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Exposing Myths, Legends and Tales About Reference Materials

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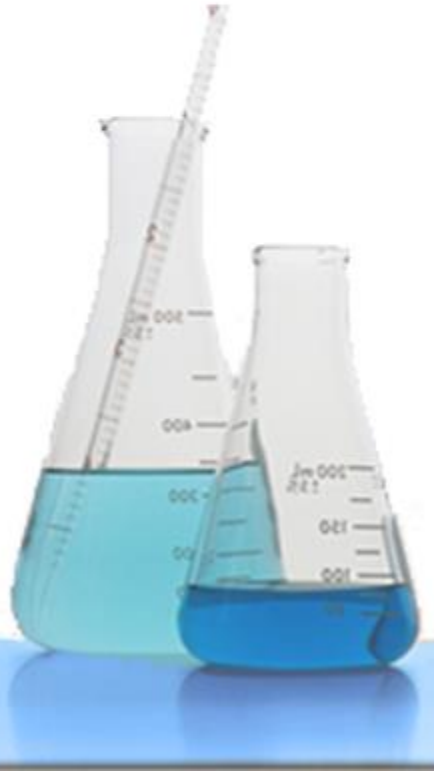

Overview

- Reference Materials Accreditation
- Reference Materials Production
- Reference Materials Definitions
- Reference Materials Use
- Second Source Lot Reference Materials

Reference Materials Accreditation

- These standards apply only to ISO GUIDE 34 ACCREDITED REFERENCE MATERIAL PRODUCERS
- There are no requirements for other producers

Reference Materials Accreditation

- NON-ACCREDITED REFERENCE MATERIAL PRODUCERS
- Potential Issues
  - Certificates
    - Traceability
    - Uncertainty

RM Related Standards

- ISO Guide 30
  - Vocabulary
- ISO Guide 31
  - Contents of certificates and labels

RM Related Standards

- ISO Guide 33
  - Good practice in using reference materials
- ISO Guide 34 (Soon to be 17034)
  - General requirements for the competence of reference material producers
- ISO Guide 35
  - Reference materials -- General and statistical principles for certification

RM Related Standards

- ISO Guide 80
  - Guidance for in-house preparation of reference materials for quality control

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Reference Materials Production

Production Flow

- Planning
- Material Selection
- Collection
- Preparation of Material
- Characterization
- Storage
- Documentation

Planning

- End-use requirements
  - Methods/technology to be served
- Market need
- What is to be certified
  - Measurands
  - Forms
  - Concentrations

Planning

- Level of certification required
- Quantities
  - Starting materials available
  - Final product needed

Material Selection

- Based on:
  - nature and physical form of the matrix desired
- Materials should be:
  - similar to real-world samples
  - Representative of materials
    - in production
    - commerce and
    - undergoing analysis

Material Selection

- In the Environmental Industry:
  - Purchase of Industrial grade materials
  - Purchase of Lab grade materials
  - Synthesis/Purify
- Determine fitness for use:
  - GC/MS
  - Optical Rotation, FTIR
  - LOD, ROI, Carl Fischer

Collection

- Selection of the collection location
  - Matrix
  - Measurand levels
- Interim transport
- Storage at processing location

Preparation

- Selection of processing equipment
- Preliminary processing
  - Cleaning, washing, separation
- Prep depending on material
  - Crushing, grinding, milling
- Considerations for homogeneity
  - particle sizes, distribution, shape and density

Preparation

- Stabilization, if needed
- Measurement of selected measurands for
  - Contamination
  - Loss control
- Stability Assessment
- Final Packaging
- Labeling
- Units required for testing and certification
  - set aside during the packaging
    - predetermined statistical design

Preparation

- Environmental RMs
  - Gravimetric Preparation
    - Weigh
    - Dilution

Characterization

- Value Assignment
- Methodologies for homogeneity testing
  - Selection
  - Development
  - Assessment
  - Use

Storage

- Environmental Conditions
  - Verification
    - stability of matrix and measurand by
      - periodic examination
      - testing

Documentation

- Collection Steps
- Processing Steps
- Characterization Procedures
- Certification (if CRM)
  - Measurand
  - Traceability
  - U_{CMR}

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Reference Material Definitions

Reference Material

- Generic Term
- Material of one or more specified properties
  - Homogeneous for intended purpose
  - Stable
  - fit for its intended use
  - Limited testing of final product
    - Verification of property

Reference Material

- No certificate to accompany material
- No stated uncertainty of material
- No statement of degree of homogeneity or stability
- Example:
  - Custom mixes

Certified Reference Material

- RM characterized by metrologically valid procedure for specified property
- Assessment to degree of
  - Homogeneity
  - Stability
- Certificate
  - Value of specified property
  - Associated uncertainty
  - Statement of traceability

Quality Control Materials

- Not a new class of RMs
- Materials used routinely to assess the precision of test procedures
  - in-house reference materials
  - quality control materials
  - check samples

Quality Control Materials

- SW846 Examples
  - 8260 & 8270
    - Stock solutions may be prepared from pure standard materials…
  - 6010 & 6020
    - Stock solutions may be prepared from ultra-high purity grade chemicals or metals (99.99% pure or greater)

Production Batch (lot)

- Produced in single manufacturing cycle
- Intended to have uniform:
  - Character
  - Quality

- Note: <u>Has nothing to do with the source of the material.</u>

Data behind CRMs

- Assessing of:
  - Homogeneity
  - Stability
  - Characterization of RM
- Establishing of:
  - Uncertainty
  - Metrological traceability
    - Identity (measurand)
    - Quantity

Homogeneity

- Homogeneity - uniform in composition or character –
  - *Within-bottle Homogeneity*
    - Checks product for stratification or precipitation
  - *Between-bottle Homogeneity*
    - Samples multiple containers from each lot to check for homogeneity

Homogeneity

- Units analyzed in random order, not ‘as bottled’
  - Separate analytical drift from bottling trends
  - ANOVA
  - Determines the contribution to the combined uncertainty from possible inhomogeneity

Homogeneity

- Assists in the assessment of the statement of minimum sample on the certificate

Stability

- Not reactive during normal use
- Retains properties
  - In expected timescale
  - In the presence of expected conditions of application
- Unstable material
  - corrode, decompose, polymerize, burn or explode under the ‘normal’ conditions

Stability

- Prior information
  - Use data from related materials
  - Use published and/or readily available information
- New stability studies
  - Accelerated testing
  - Long-term testing
  - Determines the value of the contribution to the combined uncertainty for instability

Characterization

- Single primary method in one laboratory
  - Cost effective if methodology and equipment is readily available
- Two or more independent methods in one or more laboratory
  - Requires detailed uncertainty information for methods
- Consensus certification
  - Multiple laboratory study using competent laboratories
    - Sometimes free choice of method
    - Sometimes method specified

Uncertainty

- Calculated from the standard uncertainties associated with:
  - Homogeneity assessment
  - Characterization measurements
  - Possible long-term instability
  - Other contributions
- Contributions are combined and expanded to give a 95% confidence interval

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Metrological Traceability

- Common reference point
  - SI - International System of Units
  - NMI material or higher level RM in the metrological traceability hierarchy
    - Primary Standard
  - Applies to:
    - assessment of homogeneity and stability
      assignment of values in characterization

Traceability

NMI (Primary Std)

CRMs (2ndary Std)

RMs

In-house QCMs

Increasing Traceability

Uncertainty

NMI (Primary Std)

CRMs (2ndary Std)

RMs

In-house QCMs

Increasing Uncertainty

Traceability

- **“NIST Traceable” is a misnomer**
- **The value of a reference material is created through metrological traceability.**

Metrological Traceability

- ONLY measurement results can be traceable.
- Neither a laboratory, nor a government agency can be traceable. An accredited laboratory isn't traceable, and its results aren't necessarily traceable.

Metrological Traceability

- An instrument can't be traceable. Even if an instrument was calibrated by NIST, it doesn't make its results traceable.
- A solution can be traceable.
  - **The preparation of the solution and measurement result for a solution <u>can be traceable</u>, ONLY if the solution was appropriately prepared, packaged, maintained and documented.**

Metrological Traceability

- The RMP is Responsible For Appropriate RM:
  - **Preparation**
  - **Packaging**
  - **Storage**
  - **Documentation**
- The Lab is Responsible For Appropriate RM:
  - **Handling**
  - **Use**
  - **Storage**
  - **Documentation**

Metrological Traceability

- **Documentation:** Every link in the chain must be performed and the results of these procedures must be documented.
- This documents the measurement system.

Metrological Traceability

- Competence: RMPs and their internal laboratories performing steps in the chain must demonstrate competence by:
  - Accreditation to ISO 17025 for testing labs and ISO Guide 34 for reference material producers

Metrological Traceability

- **Measurement uncertainty:**
  - Must be determined for each link in the traceability chain
  - Must be reported for the final measured result
  - Must be documented by the RMP in their CoA

Metrological Traceability

- Read the CoA provided by Accredited RMPs.
- A good CoA describes the preparation and verification of the solution
  - (e.g., gravimetric preparation with chromatographic, titrimetric verification)

Metrological Traceability

At a minimum Guide 31 requires the following essential elements to be included in a CoA:

- AB Symbol (or statement)
- Name of the material
- Producer and producer's code for the material
- General description of the material
- intended use

Metrological Traceability

At a minimum Guide 31 requires the following essential elements to be included in a CoA (continued):

- Instructions for proper use
- Instructions for appropriate conditions of storage
- Certified property value(s)
  - each accompanied by a statement of uncertainty;

Metrological Traceability

At a minimum Guide 31 requires the following essential elements to be included in a CoA (continued):

- Method(s) used to obtain property values
- Level of Homogeneity
- Period of Stability

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Reference Material Use

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RM Hierarchy

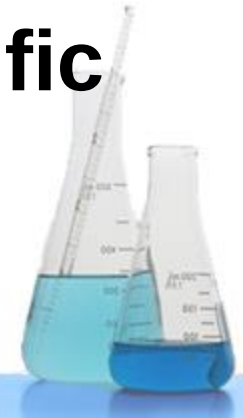
- NMI materials (i.e. NIST SRMs)
- CRMs
- RMs
- In-house QCMs

CRM Use

- Establish Traceability
- Measurement Uncertainty
- Method Validation
- Method Verification (Correct for use) (RM)
- Calibration (RM)

Reference Material

- **Guide 33 13.1.3**
- Purposes to use RM include:
  - Calibration;
  - Assignment of values to properties of other materials;
  - Quality control.
- Furthermore, **a given RM can only be used for a single purpose in a specific measurement.**



Reference Material

- **Guide 33: 2015 Clause 11.1.3**
  - Checking the consistency of values assigned to … calibrants is recommended.
  - Such checks can be performed
    - by comparing a new calibrant against an old, validated one,
    - **by assessing the effect of using the new calibrant as part of a quality control, by, e.g. measuring a QCM**.

QCM use

- Matrix matching
  - suitable for ongoing quality control
- Suitable day-to-day RM to complement a commercially available CRM
- No suitable CRM exists

QCM use

- Application does not require a material having the full characteristics of a CRM Traceability and uncertainty
  - Method development

QCM use

- Preparation of Control Charts
- Instrument Performance Checks
- Repeatability and reproducibility studies
- Check Sample
- Operator Variability
- Influence of Environmental Conditions

In Conclusion

- Choice of RM dependent upon:
  - Availability
  - Appropriateness
    - Degree of Characterization for intended use
  - Competence of Supplier

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Second Source Reference Materials

Second Source RMs

Purposes of a Second Source

1. Qualitative Agreement: Confirm Identity of Compounds in Primary Standard

2. Quantitative Agreement: Confirm Concentrations of Primary Standard Compounds

3. Degradation: Monitor and identify if occurring during analytical sequences

Second Source RMs History

1994 — ICV / QCS appears in Methods 200.8 / 6020

1994 — NELAC Draft Standard requires second source

1997 — NELAC requires 15% QC limit; AFCEE & ACoE adopt into their Manuals

1997 — AFCEE requires 15% for inorganics and 25% for organics

Second Source RMs History

1998 — *Benzidine? Really?* Presented at WTQA

1999 — NELAC drops 15% limit

2005 — ACoE Manual publishes verification limits of 90-110% for Inorganics and 80-120% for Organics.

2009 — TNI Standard still requires with laboratory established limits

Second Source RMs

Definitions

Source	Definition
SW-846 Method 6020, 1994	… a standard composed of the analytes from a source different from those used in the standards for instrument calibration
EPA Method 200.8, 1994	… - The QCS should be obtained from a source outside the laboratory
AFCEE V.2.0, 1997	A second source standard is a standard purchased from a different vendor than the vendor supplying the material used in the initial calibration standards.

Second Source RMs
Definitions

Source	Definition
NELAC, 2003 Standard	5.5.5.2.2.1.d – "…a standard obtained from a second manufacturer or lot if the lot can be demonstrated from the manufacturer as prepared independently from other lots."

Second Source RMs
Conclusion

Many methods from sources such as:

- *ASTM*
- *Standard Methods*
- *SW-846*

do not contain a reference to either the use or definition of a Second Source Lot while many more do

Requirements for Manufacturers of Starting Materials (MSMs)

ISO Guide 34:

- …there are internationally recognized requirements and an assessment processes for the evaluation of RMPs in which the competence to produce a RM is determined
- Similar requirements exist for the testing and calibration laboratories that are the users of the RMs some of which may be these second source RMs

Requirements for Manufacturers of Starting Materials (MSMs)

ISO Guide 34:

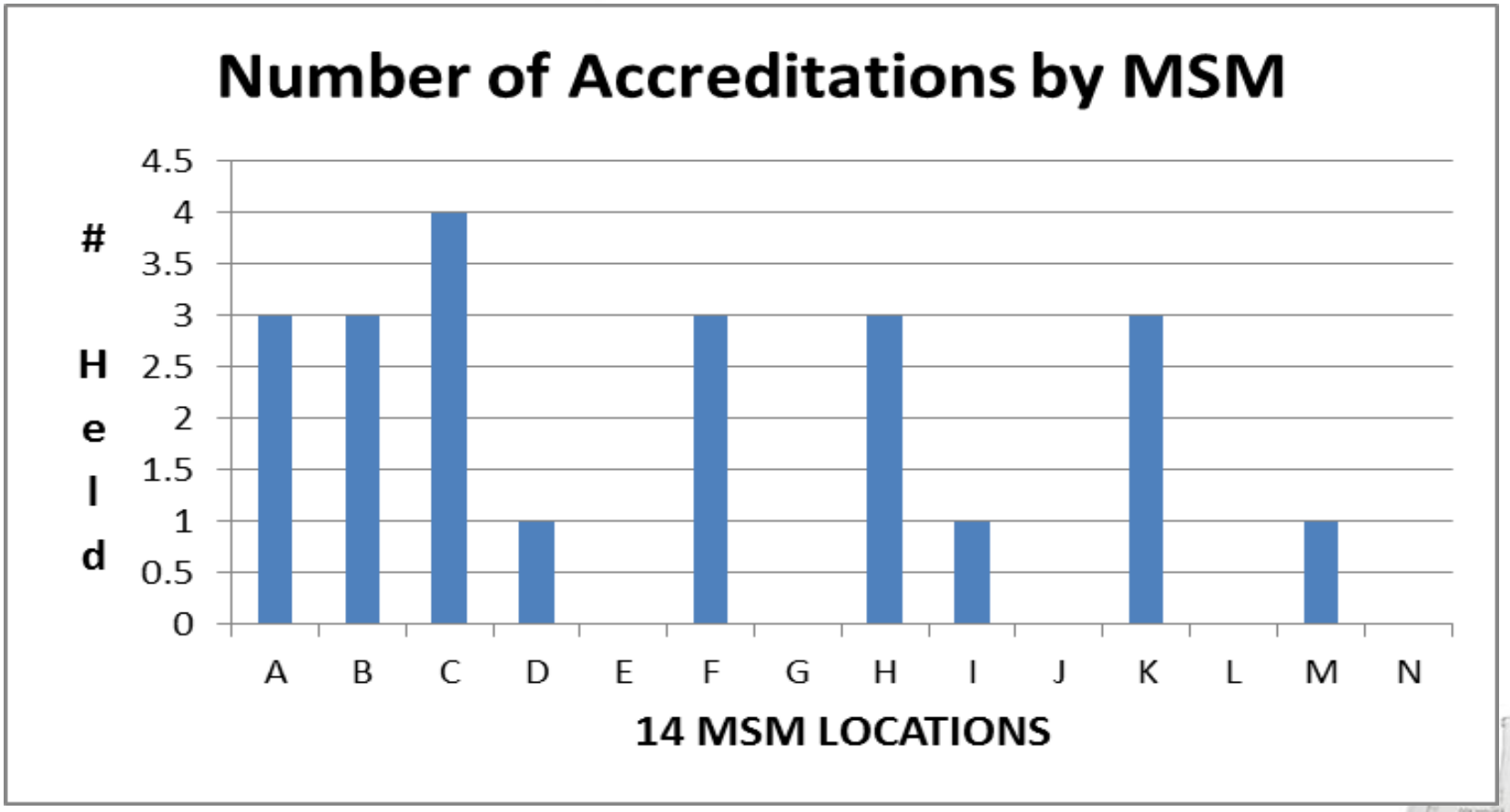
- There are no similar requirements for the MSMs (of chemicals, pesticides, etc.) from which the RMs are being produced that assess their competency to produce that starting material(SM)

- MSMs are not typically in the business of producing a product with the intent of it being used as a SM for a RM

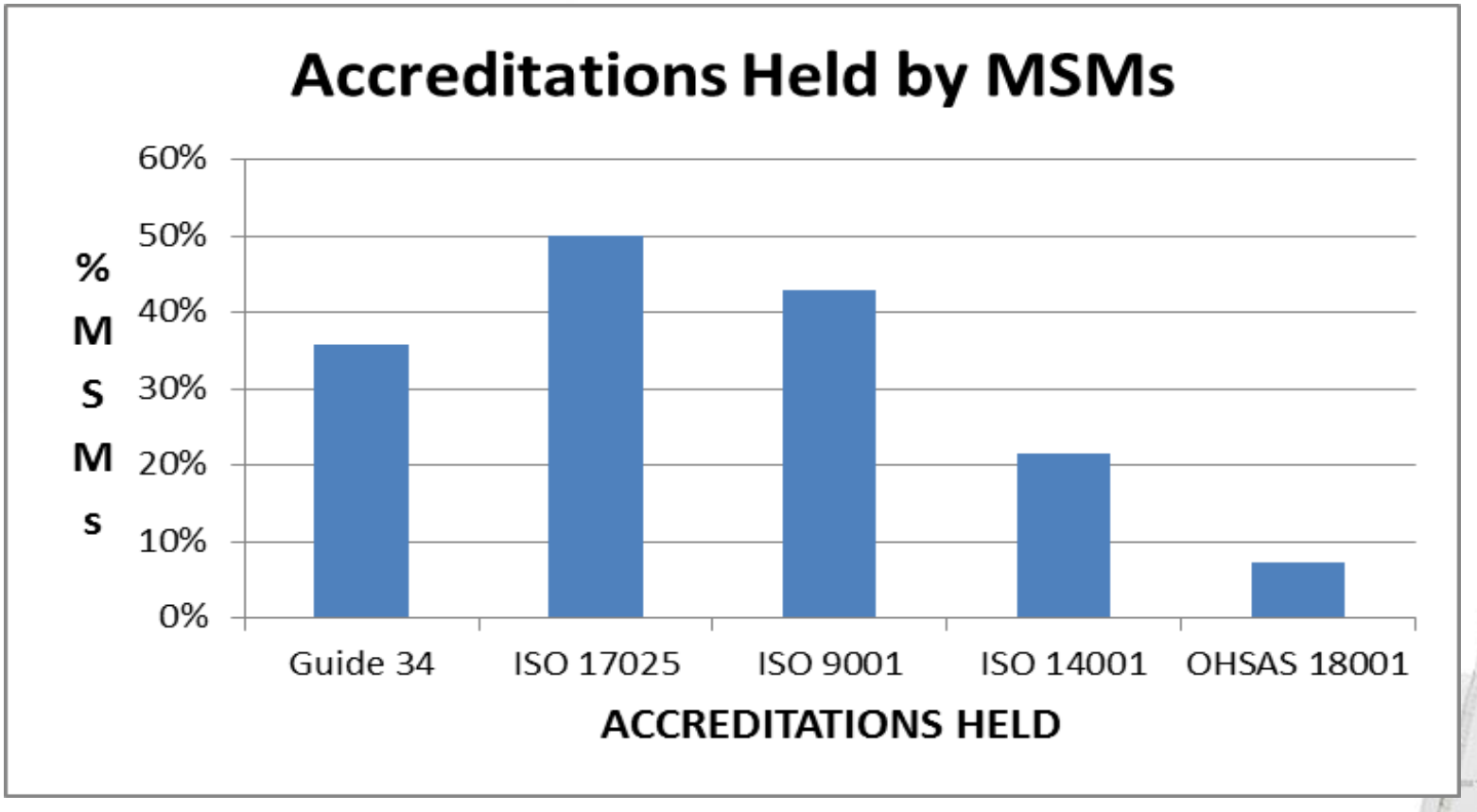
Accreditations of MSMs

Accred.	Covers	Specifically addresses chemical identity and purity
ISO 9001	Quality Management Systems	No
ISO Guide 34	Competence of Reference Material Producers	Yes
ISO 17025	Competence of Laboratories	Yes
ISO 14001	Environmental Management Systems	No
OHSAS 18001	Occupational Safety and Health	No

Accreditations of MSMs



Accreditations of MSMs



Considerations for Quantitative Disagreement Between Two RMs

- Is RM Producer Accredited?
- CRM or RM? (Custom Solution)
- Re-setting %Purity of SM based on analytical determination of impurities
  - Final concentration based on new purity vs. MSM's %purity value

Considerations for Quantitative Disagreement Between Two RMs

- Assigned expiration dates for products may vary among RMPs
- Wrong SM due to:
  - Mislabeling Error
  - Handling Error
  - Non-Specific Analytical Identification
    - Melting point, FID

Reasons for Qualitative Disagreement Between CRM and RM

- SM Manufacture Variations
  - E.g.: Toxaphene, Aroclors
- Instability
  - Artifacts, Impurities

Reasons for Disagreement Between Two RMPs

- Custom vs. Stock RMP Products
  - Are ***Custom*** RMs tested to the same QA specifications as ***Stock*** RMs?
  - Does the RMP's ISO Accreditation or Certification include their ***Custom*** RMs?
  - Varying Levels of Quality offered for Custom CRMs, or RMs
    - Level A – Gravimetric Only
    - Level B – Qualitative
    - Level C – Quantitative

Conclusions & Recommendations

- Need a better & easily understandable definition
- **Second Source Starting Materials are <u>not</u> the best solution**

A Better Definition of True Second Source RM - Proposal

The NELAC 2009 definition:

“*a standard obtained from a second manufacturer or lot if the lot can be demonstrated from the manufacturer as prepared independently from other lots”*

“prepared independently from other lots”

A Better Definition of Calibration Standard - Proposal

2015 Proposal to both PT and Chemistry Committees:

- Standards used for calibration shall be Certified Reference Material (CRM), where available. If a CRM is not available, then calibration shall be a Reference Material (RM). If a CRM and/or a RM are not available, the calibration material shall be manufactured under the requirements of ISO Guide 34.

A Better Definition of True Second Source RM - Proposal

2015 Proposal to both PT and Chemistry Committees:

Initial Calibration Verification (ICV): all initial calibrations shall be verified with a Certified Reference Material (CRM), Reference Material (RM) and/or ISO Guide 34 material as applicable. The calibration standard and the ICV standard shall be from different lots.

A Better Definition of True Second Source RM - Proposal

2015 Proposal to both PT and Chemistry Committees:

- Lot - definite amount of material produced during a single manufacturing cycle, and intended to have uniform character and quality.
- According to Guide 30(E)

Definition of True Second Source Lot Proposal - Status:

- The PT Committee accepted this proposal and has incorporated it into the new standard
- The Chemistry committee was not able to incorporate this proposal into the new standard and decided to add it to the next standard

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