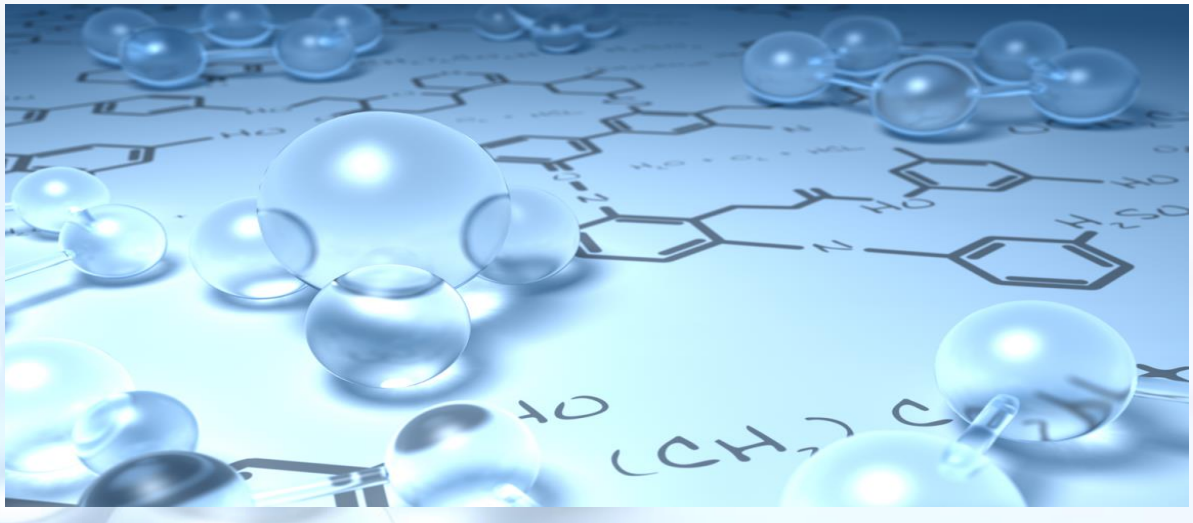
An Independently Prepared Second Source Lot Reference Material - Where Did this Come From and What Does it Really Mean?



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Presentation Content Outline

Second Source Lot Reference Material (RM)

- Purposes
- History
- Definitions & References to Use of Manufacturers of Starting Materials (SMs)
- Case Study
- Conclusions & Recommendations
- Future Work

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 History

1994	ICV / QCS appears in Methods 200.8 / 6020
1994	NELAC 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 Lot RMs History

1998 — *Benzidine? Really?* Presented at WTQA

1999 — NELAC drops 15% limit

2005 — COE 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 Lot 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 Lot RMs
Definitions

Source	Definition
EPA Method 1666, 1998	Standard solutions - Purchased as solutions or mixtures with certification to their purity, concentration, and authenticity, or prepared from materials of known purity and composition
EPA CLP, OLM04.2, Appendix E, 1999	Purchased solutions or mixtures must be verified by MS ID & purity confirmation, Chromatographic and quantitative documentation that the solution standard was QC checked

Second Source Lot RMs
Definitions

Source	Definition
ACE EM 200-1-10	An *initial calibration verification (ICV)* refers to the use of a mid-level, second-source, instrumental standard to verify the accuracy of the standards used to perform the initial calibration
FEM Glossary	The ICV is obtained from a separate source than the calibration standards, but may be from a different source from the same vendor

Second Source Lot 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 Lot RMs
References

Source	Reference to Use of
NELAC, 1997	When available, all initial calibrations shall be verified with a standard obtained from a second or different source
NELAC, 1999	All initial instrument calibrations must be verified with a standard obtained from a second source and traceable to a national standard, when available

Second Source Lot RMs

Methods Not Requiring a Definition or Use of a Second Source Lot

- ASTM
- Standard Methods
- EPA Drinking Water Manual
- EPA SW-846 Manual Organics Methods

Second Source Lot RMs

Purchasing Two Lots from Reference Material Producers (RMPs)

	Purchase from Same RMP	Purchase from Different RMPs
Perceived Advantages 	• Better Quantitative agreement between lots • Lower cost to purchase • Ease of purchase • CRMs containing same compounds for both lots	• Greater trust that systematic error did not occur • Greater trust that poor technique is not repeated • Meets auditor/QA Plan requirements Example: DoD QSM

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:

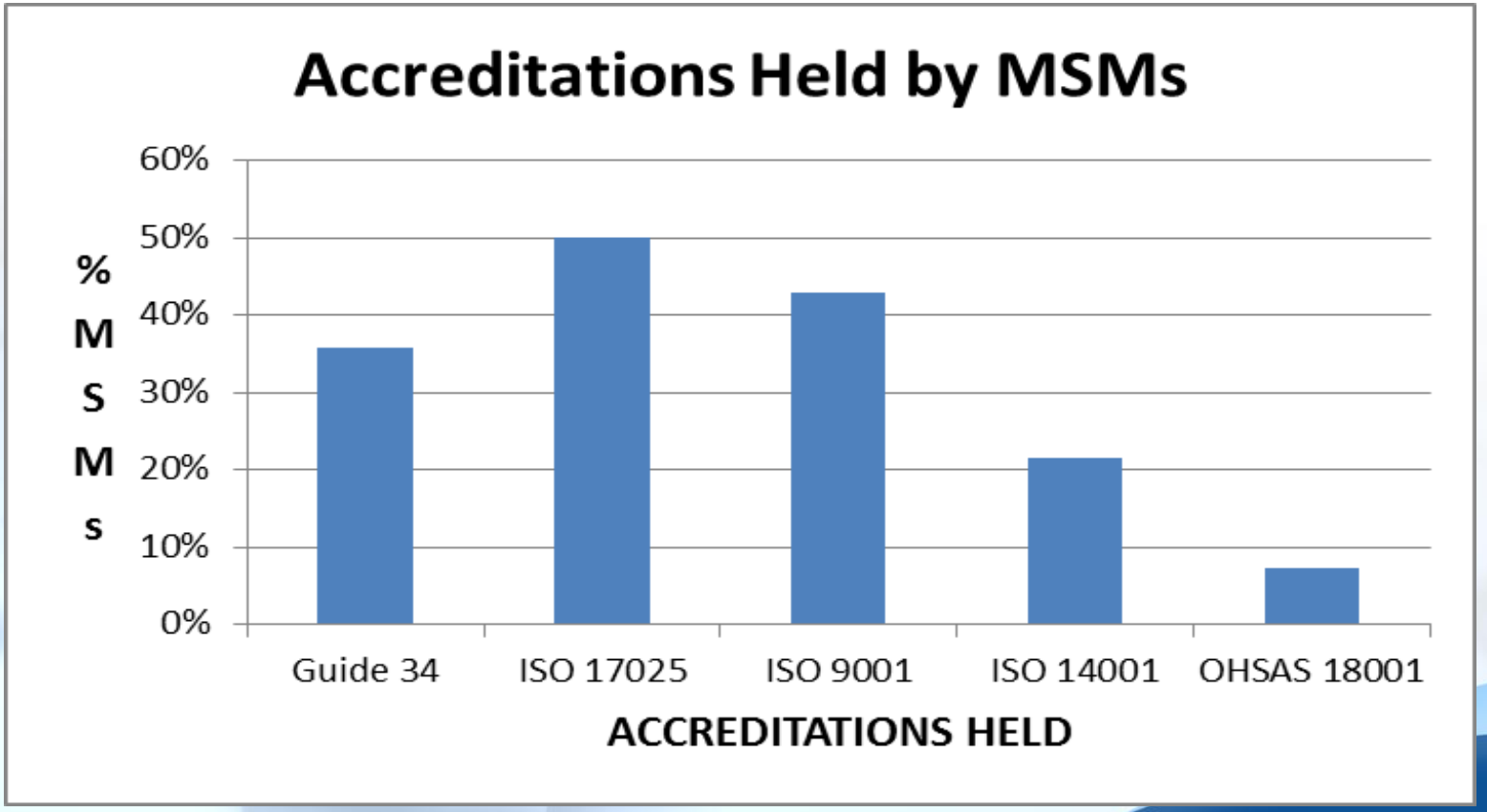
- There are no similar requirements for the MSMs (of chemicals, pesticides, etc.) from which the RMs are being produced that assess their competency to produce that starting material(SM)

- 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

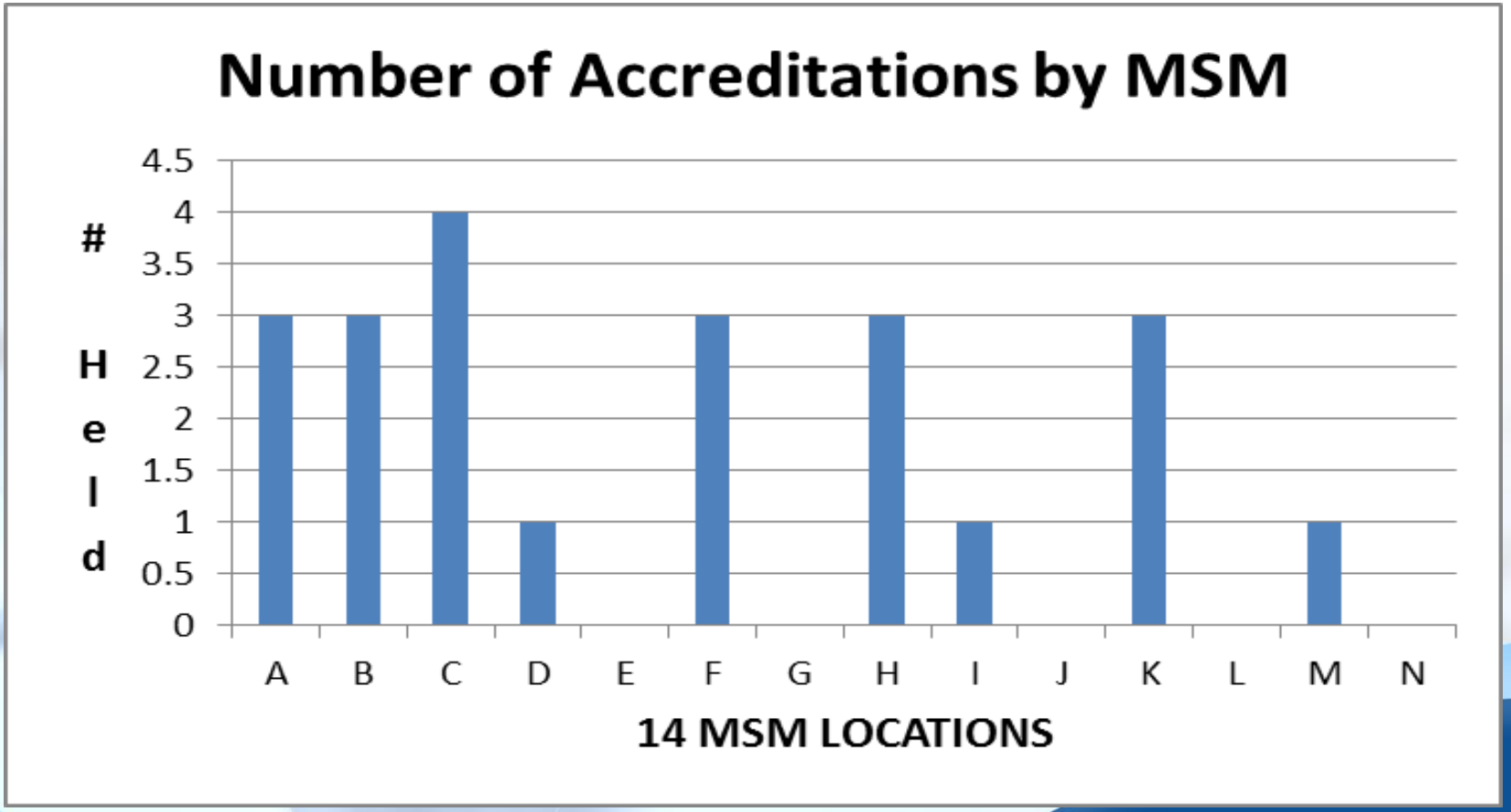
Accreditations of MSMs



Accreditations of MSMs

- 50% accredited for purity and identify of material (ISO Guide 34 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 a series of second source organic compound CRM mixtures with the intent of manufacturing an independently prepared lot using a different SM lot from different MSMs
- For EPA Methods 8260, 8270, 8081, 8082, 8141, 8151

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
  - 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 & more consistent definition
- Additional specifications are needed to ensure qualitative and quantitative accuracy of CRMs among RMPs, e.g.
  - Verification procedures for identity & % Purity
  - Validate correct concentration by independent checks
  - Policy on setting expiration dates
- Who does this?
- **Second SMs are not the best solution**

Future Work on This Topic

- Need for consistent Laboratory requirements for use of second source RMs
- Need for laboratories to validate their RMs for purity, identity and concentration based on Data Quality Objectives.
- Need for industry-standard manufacturing specifications for the manufacture of RMs

A Better Definition of True Second Source RM - Proposal

Hierarchy of Options:

Tier I: A different RM from a second RMP

Tier 2: Either Two different RMPs from same SM
or Same RMP used two different SMs

Tier 3: Two independently prepared RM lots from same RMP

(All are acceptable options)

A Better Definition of True Second Source RM - Proposal

Hierarchy of Options:

The NELAC 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"*

allows for the use of the three tiers with exception of "prepared independently from other lot"

A Better Definition of True Second Source RM - Proposal

Hierarchy of Options:

"prepared independently from other lot" is defined as:

- Prepared by a different chemist
- On a different day
- Used a different balance, or volumetric glassware

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