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Analytical Products

Application Note

Identifying Accurate Reference Materials For Water-Testing Confidence

Going through the motions of water sample testing for regulatory reporting requirements is only half the battle. It is also important that water operators use appropriately qualified reference materials and procedures to ensure the accuracy and reliability of their results. Here are some insights into reference material evaluation that can generate the highest confidence in water testing results.

The Essence Of Reference Materials

Testing is the comparison of an unknown sample with something that is known — that 'known' sample being a reference material. Accurate reference materials are important as a means of instrument calibration, method verification, validation, or monitoring. In drinking water and wastewater testing, properly calibrated instrumentation is critical for confirming the properties or measured values of various analytes in a captured sample or continuous flow of water to support compliance with regulatory reporting programs **(Figure 1).**

Levels Of Confidence In Reference Material Qualification

Not all reference materials are manufactured with the same degree of qualification or documentation. The differences are typically reflected in their pricing, which is why a low-cost reference is not necessarily a 'bargain' for critical analysis. An appropriately documented reference standard will assure the quality of the product being tested, avoid the need for repeat analyses, and save cost and time in daily lab work.

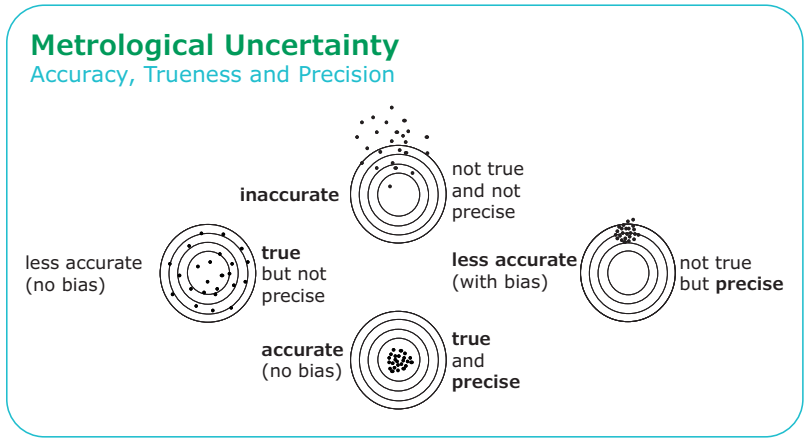

Figure 1. Choosing reference materials with consistent, traceable characteristics will mark the truest "bulls eye" to gauge the reliability of your water measurements.

MilliporeSigma

Metrological traceability and the different quality grades of standards, reference materials and certified reference materials

Metrological traceability is an important concept in the world of reference materials. A fundamental term in metrological traceability is the SI unit of measurement. The International System of Units, or SI, defines the seven units of measure as the basic set from which all other SI units can be derived. The two most common SI units of measure for traceability of reference materials are kilogram and mole.

Metrological traceability means measurements can be meaningfully compared, across difference places, at different times, by different people, using different equipment. The measurement result must be related to a reference through a documented and unbroken chain of calibrations, tracing back to the SI unit of measurement.

ISO 17034 and quality grades of standards, reference materials and certified reference materials

National Metrology Standard (NIST, JRC, NMI)
Compendial Standard (USP, EP, BP, JP, IP)*
- Issued by an authorized body
- Considered to provide the highest level of accuracy & traceability

Certified Reference Material (CRM) (ISO 17034, 17025)
- Considered to provide the highest level of accuracy, uncertainty, and traceability to an SI unit of measurement
- Manufactured by an accredited Reference Material Producer

Reference Material (RM) (ISO 17034)
- Fulfilling ISO requirements which are less demanding than for CRMs
- Manufactured by an accredited Reference Material Producer

Analytical Standard (ISO 9001)
- Certificate of Analysis available
- Level of certification varies

Reagent Grade / Research Chemical
- May come with a Certificate of Analysis
- Are not characterised for use as reference materials

Figure 2. The Hierarchy of Reference Materials - What are the Different Types?

The reference material hierarchy includes five major quality grades, from national metrology and other primary standards to Certified Reference Materials (CRMs), Reference Materials (RMs), Analytical Standards, and research grade or research chemicals. Level of certification and traceability requirements increase for each higher level. Where national governments give standardization to the top level, specific ISO guidelines provide standardization for CRMs and RMs. These ISO requirements include ISO 17034, ISO/IEC 17025 and ISO Guide 31.

Reference material producers must meet these ISO requirements to manufacture CRMs or RMs. For both of these quality grades, Certificates of Analysis must be provided, and the information contained within is defined by the aforementioned ISO guidelines. The quality specifications for the last two levels are defined by each individual producer rather than by a national government or ISO accreditations specific to CRMs and RMs.

*USP: U.S. Pharmacopeia
EP: European Pharmacopoeia
BP: British Pharmacopoeia
JP: Japanese Pharmacopoeia
IP: Indian Pharmacopoeia

Certified Reference Materials & ISO 17025:2017

Selection of Grades and Best Fit for Purpose

Type of Test	CRM	RM
Instrument qualification/ Calibration	●	○
Routine calibration/ System suitability	●	●
Method validation	●	○
Identity	●	●
Content or assay	●	●
Stability assessment /	●	●
Internal Quality Control	●	●
Regulatory / Accreditation	●	●

Fit for purpose decisions in standard selection can depend on several factors, including regulatory requirements, availability, type of testing application, level of accuracy & sample matrix

Figure 2. Choosing an appropriate grade of reference material depends on the purpose and the criticality of the application.

The Value Of Reference Materials In Metrology

Water industry professionals do not want to be, nor should they need to be, experts in reference material verification. They should, however, at least be familiar with the realities of how such verifications are generated, in order to protect their own interests related to water-testing and compliance-reporting responsibilities. Metrological traceability, as defined by the International Vocabulary of Metrology (VIM), is the "property of a measurement result whereby the result can be related to a reference through a documented unbroken chain of calibrations, each contributing to the measurement uncertainty." Such traceability requires a well-established calibration hierarchy that enables meaningful comparisons among measurements, even when they are made at different times and different places, by different people, using different equipment. Each influence should be independently, metrologically traceable, commensurate with its relative contribution to the overall qualitative or quantitative measurement.

A real-world example of consistently meaningful results in potable water applications would be ensuring an appropriate chlorine residual throughout the distribution system for the purpose of preventing water-borne illnesses. A key wastewater treatment example would be ensuring treatment to the level of Clean Water Act requirements for effluent.

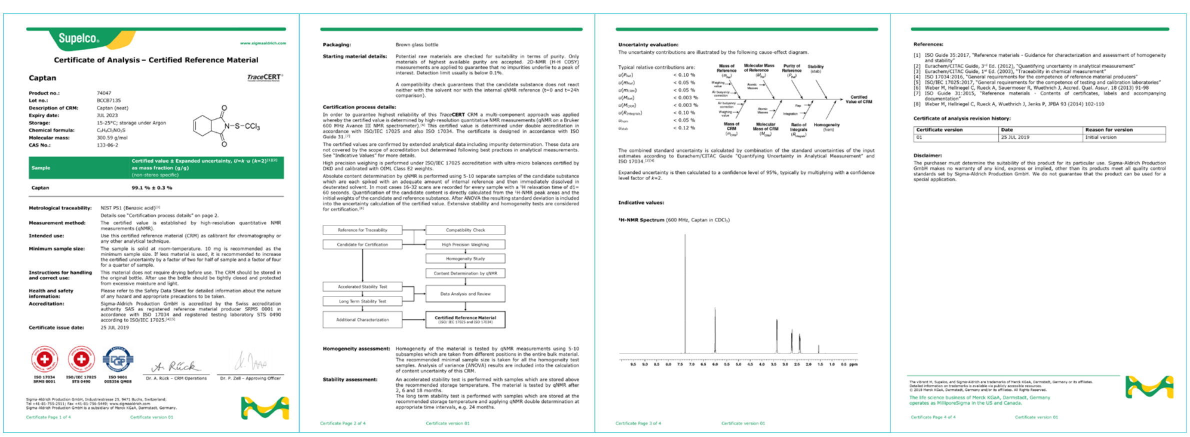

Figure 3. Whatever the grade of reference material, COAs that provide the greatest insight into critical considerations of traceability, uncertainty, and long-term stability can help to differentiate one source from another.

Key Factors To Look For On A Reference Material COA

When evaluating a reference material's certificate of analysis (COA), look for documentation of these critical considerations:

- Content Identity/Purity/Potency. A certified reference material should be well characterized for both identity and purity content. For identity, the best techniques are nuclear magnetic resonance (NMR) spectrometry or mass spectrometry. For the quantification of the mass fraction/content or potency, several techniques are applicable — single techniques (such as titration, quantitative NMR, and other types of spectrometry) or a mass-balance approach that uses multiple techniques, not chromatographic purity alone, to identify impurities.

  In addition to certified values, ISO 17034 also requires that the uncertainties associated with every step of the analysis be calculated and shown on the COA. Using a bottom-up approach (**Figure 4**) that calculates the uncertainty for each factor in the process, then adds those uncertainties, provides greater confidence in the reliability of a measurement.

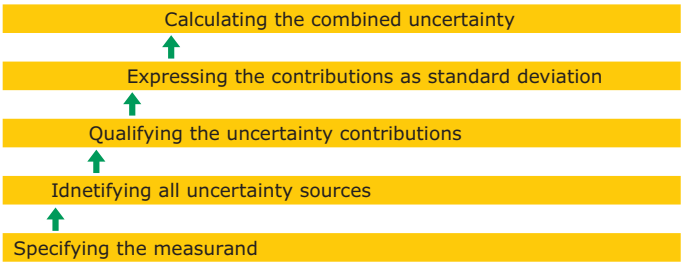

Figure 4. Uncertainty is a cumulative calculation based on a step-by-step approach to classifying and quantifying each potential point of variability in the final reference-material compound.

- **Traceability.** Always look for reference materials directly traceable to primary reference materials, issued by National Metrological Institutes.
- **Stability.** Stability studies are performed according to ISO Guide 35 and should include short-term and longterm studies at storage and elevated temperatures to ensure a reliable transportation temperature and expiry date. The uncertainty of stability refers to the two different uncertainty components – possible degradation during long-term storage and short-term storage. Be aware that stability testing that is less vigorous is also less costly, which can entice users to choose a cheaper (i.e., less rigorously tested) reference material.
- **Consistency.** Comparing lot-to-lot consistency builds confidence in the accuracy and repeatability of testing.
- **Homogeneity.** Look for excellent homogeneity — certified to ISO Guide 35 standards — across multiple vials or ampules in a batch. Ideally, the analysis of variance (ANOVA) across the whole dataset will show that the individual range of values for each sampled vial will overlap with some point of the range for every other sampled vial.

Even within a chosen grade level, not all COAs provide equal assurances. That is why it is important to inquire about the traceability of information on the COA. Improperly prepared or insufficiently documented reference materials can lead to false-positive results, false-negative results, or inaccurately quantified values.

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