Reagecon

"Delivering The Correct Result..."

Standards

A REAGECON GUIDE

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1.0 Standards

1.1 Introduction

One of the key factors affecting laboratories' capabilities to produce reliable test data is the availability of standard materials with property values that can be relied upon by their users.
The quality of a result is dependent on the quality of standards used to validate a method, or calibrate an analytical instrument. Every day, standards are used to calibrate instruments, or validate test methods, e.g. pH meters, Conductivity Systems, Auto-titrators or Karl Fisher Titrators,
If the standard is not accurate, this inaccuracy will be reflected in the test result.

"No matter how skilled the analysts or how sophisticated the analytical technique used, if the calibration of the system is in error, the analytical result will always be wrong" B. Brookman, Laboratory of The Government Chemist

1.2 Definitions

The ISO definition of a reference material (standard) is: "A material or substance one or more properties of which are sufficiently well established to be used for the calibration of an apparatus, the assessment of a measurement method, or for assigning values to materials."

Traceability of Chemical Composition Standards

SI Units

Primary Reference Standards

Certified Reference Material (CRM)

Secondary Standards

Working Standard

In the science of chemical measurements comparability of results is a primary requirement, and traceability is a tool to help achieve comparability. The term traceable is defined by ISO as the 'property of the result of a measurement or the value of a standard whereby it can be related with a stated uncertainty, to stated references, usually national or international standard, through an unbroken chain of comparisons'.

The ultimate international reference points are the Systeme International d'Unites (S.I. units). There are seven base S.I. units, these are the Meter, Second, Kilogram, Ampere, Kelvin, Candela, and Mole. These S.I. units are maintained by The International Bureau of Weights and Measures (BIPM).

The role of national laboratories, e.g. NIST, LGC, BCR, is to provide traceability to the SI units through standards and methods

A **Primary Reference Material** is one whose value is accepted without reference to other standards of the same quality. The standard must be pure, stable, have high equivalent, be soluble under the conditions in which it is to be used, react with the standard solution instantaneously and stoichiometrically.

In practice, an ideal primary standard is difficult to obtain, and a compromise between the above ideal requirements is usually necessary.

Primary Standards are produced in limited quantity, are expensive, but offer the highest accuracy.

A **Certified Reference Material** (CRM) is a reference material one or more of whose property values are certified by a technically valid procedure, accompanied by a certificate or other documentation which is issued by a certifying body. This certificate will provide detailed information on the analyte values, their associated uncertainties, methods of analysis, and traceability. Their production and certification is expensive, therefore they are not used for routine analysis.

Producers of CRM's include

- National Institute of Standards and Technology NIST (USA)*
- Commission of the European Communities BCR (Belgium)
- Laboratory of the Government Chemist LGC (UK)
- National Institute for Environmental Studies NIES (Japan)
- Laboratoire National d'Essais LNE, (France)

*CRMs are also referred to as Standard Reference Materials SRMs.

A **Secondary Standard** is a material or substance one or more properties of which are sufficiently well established to be used for the calibration of an apparatus, the assessment of measurement method, or for assigning values to materials. A secondary standard is traceable to a primary standard, or a CRM.

A **Working Standard** is used as an alternative to a secondary standard. It may be characterised by either primary or secondary methods. Typical applications would include internal quality control, and instrument performance checks. Typically it might be obtained by dilution of a Secondary Standard.

1.3 Criteria of all Standard Materials

- Stability
  The ideal standard material should be physically and chemically stable. Most materials change due to evaporation, or chemical reaction initiated by temperature, light, air, or humidity. Precipitation, bacteriological activity, and interaction with storage container may lead to instability. The producer of the standard should carry out extensive stability studies, and assign expiry dates based on these studies.

- Homogeneity
  The Standard must be homogeneous; i.e. the difference between representative sample measurements must be less than the overall uncertainty limits of the measurement.
  A material can only be said to be homogeneous at or above the weight / volume of the representative samples analysed.

- Accuracy of Reference Value
  Accuracy of the value / property of a standard material may be defined as the closeness of the agreement between the reported value and the true value of the analyte

- Uncertainty of Reference Value
  The reference value of the material must be determined with rigorous estimates of uncertainty, the value being as close as possible to the true value.
  Uncertainty of Measurement is defined as the parameter associated with the result of a measurement that characterises the dispersion of the values that could reasonably be attributed to the measurand.

1.4 Application of Standards

Standards provide vital ingredients in every day laboratory analysis; these include

- Instrument calibration, ensuring the analytical device is giving a correct result over the analyte range of interest
- Validation of test methods
- Analytical quality control
- Production of working standards
- Establish traceability
- Check equivalence of methods
- Comparability

The use of Standards allows

- the analyst to demonstrate the validity of an analysis
- the concept of measurement traceability to be realised
- the comparability of analytical data between laboratories to be improved

1.5 Production of Secondary Standard Materials

Standards should be prepared in such a way as to ensure that its final form is fit for its intended use and that it is sufficiently stable. The procedures for processing the standard need to be carefully chosen in order to achieve the required homogeneity and maximise the materials shelf life. Typical operations include drying, grinding, sieving, filtering, and mixing. Care must be taken in selecting a suitable processing procedure in order to prevent any change or degradation in the form or concentration of the analytes of interest.

The key steps in the production of Secondary Standards include

- Determine the role of the Standard
- identify accuracy required
- matrix.

- Select suitable raw materials
- high purity
- composition accurately known, preferably traceable.

- Select suitable production equipment
- high specification
- calibrated with appropriate standards
- must not cause contamination

- Production of Bulk material
- prepared in accordance to specific Standard Operating Procedures (SOPs)
- quality controlled environment
- trained operating staff.

- Testing
- finished product is tested using validated procedures, ideally using an accredited procedure
- assign a value to the standards, with a known level of uncertainty
- assessment of homogeneity
- assessment of stability of material
- trained personnel.

- Filling
- controlled environment
- packed into appropriate containers that allow safe handling, & shipping of the product
- select packaging materials that do not cause contamination

- Labelling

Information contained on the label must include

- product description
- product number
- reference or nominal value
- unique lot number

- expiry date
- pack size
- show traceability
- storage conditions
- display hazard symbols, with the relevant R (indication of danger) and S (nature of special risks) sentences.

When preparing a Secondary Standard it is important to ensure that the target value of final product is

- Accurate
- Precise (batch to batch)
- Traceable
- Stable.

To provide a secondary standard that is proven to exhibit all of the above properties requires

- high specification instrumentation
- calibration using primary standards
- method validation
- controlled environments
- trained personnel
- and a substantial amount of time.

The production and testing of Secondary Standards requires extensive resources, as indicated above.

1.6 Certification of Secondary Standards

As the reported test results forms the basis for the 'certificate of analysis' of the standard, the testing procedure is critical to the reported value.

All tests must be carried out using Validated methods.

Such methods must be technically valid, i.e.

- have a valid and well described practical foundation,
- have been experimentally evaluated so that reported results have negligible systematic errors,
- have a high level of precision,
- have high reliability,

♦ Where possible a primary method should be used, i.e.

- titrimetry
- gravimetry
- coulmetry
- depression of freezing point
- IDMS.

Sources of Uncertainty during analysis include

♦ Sample Handling

- sampling technique

- accuracy of sampling device (e.g. pipette)
- precision of sampling technique
- homogeneity of sample
- sample pre-treatment, if required.

♦ Test Instrumentation & Apparatus
- calibration of instrumentation
- accuracy of calibration standards
- readability of output reading

♦ Condition / Control of Environment
- accuracy of equipment used to monitor environment (e.g. temperature)
- calibration of monitoring device
- readability of monitoring device

♦ Method Validation
- Analyst
- reproducibility
- training.

The uncertainty associated with each step of the testing procedure should be quantified.

1.7 Stability

The stability of a standard material is defined as its ability to maintain its property / value over a specified period of time.

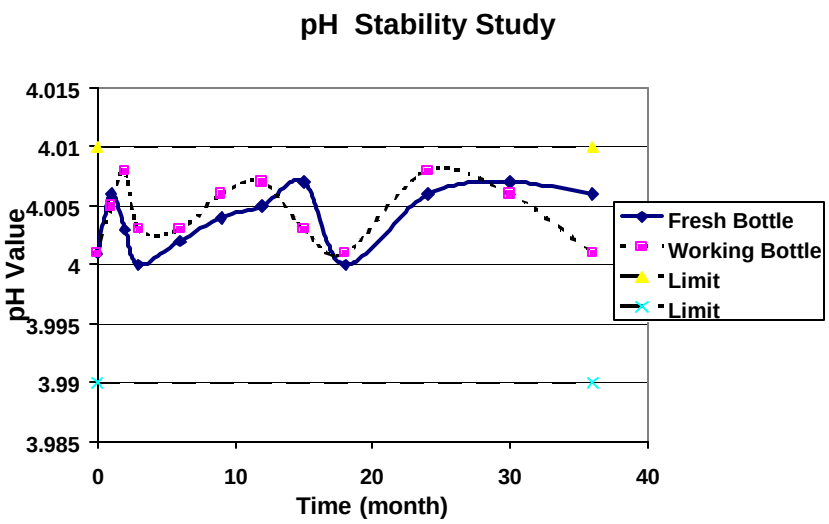
The aim of stability testing is to determine whether the standard maintains its reference value from the time of production to time of use. The frequency of stability testing depends on the risk of any change in reference value with time.

Resulting from a well defined stability trial one should be in a position to

- Identify suitable packaging materials,
- Determine shelf life of the product,
- Determine optimal storage conditions,

for the standard material being investigated.

By way of example the figure below shows the stability of pH 4.00 buffer solution over a 36 month time period.



1.8 Selection of a Standard.

When deciding on the most appropriate standards for a particular use one must first decide on the accuracy of result required.

The use of Primary Standards / CRMs are appropriate to work of highest accuracy, or when a specific procedure requires their use.

Secondary standards are more appropriate to routine analysis. They provide known accuracy, traceability, certification, and economy.

When selecting a Standard, the analyst must consider

- the accuracy of standard required
- stability of standard
- matrix of standard
- concentration of analyte (value of standard).

1.9 General Guidelines for Handling Standard Materials.

Standards, when supplied, are accurate, homogeneous, and stable. Stability studies will have been carried out to establish the best storage conditions for an optimal shelf life.

- Store in original container,
- Store in accordance with accompanying instructions,
- Check the Expiry Date before use,

- Replace cap when standard is not in use,
- Avoid contact with fumes,

- Avoid the possibility of contamination during removal of sample,
- Dispose of any 'unused' sample of Standard material; do not return to the original container.

Standards are chemicals, in some cases they may be classed as hazardous substances. One must handle, and dispose of, in accordance to local safety regulations.

Most importantly they must be accompanied by appropriate certification.