Certified Reference Materials: Beyond the Basics

spex certiprep

What is a Standard?

A standard is a 'KNOWN' to compare to an 'UNKNOWN'

An acknowledged measure of comparison for quantitative or qualitative value
- American Heritage Dictionary

ISO definitions

Primary standard:

- Highest metrological quality
- Value is accepted without reference to other quality standards
  - Example: Le Grand K

Secondary standard:

- Value is assigned by comparison to the primary standard of the same quantity

A material or substance whose property value(s) are:

- Sufficiently homogeneous & well established
- Used for:
  - Calibration of an apparatus
  - Assessment of a measured method
  - For assigning values to materials

Accreditations

ISO 9001: General requirements: Quality Management System

- Meet the needs of customers
- Meet statutory & regulatory requirements or product

ISO/IEC 17025: Testing and Calibration Laboratories

- Laboratories must demonstrate: Management system, technical competency and technically valid results
- Harmonization of standards and procedures to comply with International Standards and provide equivalent results among testing bodies

ISO Guide 34: CRM producers

- ISO Guide 34 allows for the transfer of results from CRM to labs for: Calibration of measuring equipment and evaluation or validation of measurement procedures
- Scientific and technical competence and ability to supply information about their materials

Error & Uncertainty

Differences Between Error and Uncertainty:

Error: Difference between measurement and 'TV' of the measurand

- Does not include mistakes (explain and exclude)
- Causes different values when a measurement is repeated and none are preferred
- Impossible to completely eliminate error, but it can be controlled and characterized

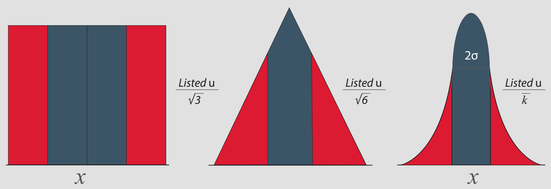
Uncertainty: Estimate attached to a certified value which characterizes the range of values where "true value" lies within a stated confidence level

- Random effects, short-term fluctuations in temperature, humidity, static electricity, and air pressure
- Variability in the performance of the analyst
- Drift can be accounted for by a correction

Error vs. Uncertainty: Error cannot be estimated and Uncertainty can be estimated

Types of Uncertainty:

- Type A: Usually associated with repeated measurements expressed as: $u_i \frac{s}{\sqrt{n}}$
- Type B: Based on scientific judgment made from previous experience, manufacturers' specifications, etc.
- Three types: Rectangular, Triangular and Normal Distribution



Rectangular Distribution

Use this when a certificate or other specification gives limits without specifying a level of confidence.

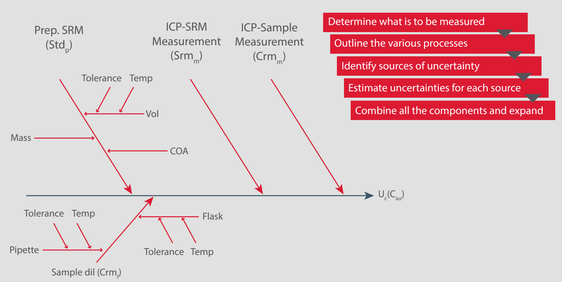
Triangular Distribution

Use this when distribution is symmetric and when values close to the target value are more likely than near the boundaries. Example: volumetric glassware.

Normal Distribution

Use this when an estimate is made from repeated observations of a randomly varying process and an uncertainty is associated with a certain confidence interval. Example: Calibration Certificate with Confidence Intervals.

Examples of Uncertainty Estimation in Creation of a Reference Standard:



Contamination & Error

Sources of error and potential contamination are found all over the laboratory from the actual chemical components used to the heating and cooling systems found in the building.

Sources of error:

- Chemical Components: Solvents, Reagents, Additives
  - Starting materials - must be tested for trace impurities
  - Impurities create: overlap of spectra, incorrect calibration curves and inaccurate results
- Common Laboratory Contamination:
  - Metals: Silicon, Calcium, Aluminum
  - Phthalates
  - Impurities
  - VOA: Chloroform, Acetone
  - Laboratory Solvent: Can be contaminated or cause contamination
    - Persistent solvents in lab: DCM & Carbon Disulfide
    - Solvent contamination includes:
    - Particles, gases, preservatives and additives
    - Leach or dissolve compounds from their containers
      - Sodium (glass), Boron (glass), Silica (pH >10)
      - Phthalates (plastics and liners)
    - Different solvent grades have different applications

Grade	Application/Use	Analytical
ACS	General Procedures	Meets or Exceeds ACS Specifications
Anhydrous	Water Sensitive Reactions and Synthesis	Low Water Levels (10-30 ppm)
Biotechnical	Biotechnical Applications	Low Water, Low Residue, Low UV
Environmental	Environmental Analysis, HPLC, Trace Organic	
Food/FCC Grade	Food and Drug Applications	Meets Specifications of Food Chemicals Codex (FCC)
GC	GC Applications	PPB Levels of Contamination
HPLC	HPLC Applications	Sub-micron Filtration, Some Low UV Absorbance
LCMS	LCMS Applications	Low Ionic Impurities < 0.1 ppm
Pesticide Residue	Pesticide, Environmental Analysis, Trace Analysis and GC-ECD, FID, MS	Meets or Exceeds ACS Pesticide Specifications
Reagent	General Laboratory Use	> 95% Purity
Spectrophotometric	UV Applications	UV, Vis, IR
Technical	General Laboratory Use	Non-critical Tasks
USP	Food and Drug Applications	Meets or Exceeds USP Specifications

- Water: Different grades or classifications of water are used for different laboratory uses
  - The same water cannot necessarily be used for all applications (inorganic or organic)
  - Bottled water has an expiration date like any other solvent

Requirement	ASTM Type			
	I	II	III	IV
Specific Resist. (megohm/cm) (max)	18	1	4	0.2
pH	N/A	N/A	N/A	5 - 8
Sodium (max)	1 µg/L	5 µg/L	10 µg/L	50 µg/L
Total Silica (max)	3 µg/L	3 µg/L	500 µg/L	High
Total Organic Carbon (max)	50 µg/L	50 µg/L	200 µg/L	N/A

Conclusions

- Contamination in Water from Phthalates
  - Laboratory components: syringes, pipettes, glassware, storage containers, scales
    - The most common source of contamination and uncertainty is labware
    - Syringes, pipettes, dispensers: carryover/cleanliness, accuracy, calibration, & maintenance
- How Clean Pipettes Charts (2)
- How Clean Syringes Charts (3)
  - Smaller volume syringe = more rinses needed
    - 10 µl syringe 5-10 rinses should go to waste in addition to another 5-10 rinses to clean syringe
    - Viscous samples may need much more cleaning
    - Pulling solvent through a vacuum system and taking the syringe fully apart
- Syringe Error Chart
  - Use calibrated syringes of appropriate range for level decanting
  - Measured volume should be no lower than 20% of syringe volume (1,000 & 100 µL syringes) for 1% or lower error
  - Measured volume needs to be > 20% for smaller syringes to decrease error
    - Laboratory glassware: Calibration/Class, TC or TD
    - Storage containers: Materials and cleanliness
- Cleanliness of Storage Containers Chart
  - Laboratory environment
    - Lab surfaces: residue and dust
  - Clean rooms, ventilation and laboratory hoods
    - Walls, ceilings and floors are sealed and dust free
    - HEPA filters mounted in the ceiling
    - No exposed metal parts
  - Contamination sources:
    - Ceiling tiles, paints, cements, and dry walls
    - Dust and rust on shelves, equipment and furniture
    - Temperature control systems
- Clean Room Packaging Chart
  - Minimize exposure:
    - Equipment, samples, blanks or standards opened in clean room, clean bench or glove box
    - Apparatus should be covered with in plastic bag or box
  - Clean work surfaces:
    - Surfaces cleaned with reagent water
  - Wear powder-free gloves:
    - Sweat contains K, Pb, Ca, Mg, SO4, PO4, and NH4 ions, Na and Cl
    - Powder gloves contain Zn
  - Use metal free containers:
    - Volumetric flasks, beakers made out of FEP, polycarbonate, and polypropylene
  - If clean room is not available, sample prep to be performed in a class 100 clean bench or glove box with a flow of air or N2
  - Use adhesive mats at entry points to control dust and dirt from shoes
  - Change shoes and/or wear shoe coverings to reduce bringing in dirt from the outside
- Laboratory Personnel
  - Jewelry, cosmetics or lotions
    - Cosmetics and lotions
    - Fragrances, solvents, phthalates
    - Al, Be, Ca, Cd, Cu, Cr, K, Fe, Mn, Ni, Pb, Ti, and Zn
    - Hair dyes: lead acetate
    - Calamine lotion: ZnO
    - Anti-dandruff shampoo: Se
    - Jewelry: Ni, Pb, Zn, Co, Au, Ag
- Wash Lab Coats Regularly
- Dust: Phthalates, Solvent Residue, Ca, Na, K, Mg, and Si
- Cigarette Smoke: Cd, VOA, SVOA