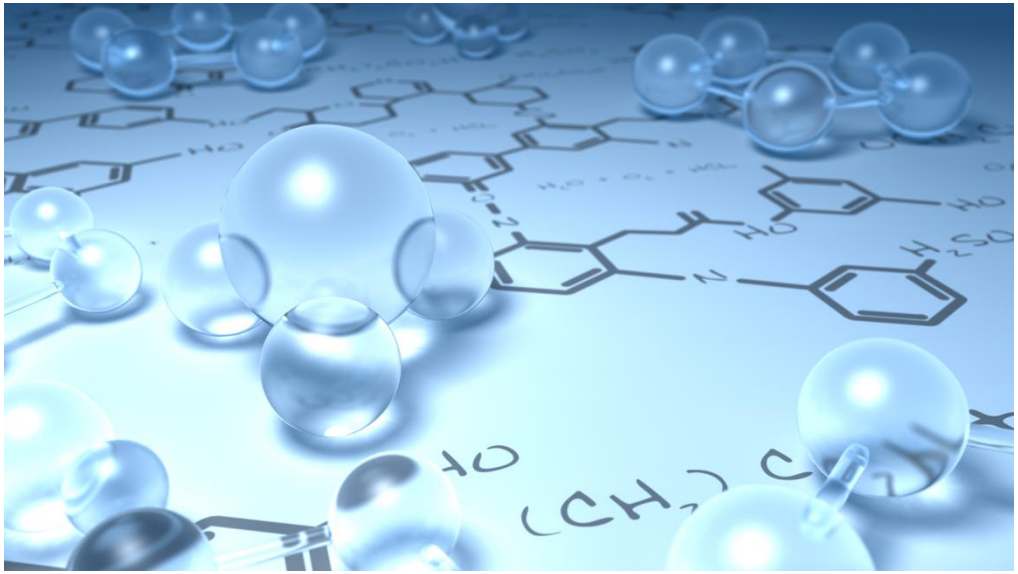
Understanding CRM Second Source and Stability



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Topics

- **Second Source Lot Reference Material (RM)**
  - Purposes & Options
  - Manufacturers of Starting Materials (MSMs)
  - Case Study
  - Conclusions & Recommendations
- **CRM Stability**

Second Source Lot RMs

Purposes of a Second Source Lot

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 Lot RMs Options:

1. Purchasing Two Lots with same Starting Material (SM) from Reference Material Producers (RMPs)

	Purchase from Same RMP	Purchase from Different RMPs
Perceived Advantages & Disadvantages 	• Better quantitative agreement between lots • Lower cost & easier to purchase • Matching lots containing same compounds • Less assurance lots are significantly different	• Less quantitative agreement between lots • More expensive & difficult to purchase • Different lots may not match exactly • Greater assurance lots are significantly different

Second Source Lot RMs Options

2. Purchasing Two Lots Made from Different Starting Materials (SMs)

	Purchase From Same or Different RMPs
Perceived Assumptions 	• Better quality assurance since they are different starting materials • More representative of a true second source
Unperceived Disadvantages	• Increased probability of error • Hard to confirm between RMPs • More expensive • Second source not available

Requirements for Manufacturers of Starting Materials (MSMs)

- **ISO 17034:**
  - …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

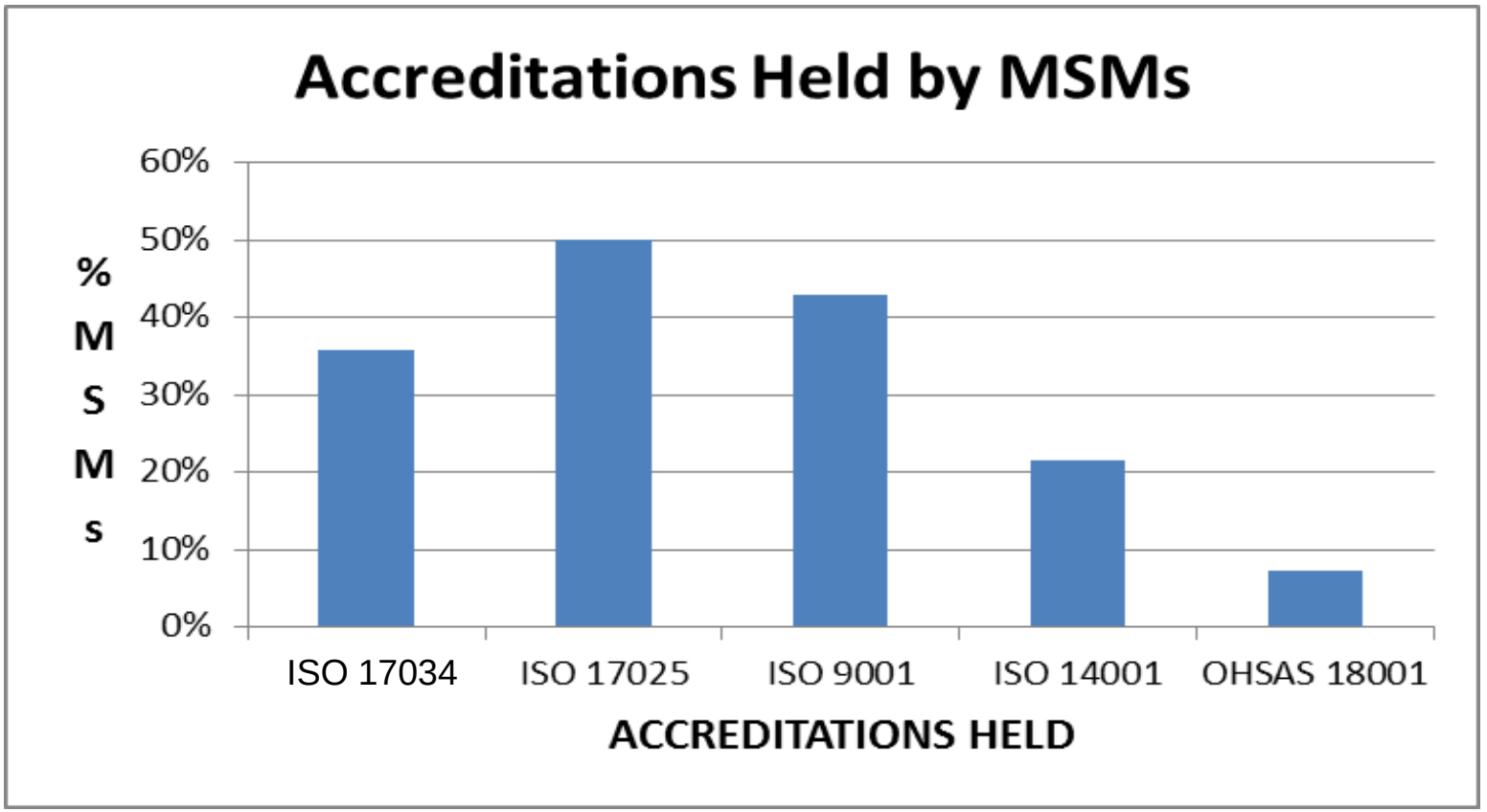
Requirements for Manufacturers of Starting Materials (MSMs)

- **ISO 17034:**
  - 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	Addresses chemical identity and purity
ISO 9001	Quality Management Systems	No
ISO 17034	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

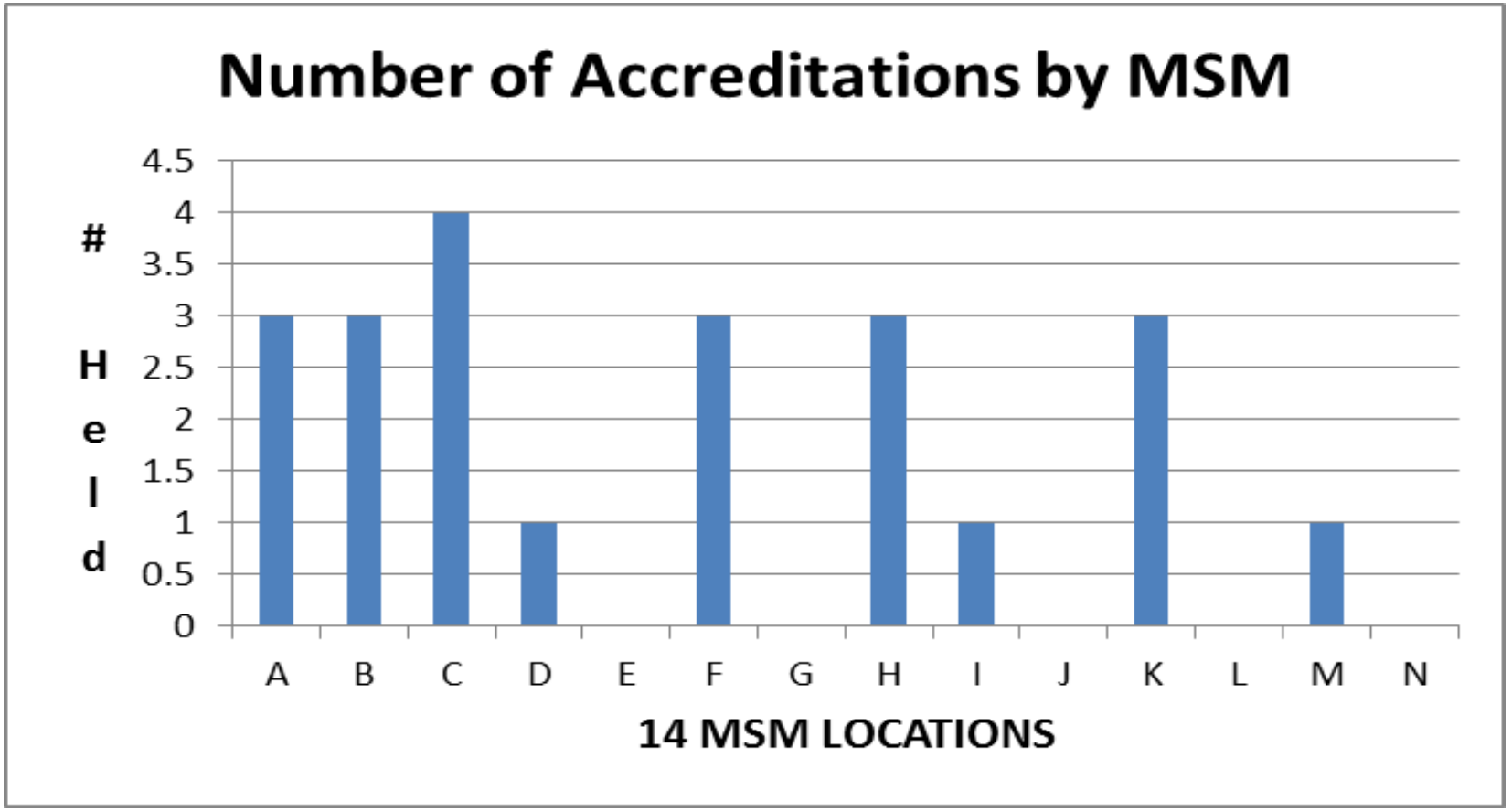
Accreditations of MSMs



Accreditations of MSMs

- 50% accredited for purity and identify of material (ISO 17034 and 17025)
- 40% accredited for Management Systems (ISO 9001)
- 20% accredited for Environmental Management (ISO 14001)
- 7% for Occupational Health (OHSAS 18001)
- **35% of 14 MSMs hold no accreditations that assess the competency to produce a SM**

Accreditations of MSMs



Second Source Lot Certified Reference Materials (CRMs): Case Study

- RESTEK created second source CRM lots of organic compound mixtures using a different SM lot from different MSMs
- EPA Methods for Volatiles, Semi-Volatiles, Pesticides & Herbicides

Second SM Sourcing Challenges

- 41 SM Challenges out of 350 Total Compounds
  - 13 Failed % Purity Criteria of 98%
  - 10 Were cost-prohibitive
  - 4 Failed Qualitative Match with Primary
  - 2 Delivery Failure (i.e. Customs, delivery time)
  - 12 No Second SM Available

- **Had to Use Single Source SM for both Lots for 22 of the 41 Compounds**

Reasons for Quantitative Disagreement Between Two RMPs

- Blunder
  - E.g., dilution error
- Poor Technique or Wrong Procedure
  - Reactivity with other compounds
  - Non-quantitative transfer (e.g., techniques for viscous liquids or gases)
  - Solubility (wrong solvent used)
- Instability - Breakdown

Reasons for Quantitative Disagreement Between Two RMPs

- Re-setting %Purity of SM based on analytical determination of impurities – final concentration based on new purity vs. MSM's %purity value
- Policy on assigning expiration dates for products may vary among RMPs

Reasons for Qualitative Disagreement Between Two RMPs

- Wrong SM
  - Mislabeling Error
  - Handling Error
  - Non-Specific Analytical Identification
    - Melting point, FID
- SM Manufacture Variations
- 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

- Understand Variations Among CRMs:
  - RMPs verification procedures for identity & % Purity of SMs
  - RMPs policies and procedures on second source CRMs vs. RMs
  - RMPs Policy on setting expiration dates
- Have a consistent definition for Second Source
- ISO 17034 does not require the use of a separate SM to create a second lot

Conclusions & Recommendations

Note: Apply ISO Guide 30(E) Definition of Lot:

- Lot - definite amount of material produced during a single manufacturing cycle, and intended to have uniform character and quality.

- Produced in single manufacturing cycle
- Intended to have uniform:
  - Character
  - Quality
- Note: Has nothing to do with the source of the material

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

CRM Stability Requirements

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

CRM Stability Requirements

- Prior information
  - Use data from related materials
  - Use published and/or readily available information
- Stability studies
  - Accelerated testing
  - Long-term testing
  - Determines the value of the contribution to the combined uncertainty for instability
  - **Ensures stability in packaged container until opened**

Thank You for Your Kind Attention

Questions?

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