

# How Certified Reference Materials Can Help Laboratories Meet Regulatory Requirements

As regulatory standards continue to increase, additional responsibility is being placed on laboratories to ensure the quality and safety of finished products. Now more than ever, traceability is a major concern. Laboratories are required to provide evidence that the reference materials being used for method validation and process controls are fit-for-purpose, homogenous, and stable. Certified reference materials (CRMs) are designed to meet these stringent standards.

## What Is a CRM?

ISO Guide 34 defines a reference material as material that is "sufficiently homogenous and stable with respect to one or more specified properties, which has been established to be fit for its intended use in a measurement process. Properties can be quantitative or qualitative (e.g., identity of substances or species)." A CRM is different than a reference material in that it is accompanied by a certificate, has metrological traceability, and each property value has an uncertainty value assigned to it. Once property values are assigned to a CRM, the values are "stored" by the CRM and then transferred when the CRM itself is transported from one location to another.

In order to become a CRM producer, the producer's methods must meet the requirements of ISO Guide 34 *General Requirements for the Competence of Material*

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*Producers.* To receive ISO Guide 34 accreditation, the producer must demonstrate that they are competent to supply CRM.

Many accrediting bodies require companies to use CRMs in their processes. For example, the American Association for Laboratory Accreditation (A2LA) will begin enforcement of ISO 17025:2005 Section 5.6.3 beginning January 1, 2012. ISO 17025:2005 Section 5.6.3 states that "Reference materials shall, where possible, be traceable to SI units of measurement or to certified reference materials." Companies not using CRMs, if available, or not providing good justification for not using CRMs, will be cited for this nonconformance starting January 1, 2012.

## Regulatory Requirements

A major regulatory change that will impact companies in the food industry is the recent amendment to the Food Drug and Cosmetic Act titled the Food Safety Modernization Act. This Act was signed into law by President Obama on January 4, 2011, and focuses on food

safety by preventing outbreaks instead of reacting to outbreaks. Food manufacturers will need to implement preventive controls to stop identified hazards from occurring. Implementation of the Act will happen over a 2-year period; however the industry must be prepared for the changes in advance. To be in compliance with the Act, food manufacturers must:

- Identify hazards
- Implement controls to prevent hazards
- Monitor controls
- Maintain records of monitoring
- Correct problems that arise

Companies will need to validate detection methods, controls, and monitoring of hazards in foods. These hazards may include allergens, bacteria, or other contaminants. In addition, the FDA will require certain testing to be done by accredited laboratories.

The FDA will be increasing its inspection of food producers. High-risk producers can expect to be inspected within the next 5 years. Following the initial

inspection, the FDA plans to revisit high-risk facilities every 3 years.

With the FDA's focus on traceability, validations, inspections, and accreditations, the use of CRMs becomes increasingly important to the laboratory's evidence of compliance to the FDA regulation.

## Advantages and Uses

As technology improves over time, the ability and need to measure more precisely and accurately increases as well. This drives the need for better reference materials to be used in testing and calibration. CRMs provide metrological traceability and known uncertainty for the property values of the material. CRMs can ensure reliable measurements for users. Traceability is provided via a certificate that documents the property values, the uncertainty, and the authoritative issuing body.

Users of CRMs are responsible for determining if the CRM is appropriate for their intended use. The user must follow all labeling instructions provided by the

CRM producer. This includes handling and storage, shelf life, and instructions for use. Failure to follow all CRM labeling could invalidate testing results for the user.

ISO 17025 states, "The laboratory shall have quality control procedures for monitoring the validity of tests and calibrations undertaken. This monitoring shall be planned and reviewed and may include...regular use of certified reference material and/or internal quality control using secondary reference materials."

Common uses of CRMs include:

**Method validation.** A laboratory or factory may need to validate the methods or equipment used for measuring or detecting a substance. A CRM may be used to validate the measurement method or the ability to detect a substance.

**Method verification.** A laboratory may need to check the process at any time to ensure the process is continuing to measure and detect as initially validated. For example, a CRM can be used to check a process and determine if a nonconformance has occurred and troubleshooting is necessary.

**Calibration.** CRMs that

are a pure substance can be utilized for calibration of equipment, which is intended to detect or measure that substance, or the CRM can be used as an independent check of the calibration.

**Method monitoring or process control.** CRMs can be used continuously to provide evidence that processes are stable and continue to measure and detect as required.

**Training.** A laboratory may use CRMs to train and/or evaluate operators by using a substance that has a known identity and property values.

#### CRM in Microbiology

Detection and control of microorganisms in food processing applications may require the use of CRMs. There are currently a limited number of options for microbiological CRMs. When choosing a microbiological CRM producer, one should look for the following attributes:

- **Stability and shelf life.** Make sure the CRM meets one's specific needs.
- **Handling and storage requirements.** Consider the ease-of-use and preparation time for all available options.

- **Traceability.** Using a microorganism with known property values allows it to be distinguished from other strains of the same species that may be found in the user's laboratory or products.

#### Obtaining CRM

A number of CRM databases are available that can assist in finding a CRM to meet an individual's unique needs. The AOAC Technical Division on Reference Materials (TDRM) is establishing a database to assist users in finding CRMs. In addition, TDRM offers a Reference Material/Method Matching list. Anyone can submit the reference material methods to be considered for inclusion on the AOAC website. AOAC has a documented process for reviewing and recommending publications.

Other databases available for finding CRMs include the COMAR International database for CRM, the Virtual Institute for Reference Materials (VIRM), and European Reference Materials (ERM).

If CRMs are not available, determine if another reference material is available

that will meet the testing needs. In *Policy on Reference Material Traceability for Life Sciences Testing Laboratories*, A2LA outlines four categories of reference materials as alternatives if CRMs are not available.

Other options include a proficiency testing program, which allows one to compare results against results from other laboratories. Care must be taken when utilizing a proficiency program as there may be method bias from the different laboratories. In addition, material used in other laboratories may not be homogenous or stable.

Spiking is another option to consider for method validation if CRMs are not available. Spiking involves taking an actual sample and injecting a known amount of the material to be measured or identified. This method does not provide traceability but can demonstrate a laboratory's ability to measure or detect a given substance.

In-house reference materials may also be considered if sufficient testing has been conducted to show the material is homogenous and stable.

#### Conclusion

CRMs have become increasingly important to the laboratory's evidence of compliance to new FDA regulation. In addition, many accrediting bodies require companies to use CRMs in their processes to provide traceability. The use of CRMs plays an integral role in meeting traceability requirements for regulatory standards. ■

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