

CRM's and the Dilemma of the 2nd Source

Shawn Kassner, Sr Product Manager

Tim Miller, Sr Organic Chemist

Phenova, A Phenomenex Company

What are we talking about?

- ISO 17025 requirements for labs and CRM providers, are they the same?
- What are the best practices of CRM Providers?
- How does this impact laboratories?
- What is the reality/status of the 2nd source requirements today?

ISO 17025 requirements for labs
and CRM providers, are they the
same?

ISO 17025 Second Source Requirement

- **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 and calibrations undertaken. The resulting data shall be recorded in such a way that trends are detectable and, where practicable, statistical techniques shall be applied to the reviewing of the results. This monitoring shall be planned and reviewed and may include, but not be limited to, the following:
 - a) regular use of certified reference materials and/or internal quality control using secondary reference materials;

Historical 2nd Source Interpretation

- Independent raw material
 - Independent reference material vendors
 - Independent manufacturing lots
 - Independent all of the above!
-
- For all ISO 17025 accreditations –
Laboratories, CRM Providers, etc!

What are the best practices of CRM Providers?

What is a CRM?

- **ISO Guide 30**
- **2.2 certified reference material CRM** - reference material characterized by a metrologically valid procedure for one or more specified properties, accompanied by a certificate that provides the value of the specified property, its associated uncertainty, and a statement of metrological traceability

NOTE 1 The concept of value includes qualitative attributes such as identity or sequence. Uncertainties for such attributes may be expressed as probabilities.

NOTE 2 Metrologically valid procedures for the production and certification of reference materials are given in, among others, ISO Guides 34 and 35.

NOTE 3 ISO Guide 31 gives guidance on the contents of certificates.

Best Practices – What do we do?

- Manufacturing and analytical requirements are found in ISO Guides 34 and 35.
- ISO Guide 31 tells us what has to be CRM Certificates of Analysis.
- But what do we really do....

Manufacturing Best Practices

- All raw materials are tested for purity and identity.
- Impurities are identified and purity values are accounted for in manufacturing.
- All balances are NIST calibrated on a schedule – usually annually.
- All glassware is Class A grade and calibrated.

WHY?

- Calibrated balances and glassware allow us to:
 - Calculate manufacturing uncertainties
 - Ensure the accuracy of our measurements
 - Ensure the consistency of our measurements
 - Ensure the quality of our measurements

Verification Best Practices

- For ISO 17025 and Guide 34 accredited providers
 - Validated analytical methods
 - Calculated method repeatability
 - Calibrate with independent CRMs,
 - Typically with 2nd and 3rd sources.
 - Verify accuracy of Certified Values.
 - Verify the homogeneity of each lot.

WHY?

- Validated methods and method repeatability allow us to calculate analytical uncertainties.
- Using independent CRM, 2nd and 3rd sources allows us to:
 - Ensure that certified values are independently verified
 - Benchmark across the industry

TOTALLY WHY?

- Each step in the process of the CRM provider involves calibrated equipment and calculated uncertainty.
- All of these uncertainties are used to calculate the expanded uncertainty on the Certificate of Analysis.

How does this impact
laboratories?

Laboratory Requirement

- Must also meet the ISO 17025 and TNI second source requirements.
- a) regular use of certified reference materials and/or internal quality control using secondary reference materials;
- The requirements have been inconsistently interpreted and applied.

Laboratory Impact

- Laboratories are purchasing CRM's that have uncertainty values calculated at each step of manufacturing and verification.
- Each CRM has been evaluated to multiple sources.

Laboratory Impact

- These steps ensure that laboratories using CRMs can rely on the fact that a single manufacturing event or CRM lot has its own manufacturing and analytical pedigree.

What is the reality/status of
the 2nd source today?

Historical 2nd Source Interpretation

- Independent raw material
 - Independent reference material vendors
 - Independent manufacturing events
 - Independent all of the above!
-
- For all ISO 17025 accreditations –
Laboratories, CRM Providers, etc!

Raw Materials Reality

- Many raw materials are only available from a single primary source.
 - PCBs, PCB congeners, PAHs
- More raw materials are moving in this direction.
- Neat chemical providers are consolidating their inventories and re-focusing their core business.

Reality - Reference Material Vendors

- Economics
 - Many laboratories and laboratory networks have business agreements with a single vendor.
 - Consolidating vendors has become a common business practice.
- Custom standards have become common for many laboratories
- Analyte offerings vary from vendor to vendor
- Not all vendors offer the same suite of CRMs

Independent Manufacturing Lots

- YES!
- Each vendor does have the ability to offer multiple lots of a CRM.
- **Lot** – a definite amount of a material produced during a single manufacturing cycle and intended to have uniform character and quality. (per *ISO/IEC 9001:2000*)

Independent Manufacturing Lots

- Each lot having its own historical manufacturing and analytical pedigree
- Each lot has its own uncertainties; manufacturing, analytical, and expanded.
- Availability of a second lot allows laboratories to meet the ISO 17025 requirements.

New Definitions

- Individual lots can be seen as separate sources.
- Starting to be adopted throughout the industry.
- TNI - the definition is being added to Quality Systems for the 2015 TNI standards.

Questions?

Thanks!

Shawn Kassner
Phenova, A Phenomenex Company

shawnk@phenova.com

866-942-2978