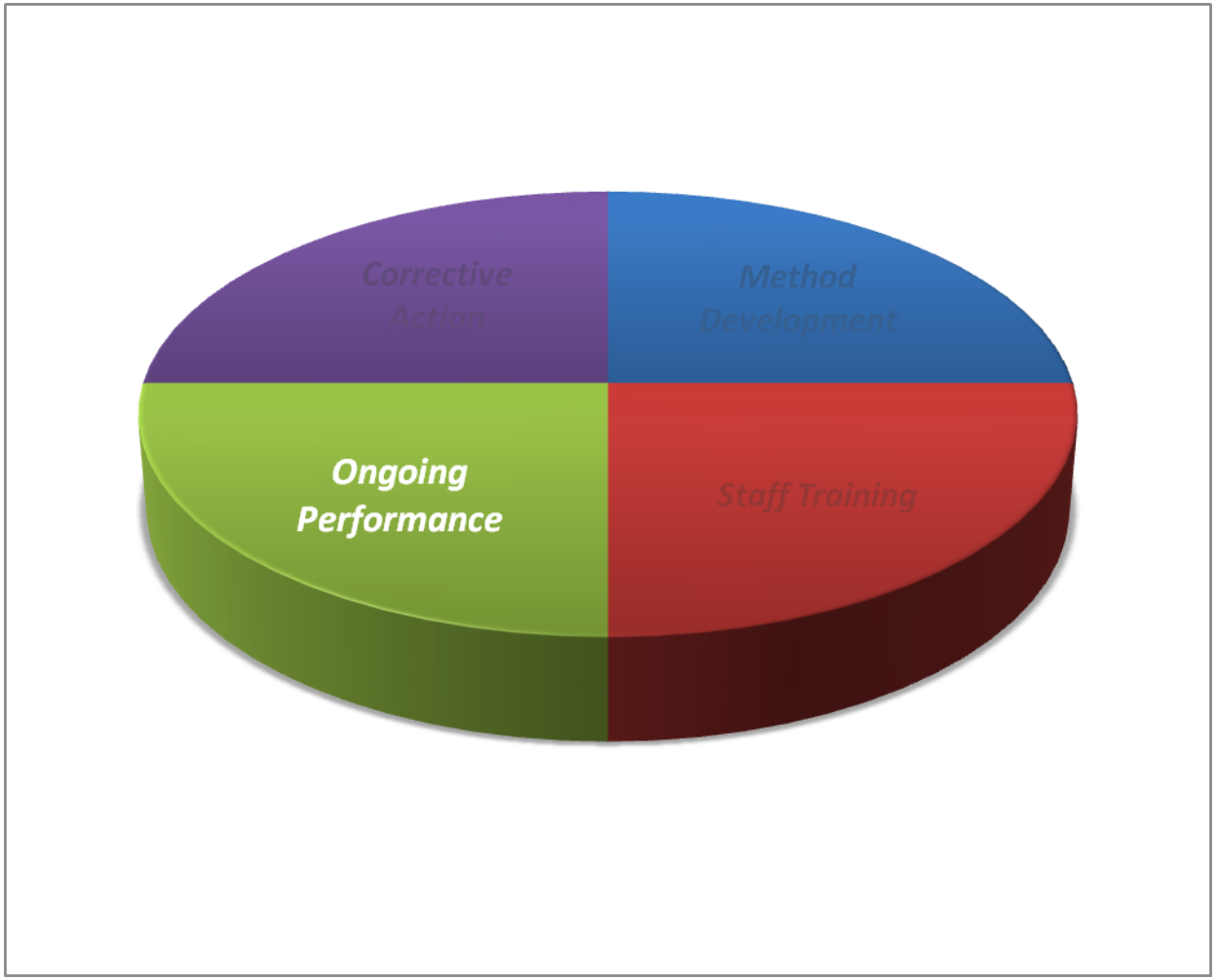
- It is also important to regularly document that the analyst is still performing with the necessary accuracy and precision
  - Ongoing performance verification
  - Use CRMs as QC samples for monitoring continued quality

Staff Training

- Gaining experience
  - Analyze samples under direct supervision
    - Use CRMs to Demonstrate Capability (DOC)

- Ongoing performance verification
  - Include CRMs as standard method QC
  - Periodic single-blind QC (lab knows it is a test)
    - PT study for each analyst
  - Inclusion of double-blind PT (lab does not know it is a test)
    - Provides a better test of the analyst's performance

Basics of Quality Control



Ongoing Performance

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- Once a method is established in a laboratory, there are still many variables that can affect its performance:
  - Analysts
  - Instruments
  - Standards and reagents
  - Laboratory environment
  - Sample matrix
  - Random errors

CRM Use in Ongoing Performance

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- CRMs can be used for Routine QC
  - Calibration
    - Fresh
    - Trusted source
    - Traceable
  - CCV: continuing calibration verification
    - Same source as calibration
    - Checking for short-term drift
  - ICV: independent calibration verification
    - Independent source
    - Generally mid-calibration range
    - Control chart the results of ICV analysis

Ongoing Performance

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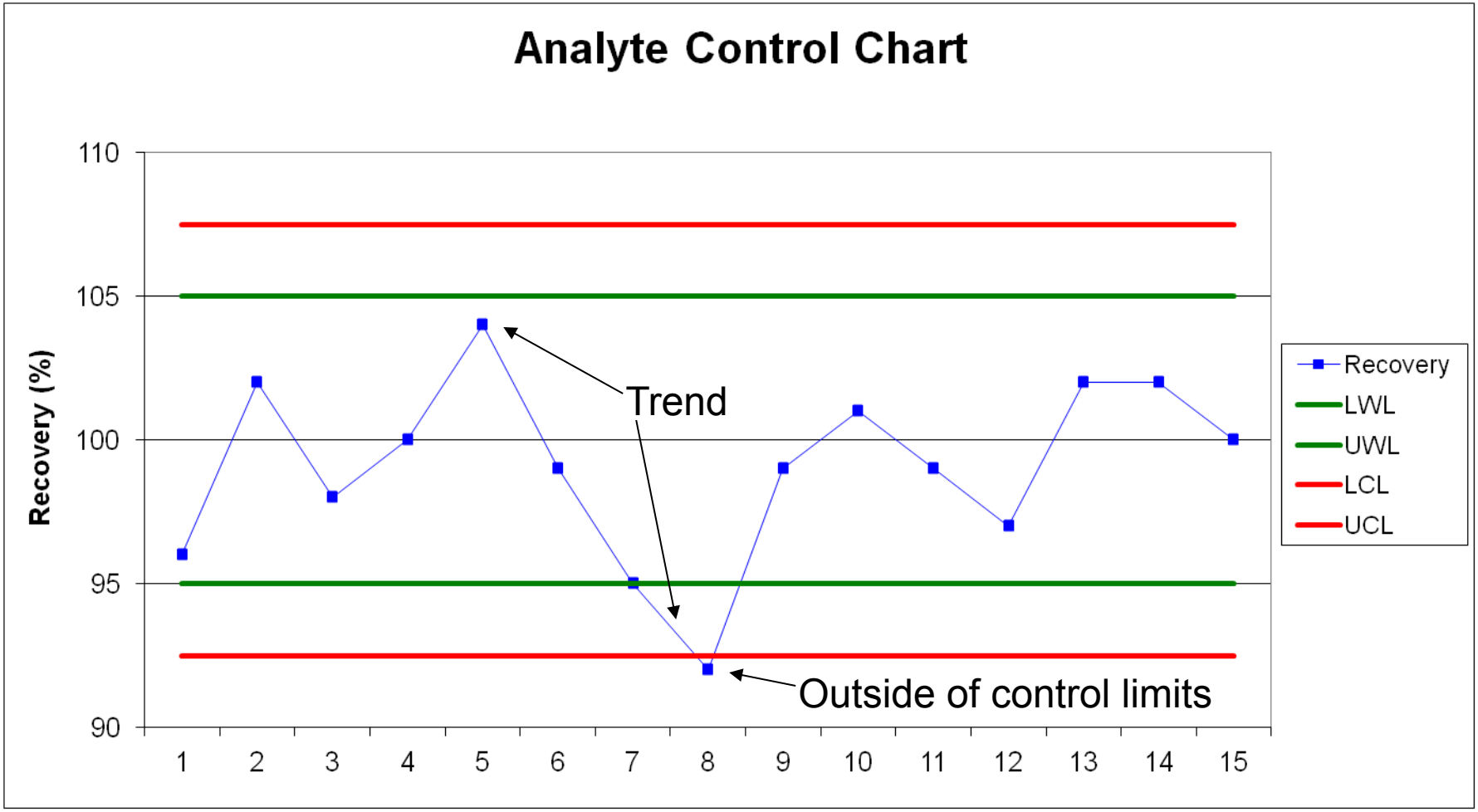
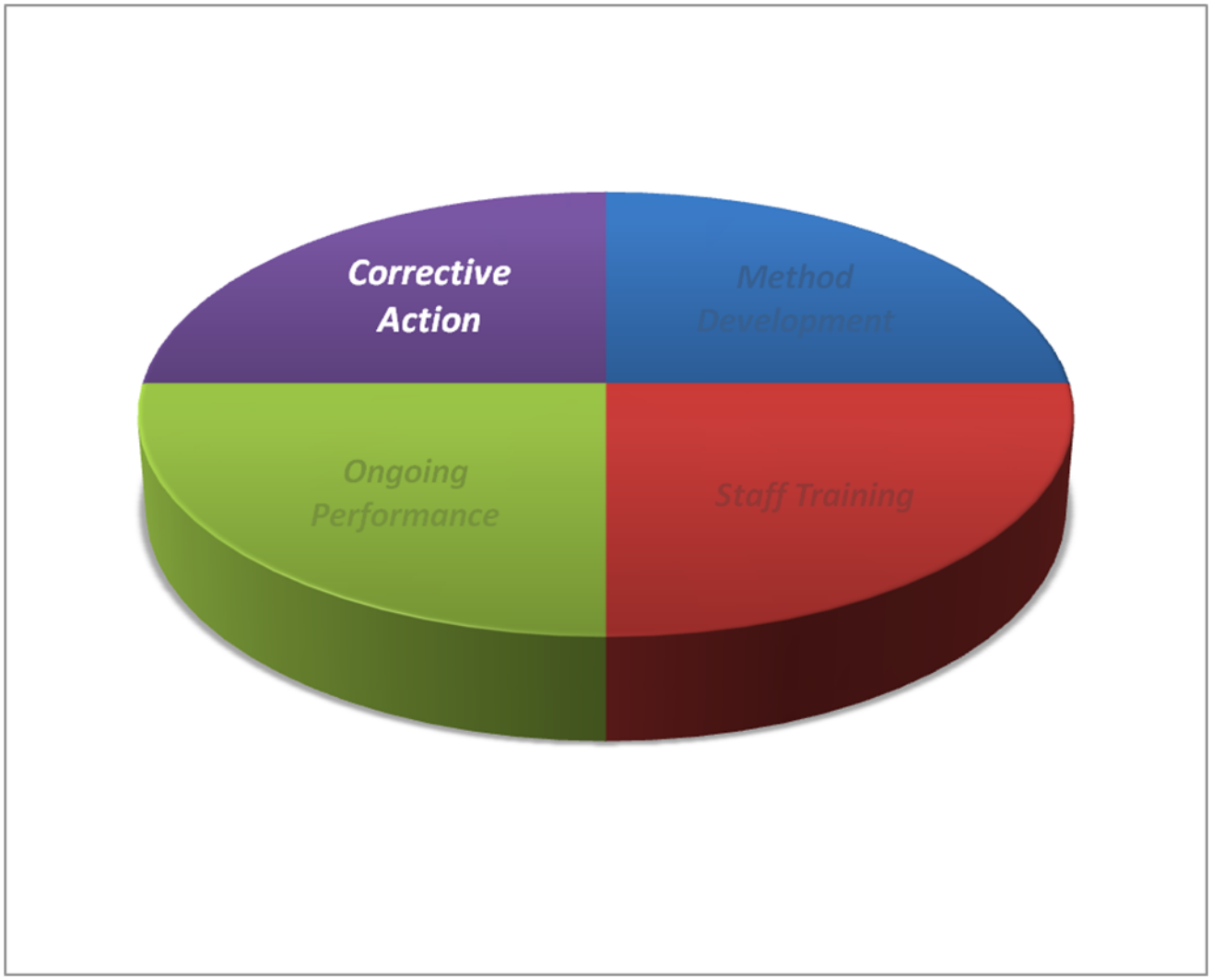
- Control charting is the process of plotting the percent recovery of a certified reference material, each time it is analyzed
- Ideally, the CRM is analyzed with each analytical batch, or at least once each day that the analysis is performed
- When possible, use the same lot number of CRM for your control charting for as long as possible
  - This ensures that any potential variations between CRMs are not affecting your control charts
  - If you consistently use CRMs from the same, accredited provider, you should not experience lot-to-lot variations

Ongoing Performance



Basics of Quality Control



Corrective Action

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- Whenever quality criteria are not met:
  - Failed PT sample
  - Calibration linear regression does not fit
  - Outside of quality control limits
    - Control chart

- Corrective action:
  - Root cause analysis
  - Implement corrections
  - Test that corrections are appropriate
  - Monitor to ensure that corrections are effective

Corrective Action – Root Cause

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- CRMs are effective when conducting root cause analysis:
  - Use to identify the source of the error (Man, Machine, Materials, Methods)
    - Analyst
    - Instrument
    - Standards
    - Procedure
  - Run using same conditions as when problem identified
  - Make adjustments, if necessary

Corrective Action

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- Once the problem is identified and a change has been implemented, CRMs are helpful to ensure effectiveness:
  - Was change appropriate
    - Verify new calibration standard, give QC standard to retrained analyst, etc.
  - Is the change effective long term
    - Routine use of CRMs will identify if the system is in control and may predict when it is trending out of control

Conclusion

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- CRMs can be used to improve the defensibility of your data. They are a critical part of 17025 accreditation.

- CRMs are critical in establishing and maintaining a quality control program. By incorporating CRMs into a QC program regularly, a lab can help ensure both reliability of results and successful PT performance.

- CRMs are certified by an outside source, giving you added confidence that your standard is made correctly.

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THANK YOU