Critical QA/QC Factors

Basic Steps of Environmental Analysis

Sampling

↓

Sample Preparation

↓

Calibration

↓

Analysis

↓

Data Reporting

QC for Environmental Measurement

- The PARCC parameters help evaluate sources of variability and error
  - Precision
  - Accuracy
  - Representativeness
  - Completeness
  - Comparability

What are the Critical Concepts?

- Representativeness (Covered in previous lecture)
- Accuracy-Precision- Reduction of bias
- Interference Effects-Matrix Effects-Selectivity
- Calibration – External standards- Internal standards- Standard Addition- Drift and Stability
- Sensitivity-Dynamic Range

The Basic Elements of Quality Control

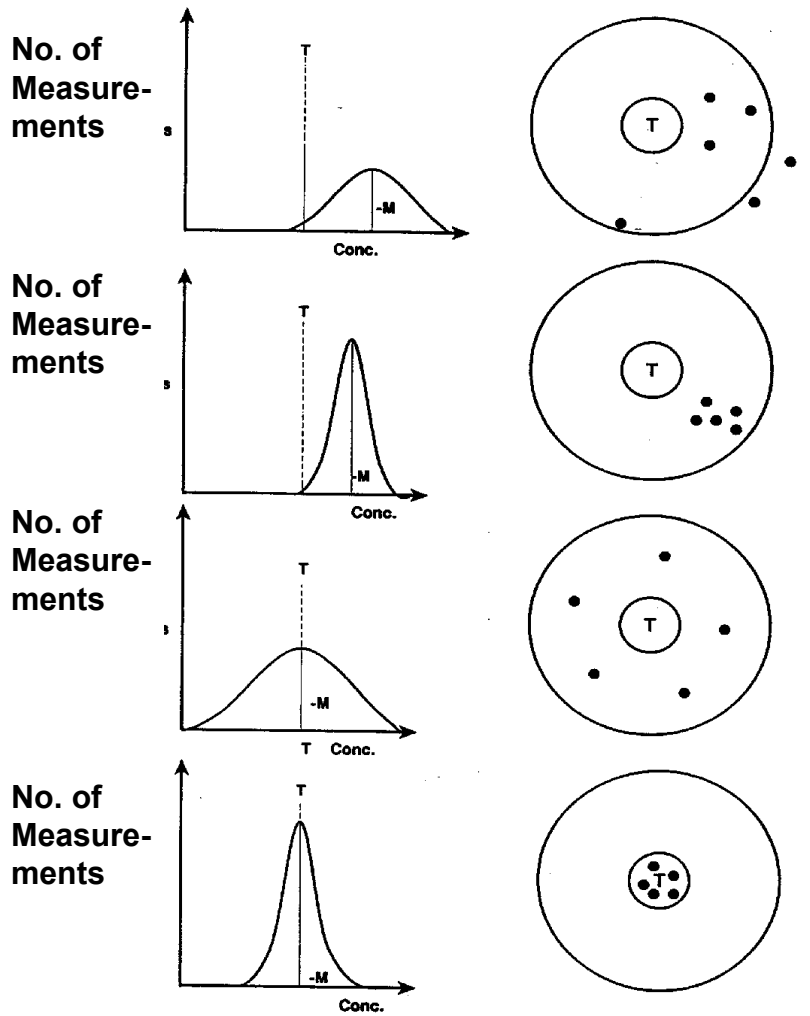
- Technical Competence of Staff
- Suitable Facilities and Equipment
- Good Laboratory Practices (GLP)
- Good Measurement Practices (GMP)
- Standard Operating Procedures (SOPs)
- Inspection
- Documentation
- Training

QC for Environmental Measurement

- **Data Quality Objectives (DQOs):**
  - Unique to the goals of each environmental evaluation
  - Address usability of data to the *data user(s)*
    - Those who will be evaluating or employing data results
  - Specify quality and quantity of data needed
  - Include indicators such as precision, accuracy, representativeness, comparability, and completeness (PARCC); and sensitivity.

Errors Determine Precision and Accuracy

- Low Precision-Low Accuracy (↑random, ↑systematic)
- High Precision-Low Accuracy (↓random, ↑systematic)
- Low Precision-High Accuracy (↑random, ↓systematic)
- High Precision-High Accuracy (↓ random, ↓systematic)



CSP CHEMICAL SECURITY ENGAGEMENT PROGRAM
SAFETY AND SECURITY TRAINING

Accuracy

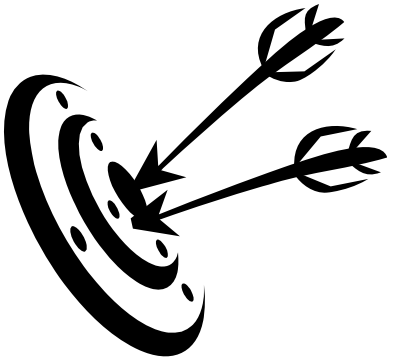
Accuracy may be defined as: *The closeness of the mean value from a replicate set of results to the true or accepted value*

Precision may be defined as: *The spread of results from a replicate set of measurements*

The difference between the true value and the mean measured value is termed **bias**. The spread of replicate data is measured in terms of **standard deviation (s) or variance (s^2)**

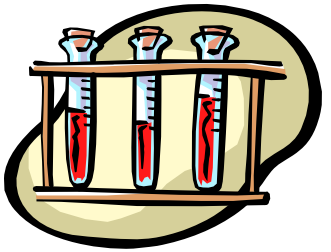
Characteristics of Precision

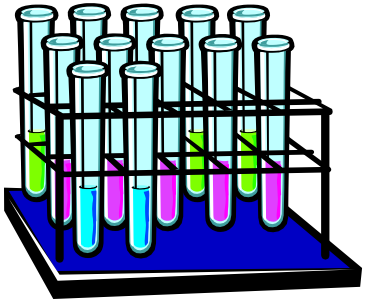
- **Precision is characterized by <u>random error</u>.**
  - **Sometimes the measured value will be higher than the true value and sometimes lower than the true value. It is random in nature.**
  - **If you measure many samples the errors caused by imprecision tend to "cancel out" and the average tends to be closer to the true value.**

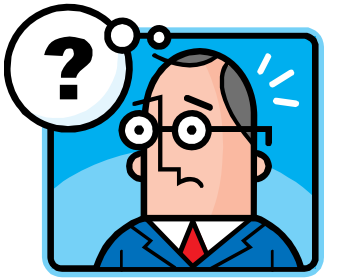


Characteristics of Bias

- Bias (which results in inaccuracy) is characterized by <u>systematic error.</u>
  - The error is always in the same direction; it causes inaccuracy to be more or less than the true answer.
  - Thus no matter how many samples you analyze you will never get closer to the true answer.



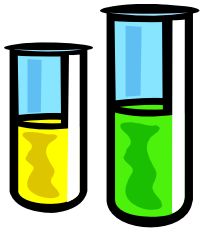




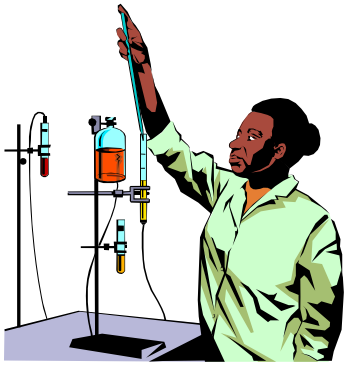
Interferences Are One Cause of Bias

- A good example of a source of bias is an interference in the analytical method.

- There are two kinds of interferences:



  - Those that are inherent in the samples, and
  - Those caused by procedures in sampling & analysis



CSP CHEMICAL SECURITY ENGAGEMENT PROGRAM
Chemical SAFETY AND SECURITY TRAINING

Inherent Interferences

- ***Inherent interferences are part of the sample.***
  - **Characteristics of inherent interferences:**
    - **Cannot be compensated for using the method.**
    - **Require modification or changing of the method employed OR require resampling and reanalysis with a different method after their source has been identified.**
    - **Their importance is that they may mask the signal of the pollutants (causing low values) OR they may add to it (causing higher than true values).**
    - **Thus, their presence causes systematic bias - always producing either higher or lower than true values.**

Procedural Interferences

- ***Procedural interferences are those that may be added during sampling, storage, sample preparation or analysis.***
  - **Characteristics of procedural interferences:**
    - **Can be removed and the existing method used again.**
    - **Importance is that they may mask the signal of the pollutants (causing low values) or they may add to it (causing higher than true values).**
    - **Thus, their presence causes systematic bias - always producing either higher or lower than true values.**

Examples of Interferences

Inherent in Sample

- Unresolved peaks on chromatogram
- Similar emission/absorption lines
- Signal quenching by other compounds
- High ionic strength affecting elemental activity

Procedural interferences

- Sampling contamination
- Sample storage/preparation contamination (VOCs)
- Lack of selectivity of method

Matrix Effects

Definition - The combined effect of all components of the sample other than the analyte on the measurement of the quantity. If a specific component can be identified as causing an effect then this is referred to as interference. – IUPAC

Matrix Effects – A Few Examples

- Background chemical matrix are characterized by:
  - High concentration of elements that are not being analyzed for
  - High or diverse ionic strength
  - Reactive materials

- Affects chromatographic resolution
  - Co-elution
  - Detector saturation
- Affects spectroscopic signal
  - Spectral overlap
  - Chemical ionization (Alkali metals)
  - Nebulizer performance erratic
- Affects recoveries
  - Adsorption on to clay matrix (for soils)
  - Co-precipitation

Instrument Drift and Matrix Effects can be Addressed in Method

- Instrument drift is often due to environmental effects, tuning, sample introduction.
- Drift and matrix effects can often be corrected by running standards (spikes) interspersed with samples.

Corrected sample = observed sample x (spike added/spike found)

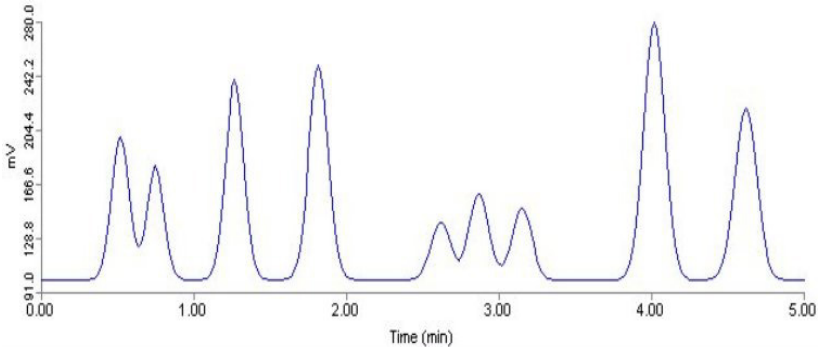
Reference: *Chemical Analysis of Metals* – Francis T. Coyle

Selectivity

- (qualitative): The extent to which other substances interfere with the determination of a substance according to a given procedure.
- (quantitative): A term used in conjunction with another substantive (e.g. constant, coefficient, index, factor, number) for the quantitative characterization of interferences.

Selectivity can be Enhanced by Method

- Selectivity refers to the extent to which a method can determine particular analytes in mixtures or matrices without interferences from other components.
  Source: IUPAC

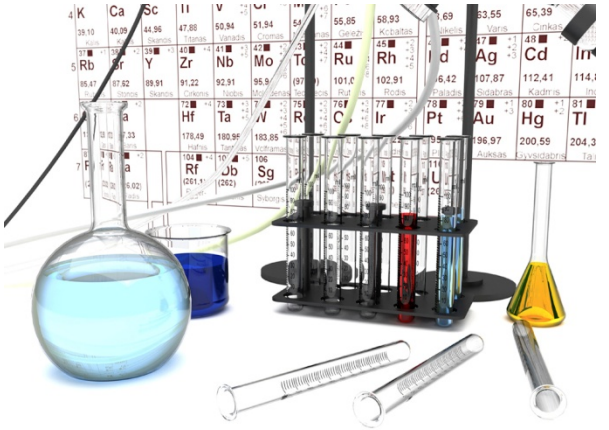


QC for Environmental Measurement

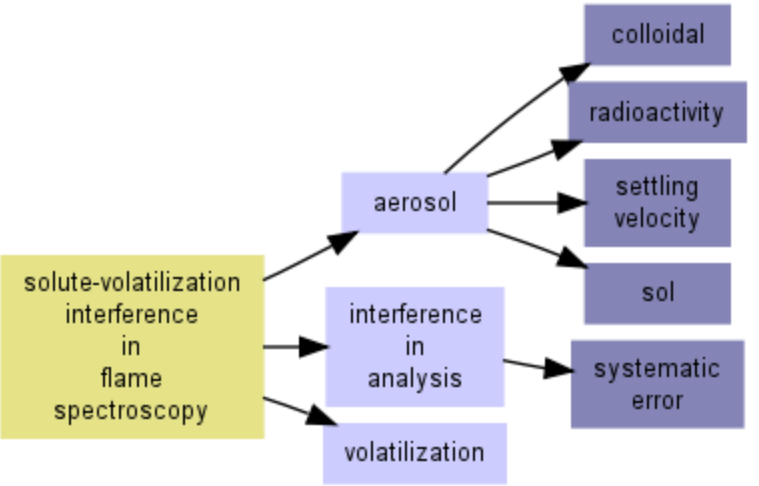
- Sensitivity
  - Ability to discriminate between measurement responses
- Detection limit
  - Lowest concentration accurately detectable
    - Instrument detection limit (IDL)
    - Method detection limit (MDL)
- Measurement range
  - Extent of reliability for instrument readings
  - Provided by the manufacturer

Quality Control Methods: QC Samples

- Greater that 50% of all errors found in environmental analysis can be directly attributed to incorrect sampling
  - Contamination
  - Improper preservation
  - Lacking representativeness
- FIELD QA/QC SAMPLES
  - Equipment/ rinsate blanks
  - Field blanks
  - Trip blanks
  - Field replicates
  - Co-located samples
  - Background samples
- LABORATORY QA/QC SAMPLES
  - Blanks to assess contamination
  - Spikes used to measure % recovery (accuracy)
  - Replicates used to measure precision



Example: All Steps in a Method can Contribute to Error



http://goldbook.iupac.org/

Reference Materials

- Standard Reference Materials and other standards are prepared by chemical service companies. They are usually traceable to a standards organization.
- Inorganics may be purchased in liquid form
- Organic mixtures for GC and HPLC are available in small sample vials.
- Reagent water, ultra pure acids and solvents are used in standard preparation

Calibration

- Calibration curve shows the uncertainty in a measurement
- Provides an empirical relationship between concentration and response.
- Provides an instrumental constant that is related to a physical law

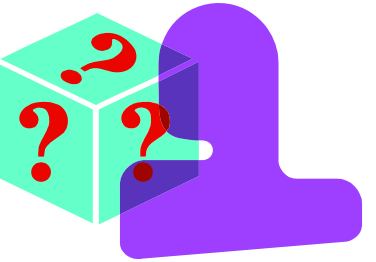
Analytical Method Performance Characteristics

A method's performance is defined by a number of important individual characteristics. These are:

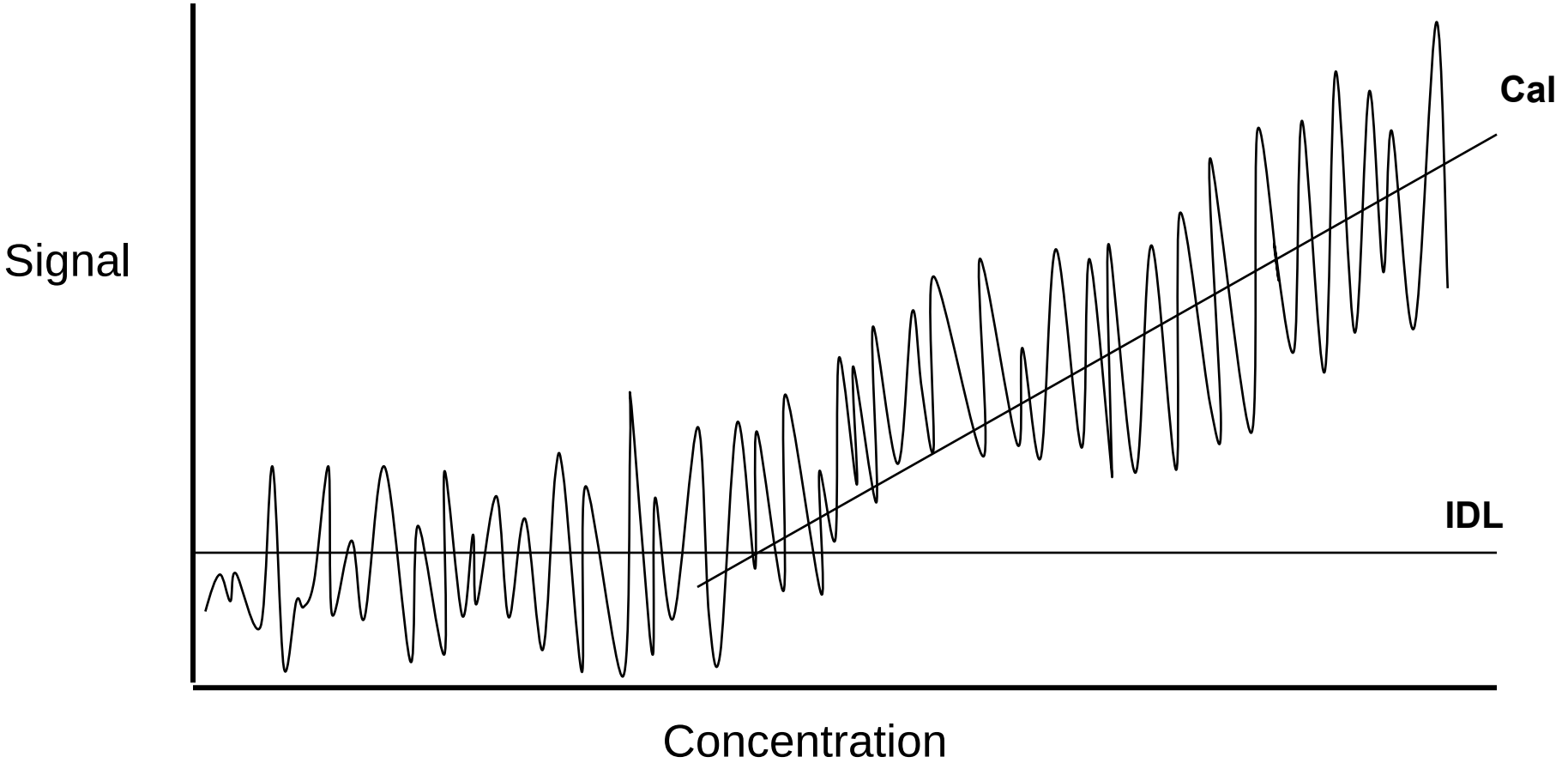
Accuracy
Precision
Sensitivity
Limit of Detection
Limit of Quantitation
Bias
Selectivity
Linear Range
Dynamic Range

Detection Level

- Expressing uncertainty with the limit of detection is very important
- Some abbreviations
  - LOD - Limit of Detection
  - LOQ - Limit of Quantitation
  - LOL - Limit of Linearity
  - IDL - Instrument Detection Level
  - MDL - Method Detection Level

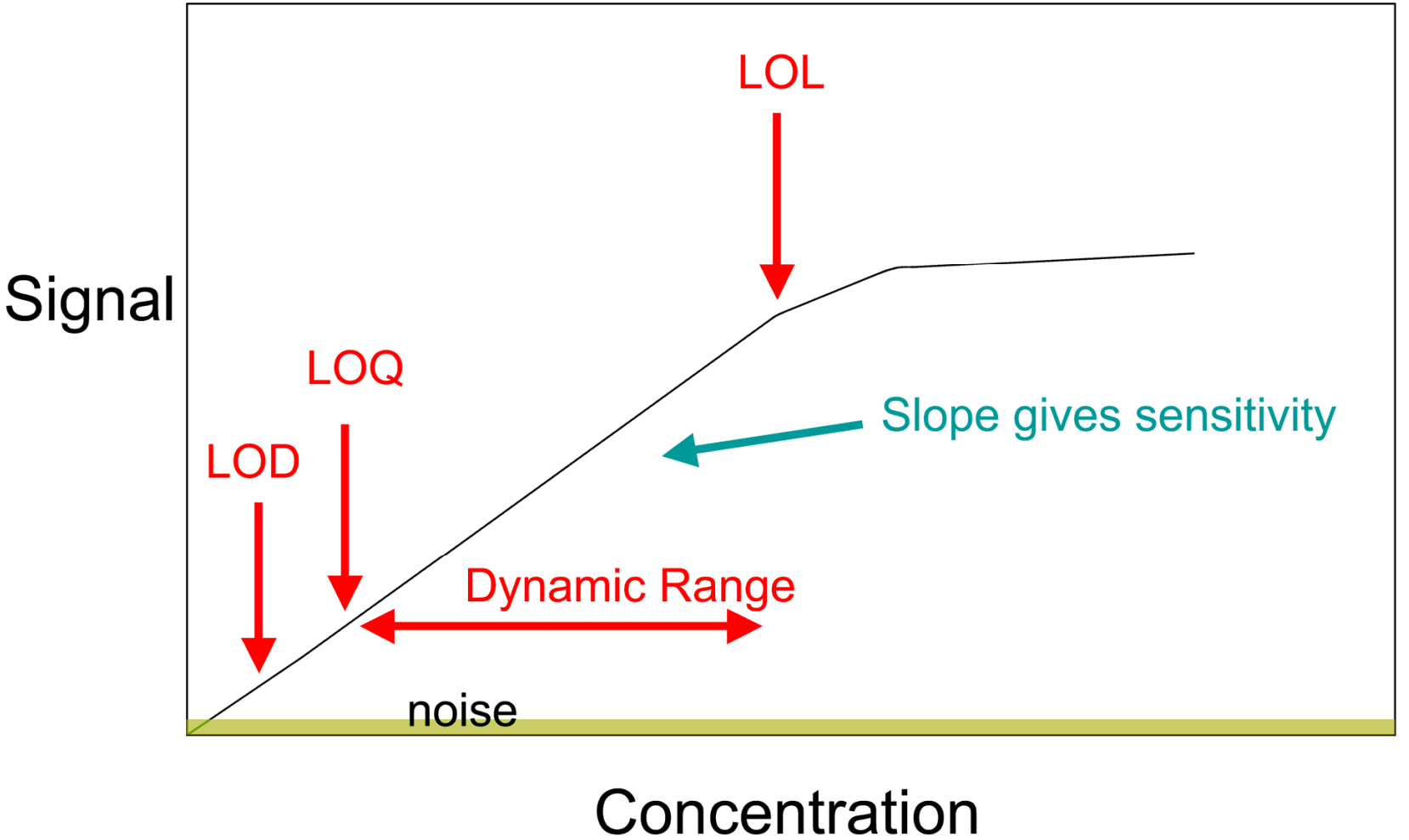


Sensitivity- Signal to Noise Ratio Intersection of IDL with Calibration Curve



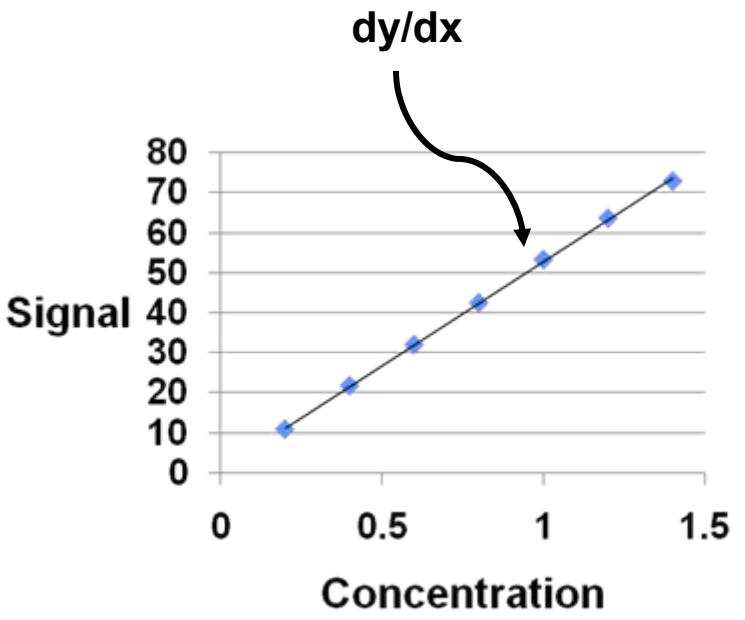
IDL = Instrument Detection Level

Calibration Curve

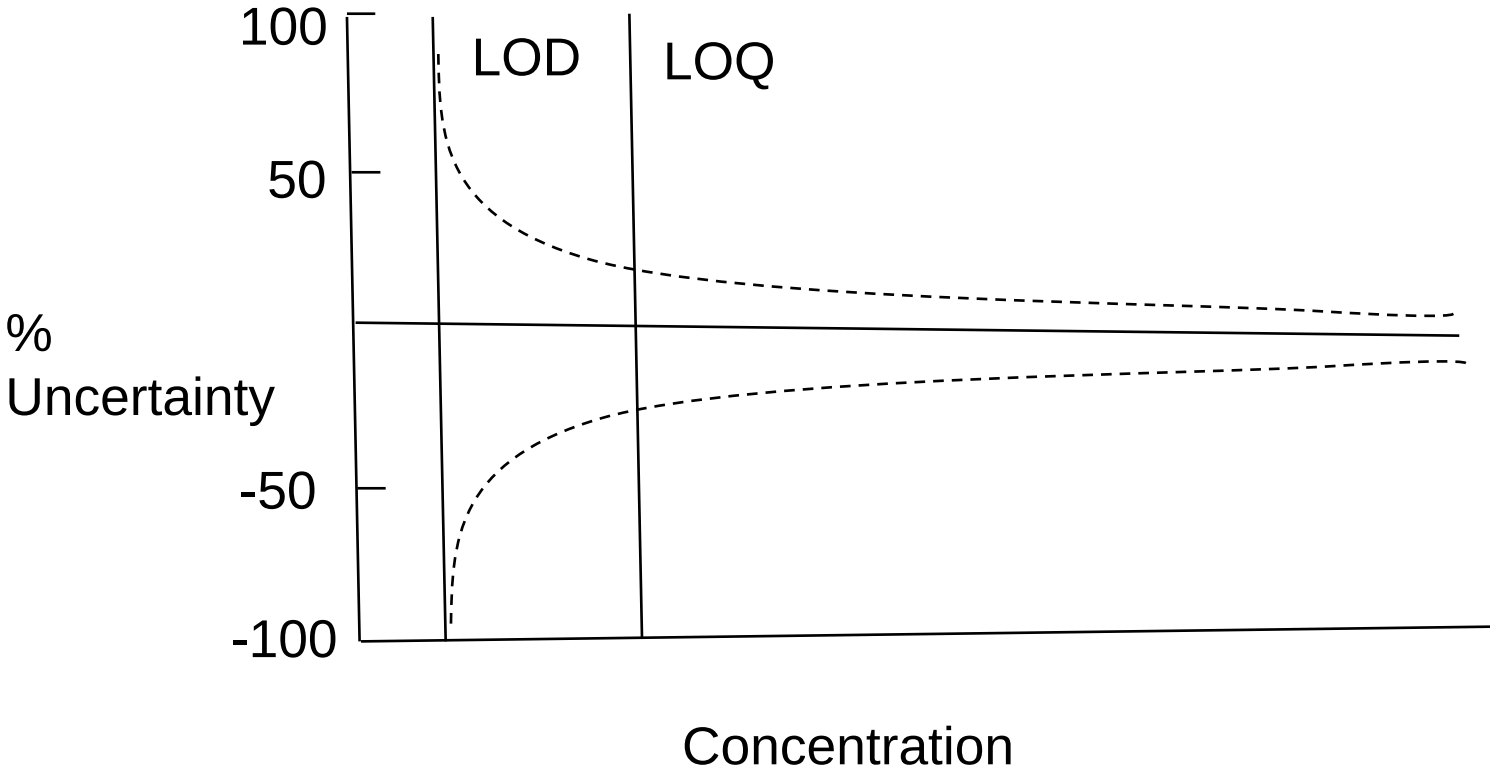


Sensitivity

- The slope of the *calibration curve. If the curve is in fact a 'curve', rather* than a straight line, then of course sensitivity will be a function of analyte concentration or amount. If *sensitivity is to be a unique performance* characteristic, it must depend only on the *chemical measurement process*, not upon scale factors.



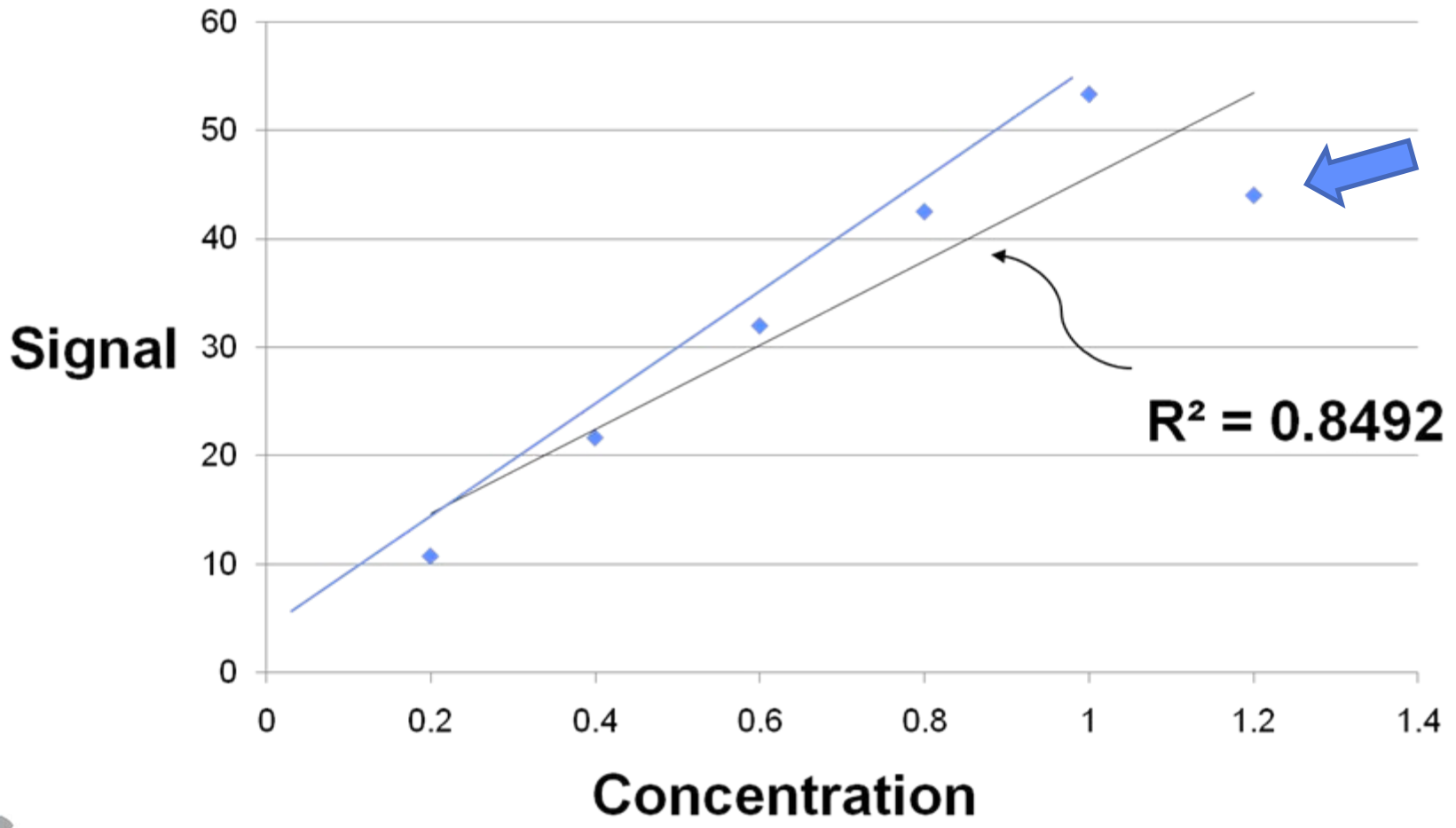
Uncertainty of Measurement Increases Near the Limit of Detection



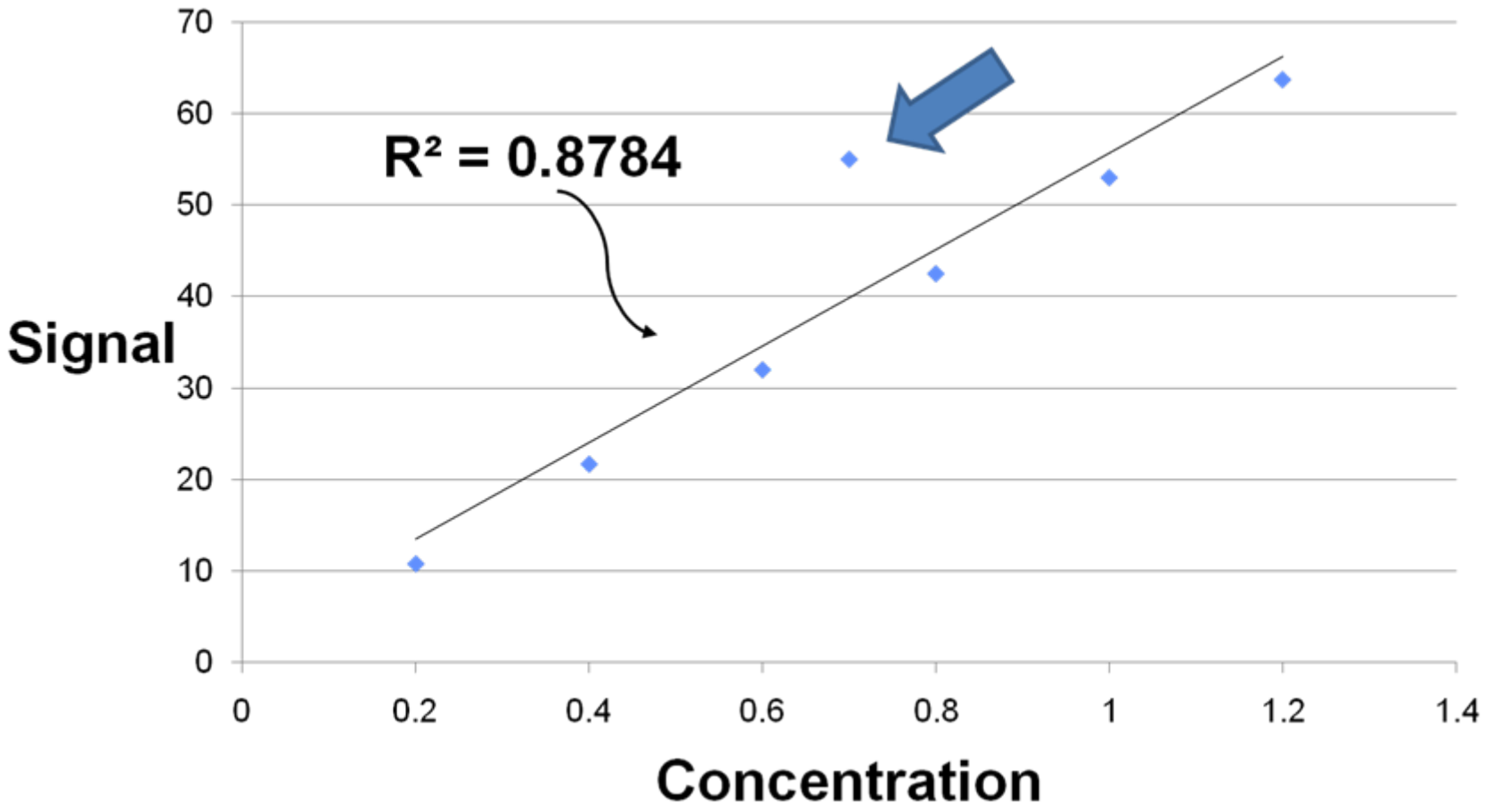
LOD-limit of detection
LOQ-limit of quantitation

Reference : Quality Assurance of Chemical Measurements- L.K. Taylor

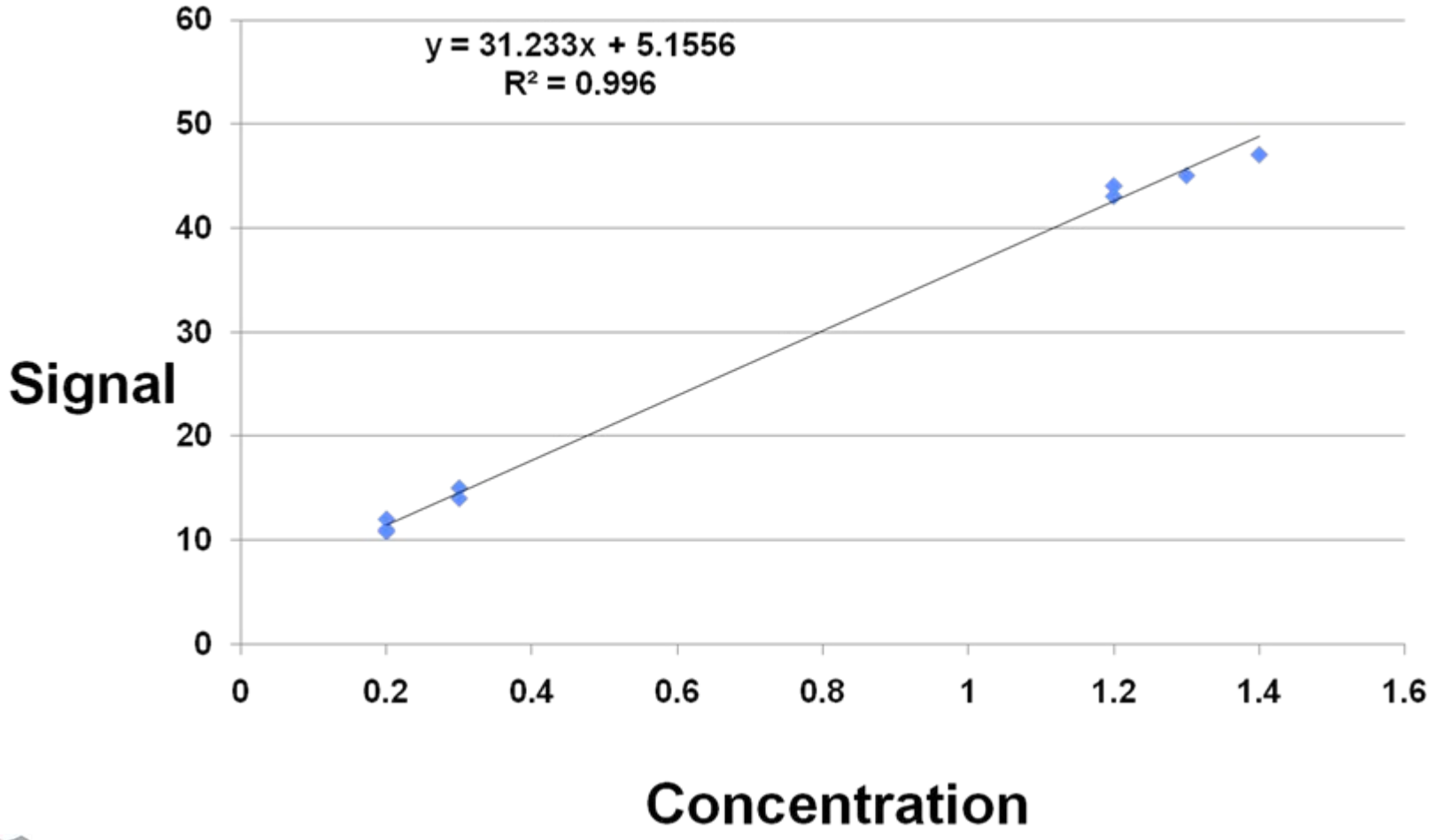
Outlier Influence



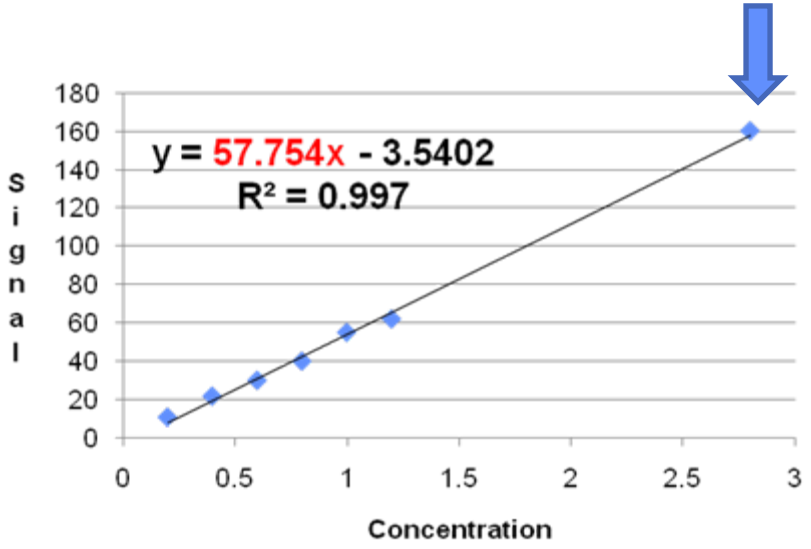
Point of Influence Bias

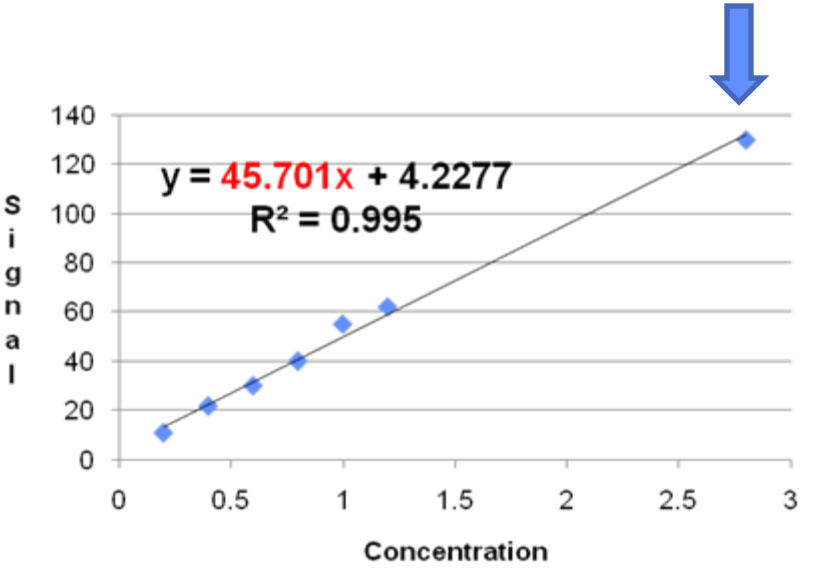


Poor Experimental Design



Point of High Leverage





Final point – (2.8, 160)

Final point – (2.8, 130)

Sources of Non-linearity

- Beers law deviation at high or low concentrations (15-80% Transmittance)
- Detector quenching due to sample volume (Electrospray, Flame Photometry)
- Injector discrimination in gas chromatography
- Electronic saturation of amplifiers

Internal Standards

- An internal standard is a known amount of a compound, different from the analyte, added to the unknown. The signal from the analyte is compared (ratio) with the signal from the internal standard to determine analyte concentration.

- Internal standards are used when the quantity of sample analyzed or the instrument response varies from run to run and difficult to control. Also used when sample loss is unavoidable during sample preparation steps prior to analysis.

Internal vs External Calibration Standards

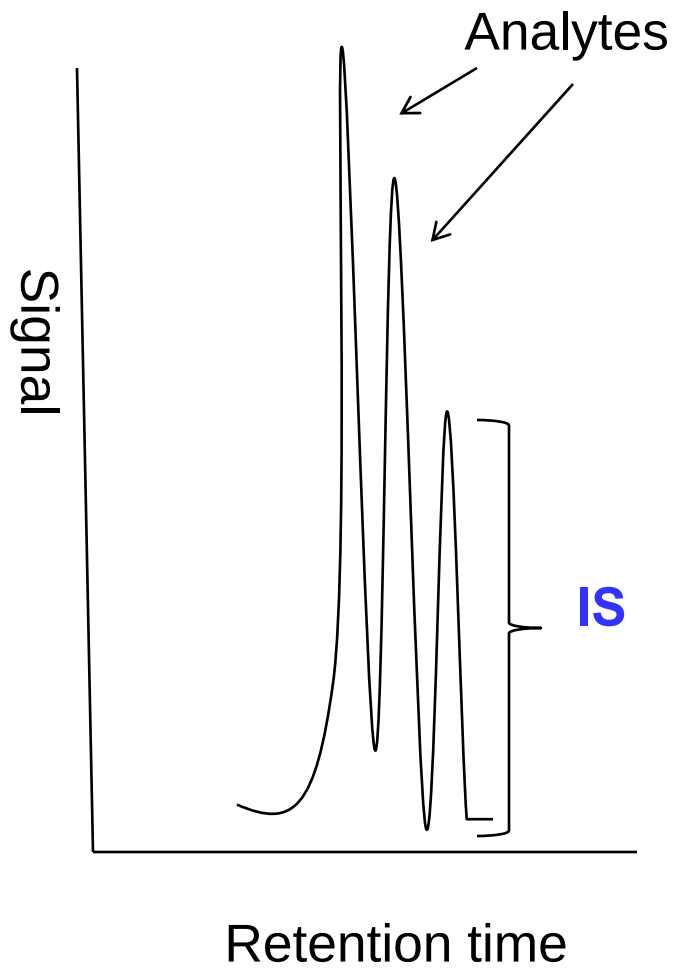
- External standards are the typical way calibration curves are produced (slope =sensitivity)

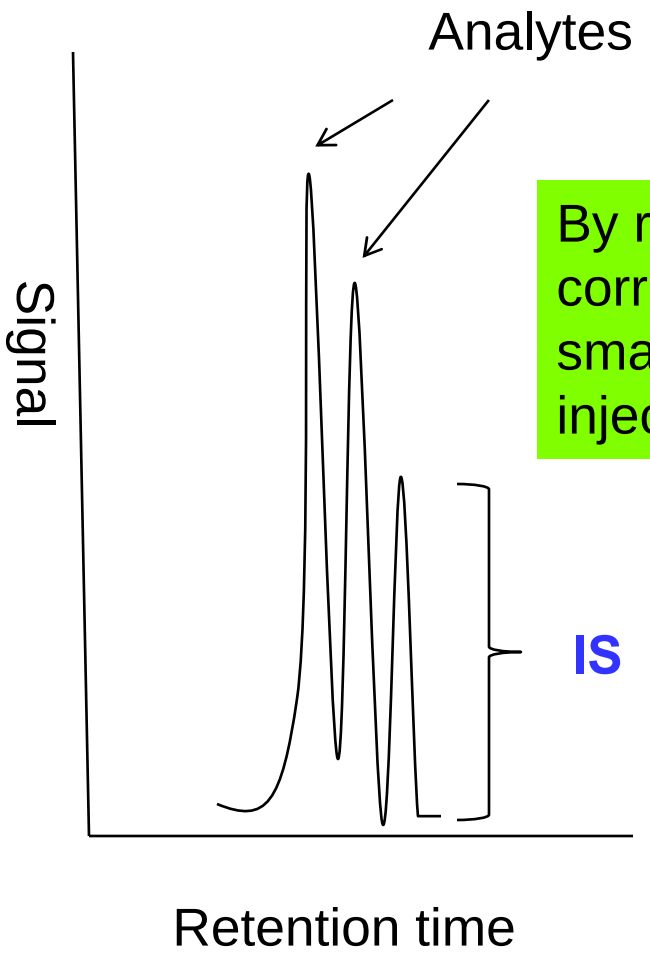
- Internal standards are often used to bracket a sample and are not present in the unknown matrix

$$\frac{\text{Analyte signal}}{\text{Analyte concentration}} = \frac{\text{F x (Standard signal)}}{\text{Standard concentration}}$$

- We assume that the internal standards behave the same way as analytes

Chromatography Example: Sequential Injections – Internal Standard Mimics Analytes



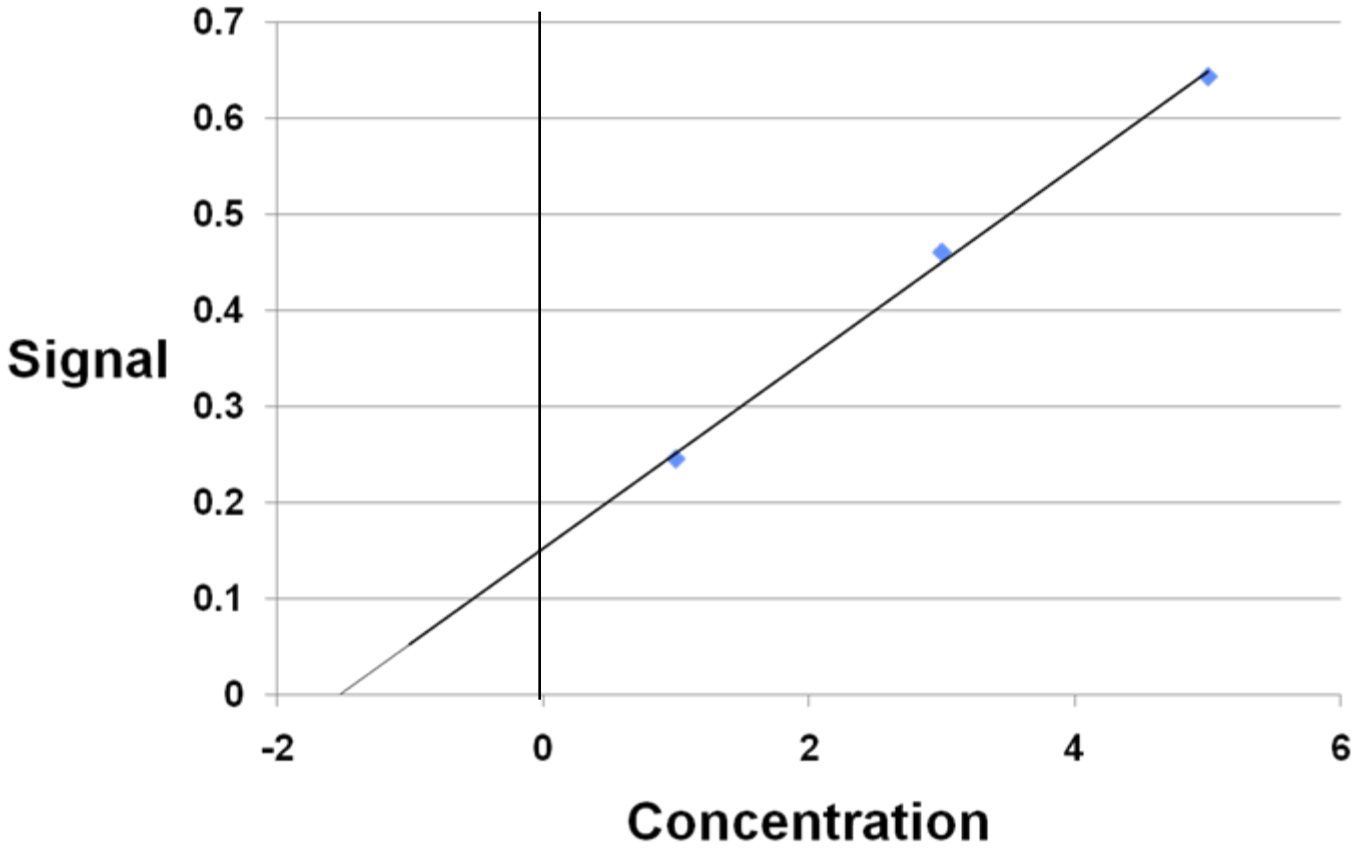


By ratio we can correct for the smaller injection

Method of Standard Additions

- Adding a standard solution of known concentration of analyte to an unknown solution so that impurity effects are accounted for.
- The analyst can then extrapolate to the actual concentration

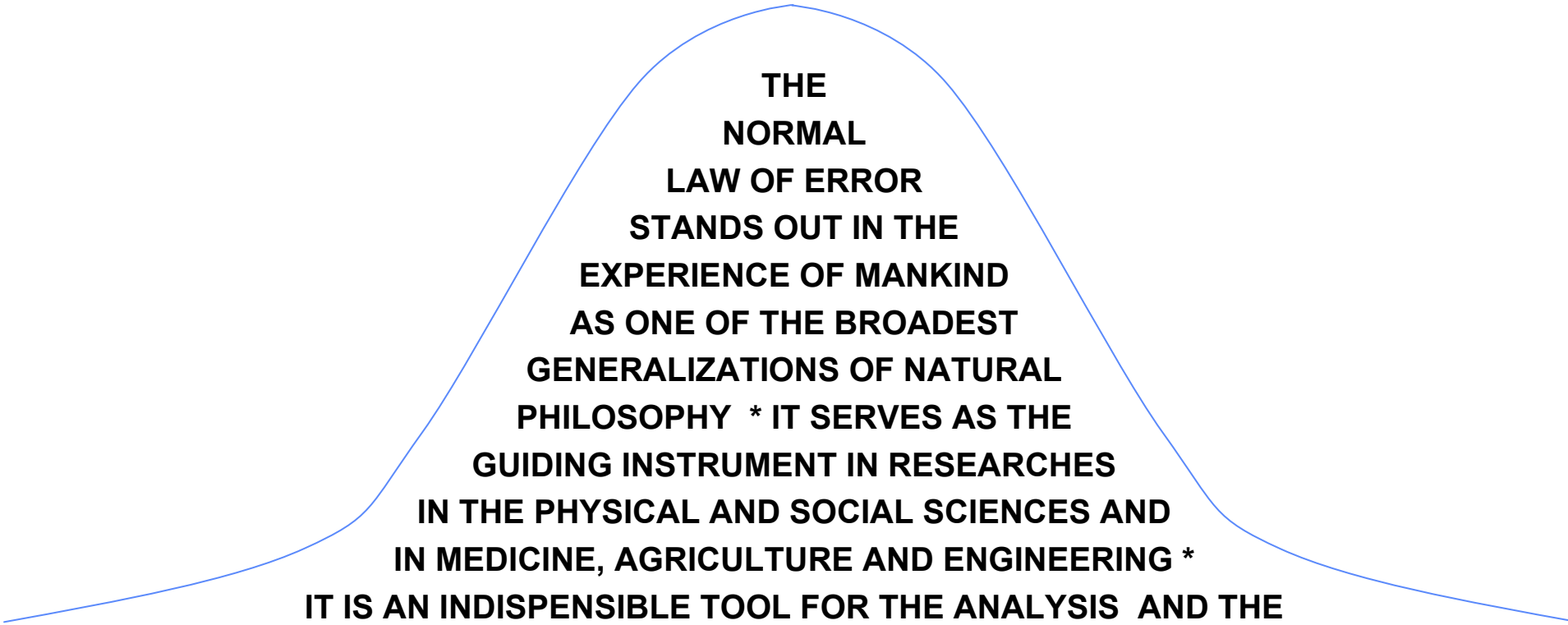
Method of Standard Additions May Help with Matrix Interferents



Concentration = -1.516 + (10.029*Signal)

R^2=0.998

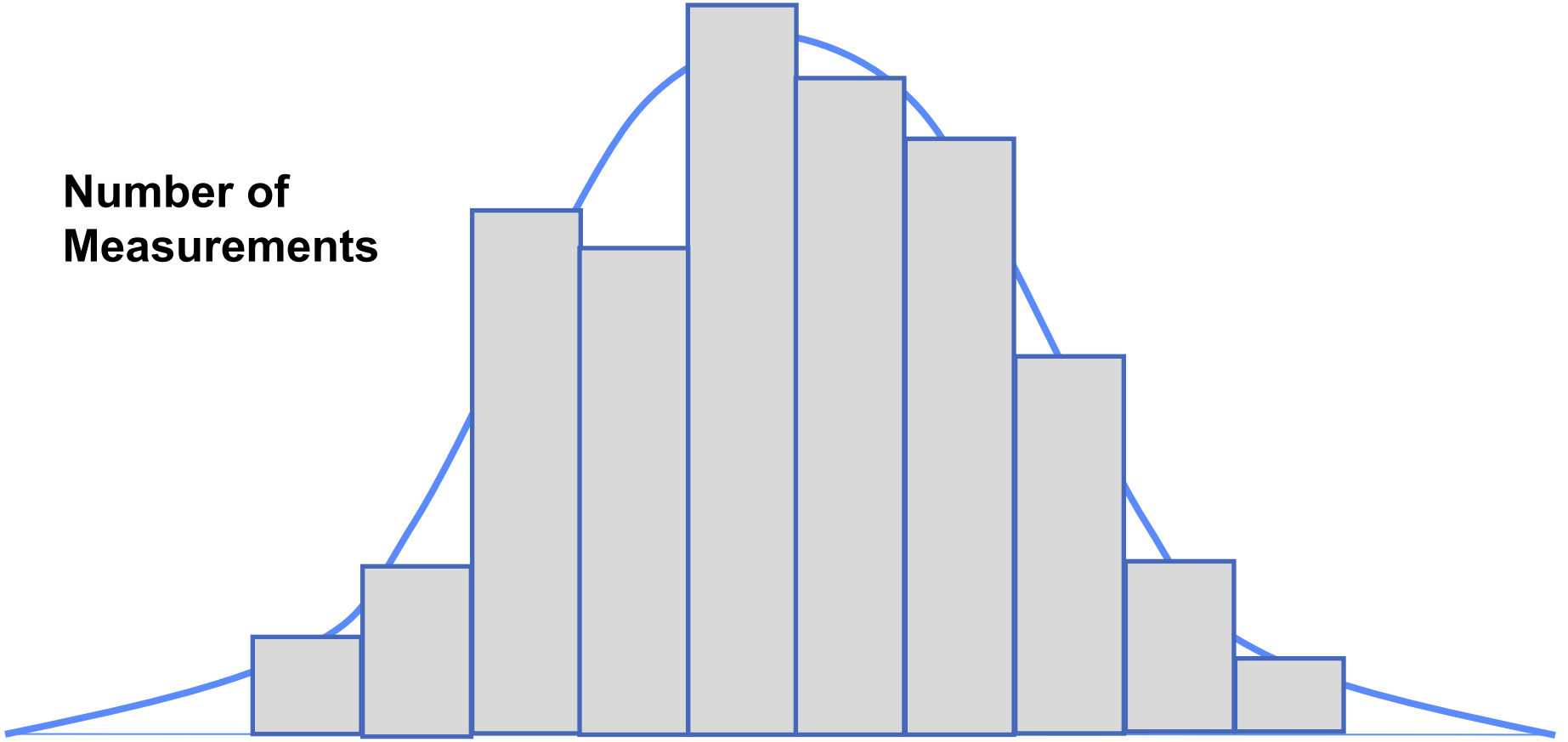
The Normal Law of Error



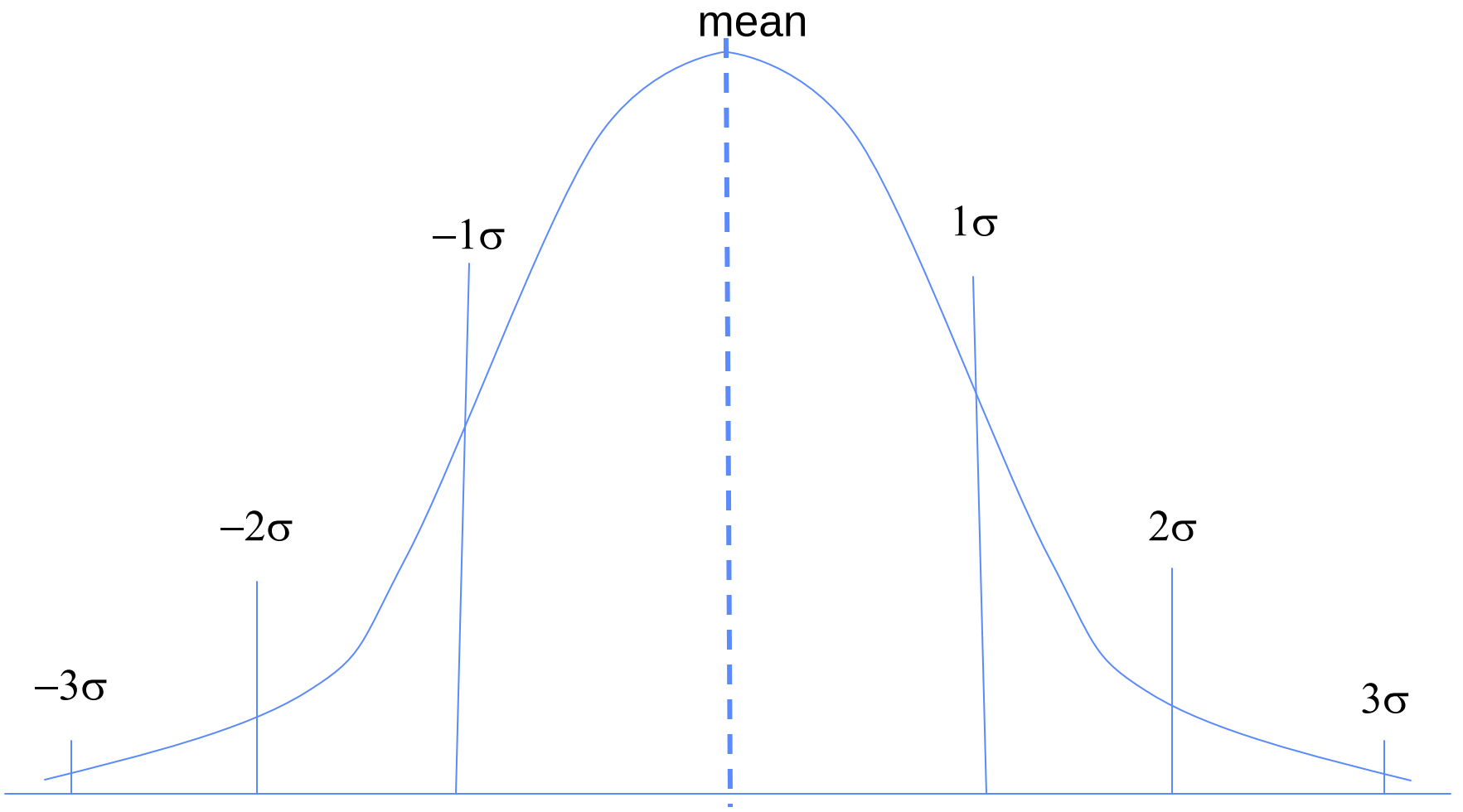
THE
NORMAL
LAW OF ERROR
STANDS OUT IN THE
EXPERIENCE OF MANKIND
AS ONE OF THE BROADEST
GENERALIZATIONS OF NATURAL
PHILOSOPHY * IT SERVES AS THE
GUIDING INSTRUMENT IN RESEARCHES
IN THE PHYSICAL AND SOCIAL SCIENCES AND
IN MEDICINE, AGRICULTURE AND ENGINEERING *
IT IS AN INDISPENSIBLE TOOL FOR THE ANALYSIS AND THE
INTERPRETATION OF THE BASIC DATA OBTAINED BY OBSERVATION AND EXPERIMENT

From: W.J. Youden -NIST Publication 672

Histogram of Data Compared to Normal Distribution



The Normal Law of Error



Standard Deviation can be Calculated for the Normal Distribution

- $SD = [\ \Sigma(x_i - x)^2/(n - 1)]^{1/2}$

Where :

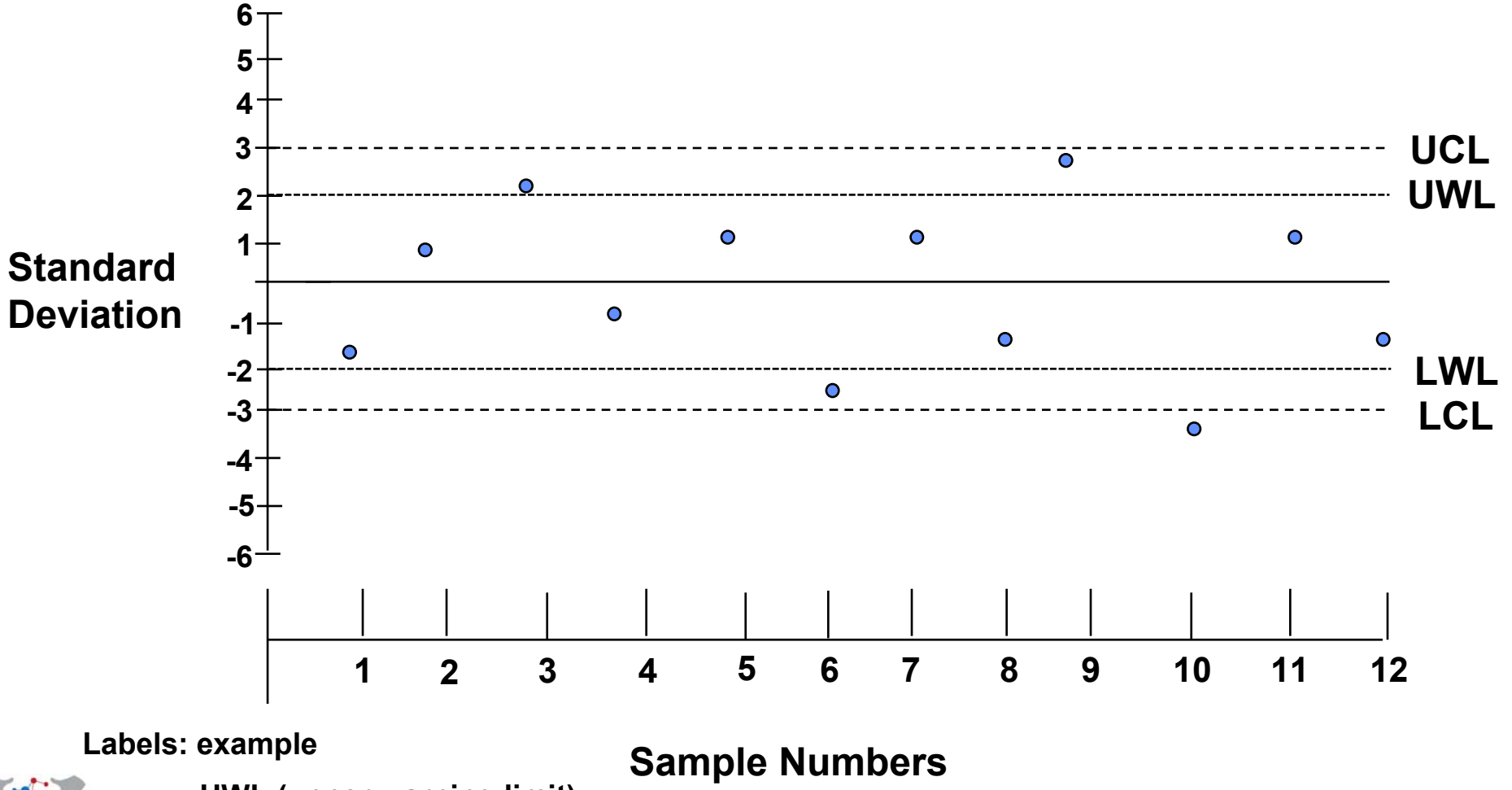
x_i= individual data point

x= mean value of the data points

n= number of points

- Need at least 8-10 data points

Control Chart can Define Acceptable Limits of Analysis



Labels: example

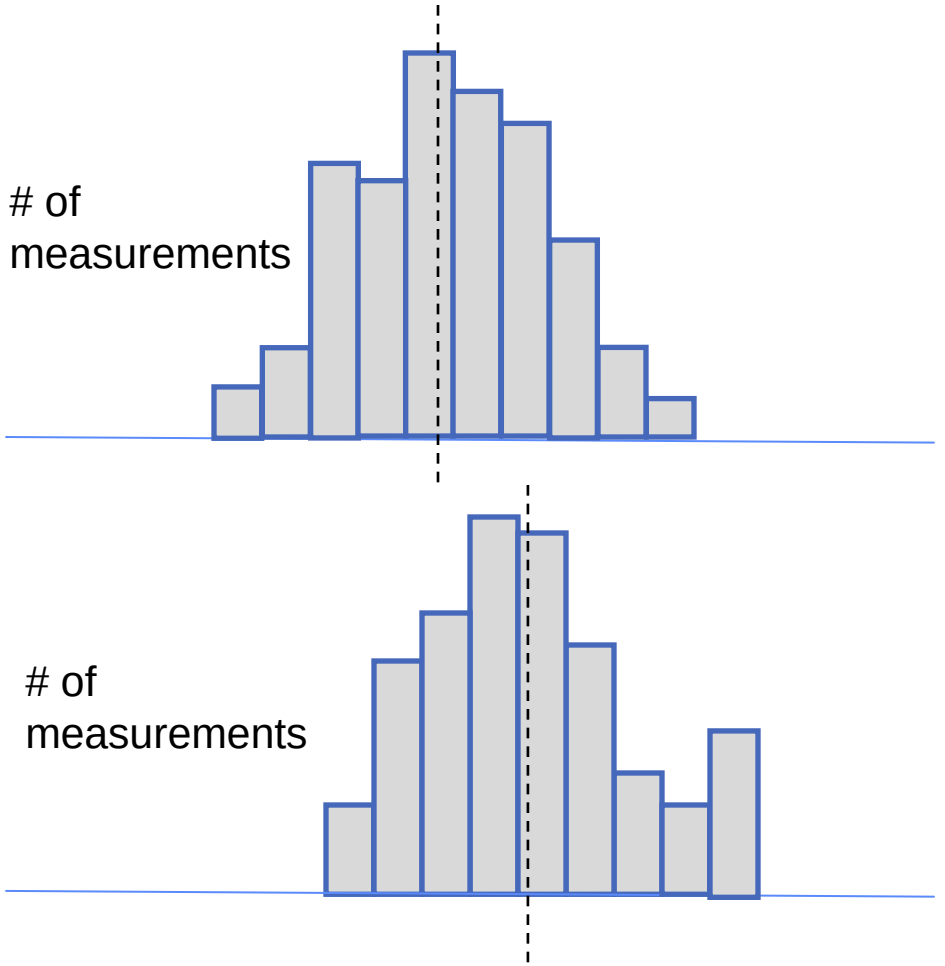
UWL (upper warning limit)
LCL (lower control limit)

Uncertainty of a Measurement Result

- **In general, the result of a measurement is only an approximation or estimate of the value of the specific quantity subject to measurement, that is, the measurand, and thus the <u>result is complete only when accompanied by a quantitative statement of its uncertainty</u>.**

Reference: *Guidelines for Evaluating and Expressing the Uncertainty of NIST Measurement* Results- B. N. Taylor and C. E. Kuyatt –NIST Technical Note 1297.

Two Sets of Replicate Data Analyzed on Separate Days



Here we see a slight change in the mean, possibly due to method drift

References

- *Quality Assurance of Chemical Measurements* –J. K. Taylor CRC Press (1987) ISBN:0-87371-097-5
- *Environmental Sampling and Analysis* – L.H. Keith CRC Press (1991) ISBN:0-87371-381-8
- *Handbook of Environmental Analysis* – R.K. Smith Genium Publishing (1995) ISBN:0-931690-77-3
- *Experimentation And Measurement* – W.J. Youden NIST Special Publication 672 (1991)
- *Eurachem Guides: http://www.eurachem.org*

Data Handling -Laboratory Audits

Basic Steps of Environmental Analysis

(Data Reporting)

Sampling

↓

Sample Preparation

↓

Calibration

↓

Analysis

↓

Data Reporting

Essential Documentation

- Laboratory Quality Assurance Plan
- Sampling Plans
- Chain of Custody
- Standard Operating Procedures
- Data Reports
- Audit Reports
- Proficiency Test Results

Laboratory Documentation –Sampling and Sample Preparation

- Sampling logs
- Sample Preparation logs
- Standard Preparation logs
- Refrigerator logs
- Oven logs
- Water quality logs
- Analytical balance certification
- Pipette logs

Laboratory Documentation

- Calibration records
- Reference standards
- Instrument logs
  - Maintenance
  - Calibration- tuning – instrument drift
  - Deficiency correction
- Instrumental methods
  - Raw data
  - Calculations
- QA/QC Charts
- Data reports

Temperature Monitoring Log

(see resource section of notebook)

Device: Thermometer Cal #: Set point Range:

Date	AM Reading	Initials-Time	PM Reading	Initials-Time	Notes

The Following “Sample Forms” are in Your Notebook

- Analytical Balance Calibration Log
- AutoclaveOperationLog.doc
- BOD Bench Sheet
- Chemical Purchase Log
- COD Bench Sheet.
- Conductivity Meter Calibration Log
- DI Water QC Log
- Fecal Coliform Bench Sheet
- Glass Fiber Filter Wash Bench Sheet

- Inhibitory Residue Bench Sheet
- Maintenance Log
- Membrane Filter QC Log
- m-fc Broth
- pH Meter Calibration Log
- Phosphate Dilution Water Log Bench Sheet
- Spectrophotometry Bench Sheet
- Temperature Log.
- Titration Bench Sheet
- TSS Bench Sheet

Data Reporting- Example Report

Environmental Protection Laboratory
Address-Telephone-Email
Laboratory Report

Report # 1234 **Date: 1/1/2010**
Sample: Water, grab, 25/12/2009 received 28/12/2009

method

Results

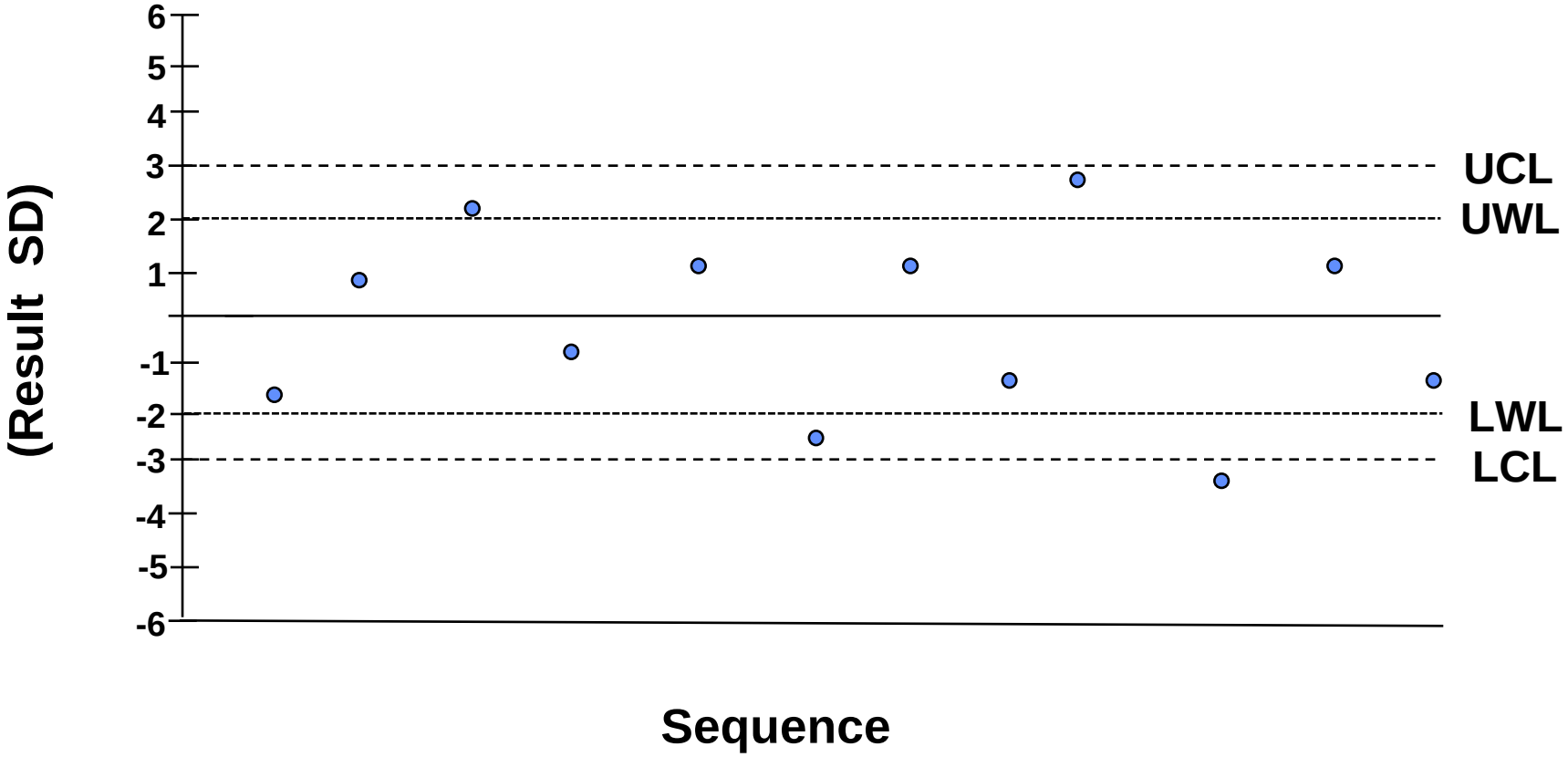
	Result	Detection Limit
Total Lead (Pb) (mg/L) (M-239.2)	1.41*	0.005
Total Copper (Cu) (mg/L) (M-220.2)	0.12*	0.002

* Sample incorrectly preserved –not acidified

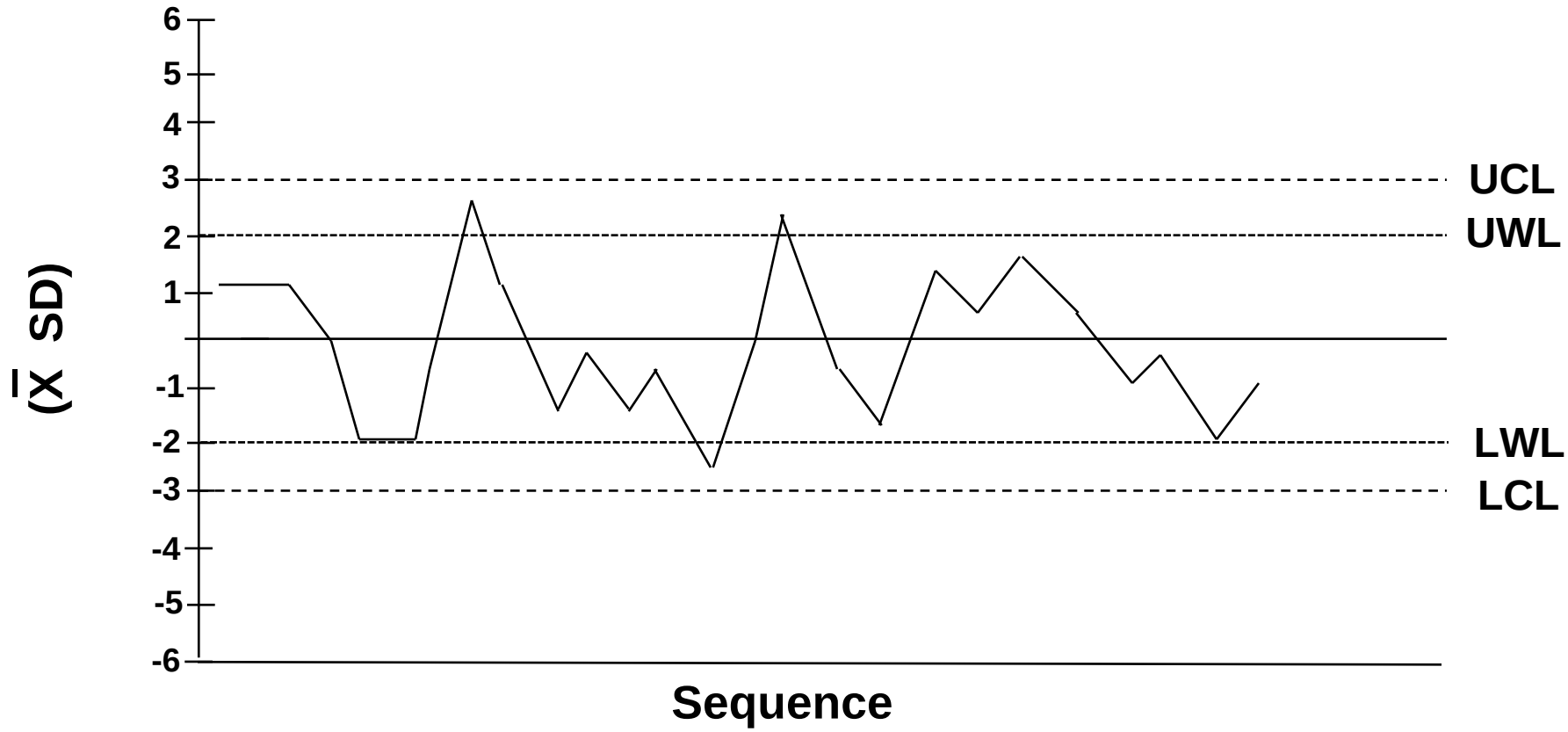
Significant Figures

Reported Number	Implied Precision
2	1 to 3
2.0	1.9-2.1
2.00	1.99-2.01
2.000	1.999- 2.001

Typical X Control Chart
(single measurement)



Typical $\overline{X}$ Control Chart
(mean of several measurements)



Means chart is less susceptible to outliers and more likely to be “normally” distributed

Audits

- Types of audits
  - Processes-documents-policies-training
  - Performance samples
  - Data audits
- Preparing for the audit
- Management involvement
- Training
- Data packages
- Corrective measures
- Peer review

Laboratory Certification

- Certification - ISO 17025 Review
- Chemical Management and Waste

Lab Certification Involves all Parts of a Labs Operations

- Laboratory Management
  - Quality Manual and QA Plans
  - Personnel Quality
  - Supplier quality
- Laboratory Staff
  - Use written and appropriate procedures
  - Document results
  - Proficiency testing
  - Best practices for chemical handling

ISO 17025 is the International Standard for Chemical Analysis Laboratories

Management

- Document control
- Consistent analytical methods
- Monitor supplier performance
- Contract review to document customer requirements
- Corrective and preventive action procedures and audits
- Quarterly management review

Technical

- Personnel training plans and detailed records
- Method development and validation procedures
- Measurement of method uncertainty
- Defined equipment calibration and maintenance program
- Defined sample preparation processes
- Quality Control monitoring

Management Requirements - Clause 4

Quality Manual

Quality Policy
Overview and Maintenance of Quality Documentation
Requests and Contracts

4.1 Organization

- Treat customer information with confidentiality
- Specify responsibilities, authority and relationships
- Experts supervise testing and calibration staff including trainees
- Technical management staff
- Quality manager
- Ensure people know the importance of job

Elements of a Quality Manual

Quality Policy
Overview and Maintenance of Quality Documentation
Staff Responsibilities
Staff Selection
Staff Training
Equipment
Calibration
Tests & Calibration Procedures
Sample Handling
Support and Supplies
Complaints
Internal audits
Management Reviews

Management Requirements - Clause 4

4.2 Management System

- Quality policy to comply International Standards – then improve
  - Specify requirements for tests and calibration
  - Regulatory and statutory
- Quality manual shall include or make reference to supporting procedures including technical procedures.
- Define responsibilities

Management Requirements - Clause 4

4.3 Document Control

The laboratory shall establish and maintain procedures to control all documents that form part of its management system (internally generated or from external sources), such as regulations, standards, other normative documents, test and/or calibration methods, as well as drawings, software, specifications, instructions and manuals.

Document approval - Change/Edit procedures

Management Requirements - Clause 4

4.4 Review requests, tenders and contracts
4.5 Subcontracting guidance for test and calibration
4.6 Purchasing services or supplies
4.7 Customer service
4.8 Complaints
4.9 Control of non-conforming work
4.10 Improvement
4.11 Corrective action - Cause analysis – monitor - additional audit
4.12 Preventive Action

Management Requirements - Clause 4

4.13 Control of records

- Maintain procedures for identification, collection, indexing, access, filing, storage, maintenance and disposal of quality and technical records.
- Accessible, legible, confidential, safely stored, electronic and hard copy

Technical records

- Laboratory shall retain records of original observations, derived data and sufficient information to establish an audit trail, calibration records, staff records and a copy of each test report or calibration certificate issued, for a defined period.

- Forms, contracts, work sheets, work books, check sheets, calculations, work notes, control graphs, external and internal test reports and calibration certificates, customers' notes, papers and feedback.

Management Requirements - Clause 4

4.14 Internal Audits

- Management system including calibration and test activity
- Expert independent of the activity being audited

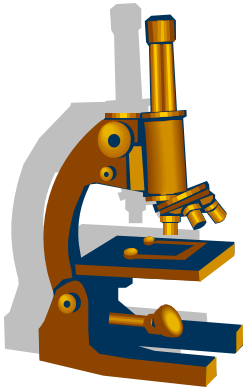
4.15 Management Reviews

- Predetermined schedule
- Includes
    - Results of internal audits
    - Lab proficiency tests
    - Assessment by external bodies
    - Corrective and preventive actions
    - Customer feedback, complaints
    - Quality control and training

Technical Requirements - Clause 5

5.0 Technical Requirements

- 5.2 human factors
- 5.3 accommodation and environmental conditions
- 5.4 test and calibration methods and method validation
- 5.5 equipment
- 5.6 measurement traceability
- 5.7 sampling
- 5.8 the handling of test and calibration items



Assessment is the Cornerstone of the Accreditation Process

- **Application**
- Provide Laboratory Quality Manual for Review, Application

- **Pre-assessment**
- Assessors visit ISO 17025/15189 – **in practice**
  - Work observed
  - Records examined (operating procedures etc.)
  - Establish competence of lab to perform performed analysis
  - Discuss any shortcomings
  - Discuss technical requirements
    - Uncertainty of measurement
    - Proficiency testing
  - Lab can carry out corrective actions before assessment
  - Assessors and labs agree on the **scope** of the assessment.

Source: Pakistan National Accreditation Council http://www.pnac.org

Full Assessment Procedure

Assessment

- Opening meeting - assessment team and lab representatives
  - Discussion of laboratory's quality system documentation: documented in-house procedures
  - Detailed observation of lab work
    - Lab manuals-calibrations
    - Examine data –uncertainty competence
- Closing meeting- Lead assessor summarizes
- Summary report - recommendations
  - Unconditional acceptance
  - Acceptance deferred until corrections made
  - refusal

Source: Pakistan National Accreditation Council http://www.pnac.org

Full Assessment Procedure

Post- assessment

- Evaluate corrective actions
- Visit to observe corrective actions
- Agreement on terms of accreditation
- Pay license

• Surveillance and reassessment

- First surveillance visit may be six months after the date of accreditation.
- Subsequent surveillance visits are carried out at yearly intervals.
- Full re-assessment in three years

• Extensions to scope- apply anew

Source: Pakistan National Accreditation Council http://www.pnac.org

Demonstrating Competence in the Laboratory is Important

Technical - Demonstrate competence for specific tests

- ILAC
- APLAC (regional) recognize accrediting bodies
- ISO/IEC 17025:2005
- Surveillance of ongoing performance by reassessment at periodic intervals by proficiency testing

Administrative-Submit quality manual-Technical staff matrix

Demonstrating Competence in the Laboratory is Important

Peer assessors
Technical procedures
Assessment
Deficiency

Competence - demonstrate the technical task
Procedures should be documented
Procedures should be followed

Address deficiency

Proficiency Tests should be performed twice per year
Specific tests that cover all matrices in 4 yrs

Interlaboratory and Proficiency Testing – Available Services

http://www.lgcpt.com/

http://www.forensic-testing.net/

http://www.nelac-institute.org/PT.php

http://www.labnetwork.org/actual_index.php?show=35

IUPAC Proficiency Testing

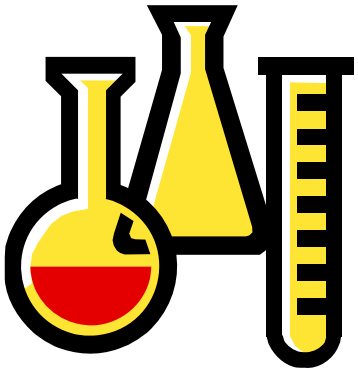
The *harmonised protocol for the proficiency testing of analytical chemistry laboratories* is a technical report issued by IUPAC. The international standardizing organizations - International, ISO, and IUPAC - cooperated to produce the International Harmonized Protocol for the Proficiency Testing of (Chemical) Analytical Laboratories. The Working Group that produced the protocol agreed to revise that Protocol in the light of recent developments and the experience gained since it was first published. This revision has been prepared and agreed upon in the light of comments received following open consultation.

http://www.iupac.org/objID/Article/pac7801x0145

Chemical Management Program Helps with Assessments

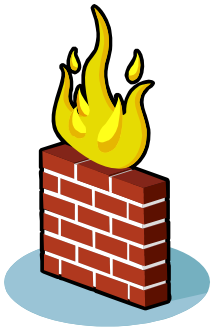
Chemical Management Elements

- Source reduction
- Procedure for chemical ordering and disposal
- Inventory and tracking
- Storage in stockrooms
- Access control
- Recycling of chemicals, containers and packages



Best practice: Access Control

- Proper training of chemical handling personnel



- Only trained and approved personnel
  - have access to stock room and keys
  - administrative privileges to inventory and database

- Locked doors and cabinets for controlled substances
  - Radioactive materials
  - Drugs and consumable alcohol
  - Explosives (special handling facility)
  - Dual use chemicals
  - Hazardous waste - high toxicity chemicals

Waste Management: General Guidelines

- Insure against leakage; dyke area if possible
- Label all chemicals, containers, vials
- Separate incompatible chemicals
- Keep gas cylinders separate
- Keep radioactive material separate
- Know how long waste can be stored
- Provide for timely pick-up

Wastes are Usually Characterized in Four Ways

- **Ignitability**
  - Liquid with Flashpoint <60C
  - Non-liquid that may start fire by friction, reaction
  - Ignitable compressed gas
  - Oxidizer
- **Corrosivity**
  - **pH >12.5 or pH <2**
  - **Corrodes steel at a specified rate**
- **Reactivity**
  - **Unstable, may detonate with heat or by chemical reaction**
  - **Reacts violently with water, may produce toxic gases**
  - **Is an explosive**
- **Toxicity**
  - **Toxic compounds may be leached from the waste in a landfill**

References

"Less is Better," American Chemical Society, Washington DC, 2003, available online: http://membership.acs.org/c/ccs/publications.htm

"School Chemistry Laboratory Safety Guide," US NIOSH Publication 2007-107, Cincinnati, OH, 2006, available on-line: http://www.cpsc.gov/CPSCPUB/PUBS/NIOSH2007107.pdf

"Prudent Practices in the Laboratory: Handling and Disposal of Chemicals," National Academy Press, 1995, available online: http://www.nap.edu/catalog.php?record_id=4911

Green

Analytical

Methodology

Curriculum Content

1. **Green Chemistry Background**
   - **What green chemistry is**

2. **Introduction to Green Analytical Methodology**
   - **How this is different from green chemistry**

3. **Where to Find Green Analytical Methods**
   - **Useful Internet sources are provided**

4. **Examples of Green Analytical Methods**
   - **Benefits and examples of green analytical methods**

1.0 Green Chemistry Background

- **Green chemistry is a science-based, nonregulatory, economically driven approach toward sustainable development**
  - **1987 United Nations report "Our Common Future" was a key event for green chemistry.**

1.1 What Green Chemistry is and What it Means

- ***Definition:*** **the use of chemistry techniques and methodologies that reduce or eliminate the use or generation of feedstocks, products, byproducts, solvents, reagents, etc. that are hazardous to human health or the environment**
  - ***From the American Chemical Society (ACS) Green Chemistry Institute***

1.1 What Green Chemistry is and What it Means – (Continued)

- **Twelve Principles of Green Chemistry provide a framework for scientists and engineers to use when designing new materials, products, processes and systems**

  - **They focus thinking in terms of sustainable design criteria**
  - **Six are applicable to green analytical methodology and are discussed on the next slide**

1.1 What Green Chemistry is and What it Means – (Continued)

1. Prevention of waste
2. Use safer solvents
3. Design for energy efficiency
4. Reduce use of derivatives
5. Use real-time analysis
6. Select safe substances to use

1.1 What Green Chemistry is and What it Means – (Continued)

- In summary, for analytical methods, green chemistry means using or designing methods that reduce or eliminate hazardous substances used in or generated by a method

1.2 Advantages of Green Chemistry – Financial and Sociological

- Faster and cheaper ways to work
- Cleaner and healthier environment
  - Cleaner air and water, enjoyable recreation areas, and conservation areas in nature
- Alternative reactions and separations can result in cost savings

1.3 Sources of Information on Green Chemistry

1. Green Chemistry Institute (GCI)
2. U.S. EPA Green Chemistry Web Site
3. Greener Educational Materials (GEMS)
4. Green Chemistry Network (GCN)
5. Green Chemistry Resource Exchange

1.3.1 – Green Chemistry Institute (GCI)

- **GCI, a part of the American Chemical Society, is the foremost source of information on green chemistry.**
  - **Link to it at www.GreenChemistryInstitute.org**
  - **Topics covered include:**
    - Mission, history, governance, chapter affiliates, staff members.
    - Conferences & Events – both future and past years.
    - Educational Resources – including books, online resources, and activities and experiments listed by grade level.
    - Grants to promote research in green chemistry.
    - Awards recognizing outstanding research in green chemistry.
    - Industrial innovation through application of green chemistry & engineering principles.

1.3.2 - U.S. EPA Green Chemistry Page

- **U.S. Government green chemistry source**
  - **Link to it at www.EPA.gov/greenchemistry**
  - **Topics covered include:**
    - **Basic information on green chemistry**
    - **EPA projects and programs**
    - **Software tools and literature such as:**
      - Green Chemistry Expert System
      - Green Chemistry Assistant
      - Green Chemical Alternative Purchasing Wizard

1.3.3 - Greener Educational Materials (GEMS)

- **Interactive collection of green chemistry education materials in an online searchable database**
  - **Link to it at http://greenchem.uoregon.edu/gems.html**
  - **University of Oregon project funded by National Science Foundation (NSF)**
  - **Search by keyword, category, or both**

1.3.4 – Green Chemistry Network

- **Website at Univ. of York Chemistry Dept.**
  - **Link to it at http://www.rsc.org/chemsoc/gcn/index.html**
  - **Facilitates education in green chemistry by**
    - Providing links to other organizations and government departments.
    - Organizing conferences / workshops and training courses.
    - Providing educational material for universities & schools.
    - Newsletters and books with close links to the Green Chemistry journal
    - Providing prizes and awards for companies & university researchers.

1.3.5 - Green Chemistry Resource Exchange

Sponsored by the American Chemical Society (ACS)

A database of information on numerous green chemistry categories

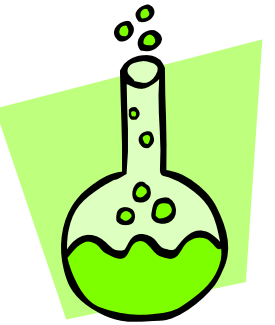
- **Link to it at http://www.greenchemex.org**
  - Categories of information include:
    - Chemicals/Materials,
    - Designing Safer Chemicals,
    - Greener Feedstocks,
    - Greener Process,
    - Greener Reagents,
    - Greener Solvents and
    - Industries/Sectors.

2.0 Introduction to Green Analytical Methodology

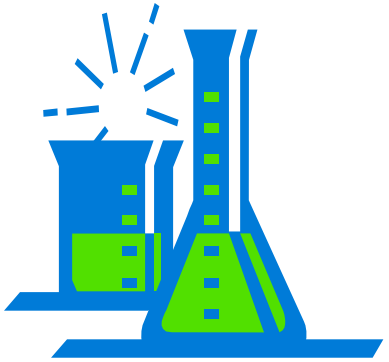
- Analytical chemistry has not been a focus of green chemistry until very recently
- Green analytical methods also have not been easy to identify
  - They must meet one or more of the twelve principles of green chemistry listed on the GCI web site

2.1 What Makes an Analytical Method Green?

- Since "green" was not usually used to describe analytical methods literature searches for green analytical methodology usually fails to find green developments in analytical chemistry



A 2007 article in Chemical Reviews defines "what makes a method green" (Dr. Keith)



This article also serves as a basis for discussing "Green Analytical Methodology"

A copy is provided on your CD-ROM

2.2 Defining Green Analytical Methodology

- **Dr. Keith's definition: "The *use of analytical chemistry techniques and methodologies that reduce or eliminate solvents, reagents, preservatives, and other chemicals that are hazardous to human health or the environment and that also may enable faster and more energy efficient analyses without compromising required performance criteria.***

- **This definition encompasses three key concepts**
  - **<u>Primary consideration</u> for selecting or modifying an analytical method is that it be able to meet specified performance criteria**
    - These criteria are "measurement quality objectives" (MQOs).
    - To use a method that fails to meet MQOs would result in wasted time and money because the analytical data produced by it would not be able to be used.

2.2 Defining Green Analytical Methodology – (Continued)

- **Second** key concept is to use less toxic or hazardous solvents or chemicals in sample preparation and analytical measurements
  - If possible replace hazardous chemicals with less hazardous chemicals.
  - If hazardous chemicals can't be replaced then use smaller amounts of them
  - Sample preservation and/or preparation steps are best places to look for opportunities

2.2 Defining Green Analytical Methodology – (Continued)

- **Third key concept is to decrease the amount of time and/or energy required to perform an analysis**
  - **Accomplished by using smaller samples or by using in-situ measurements**
    - Example: make method more sensitive so less sample is needed for analysis
    - Example: replace a method requiring sample preparation (for example, atomic absorption) with in-situ analysis (for example, x-ray fluorescence)

2.2 Defining Green Analytical Methodology – (Continued)

Biodiesel Factory in Monroe, Georgia - 2009

- **Dr. Keith'sPersonal Example**
  - **Problem: Try many different reactions to make biodiesel using new technology**
  - **Solution: Instead of using typical 300 mL reactions he used 3 mL reactions.**
    - **Saved chemical costs**
    - **Faster analysis**
    - **Saved time**
    - **Only needed 1 uL sample for GC analysis**

2.3 Advantages of Green Analytical Methods – Financial and Sociological

- **Green analytical methodology usually results in financial advantages**

- **Green analytical methods reduce health and safety hazards for the analysts**

- **Green analytical methods reduce amounts of toxic chemicals into the environment**

3.0 Where to Find Green Analytical Methods

NEMI
National Environmental Methods Index

- **The best and easiest way to find green analytical methods is to use the National Environmental Methods Index (NEMI).**
- **Go to www.NEMI.gov**
  - Free Internet-searchable database of environmental methods
  - Has over a thousand methods in it and is continuously being improved and enlarged.
    - Dr. Keith was the initial project manager of NEMI.

3.1 Green Analytical Methods Capability in NEMI

- Information Covered Here
  - Background and construction of NEMI information is provided so that students will understand its purpose and advantages
  - The “business rules” for determining greenness profiles of analytical methods are described

  - Next, examples of searches provide direct comparisons of methods that are green versus those that fail greenness profile criteria.
  - Causes of failure to meet greenness profile criteria are also discussed with examples

3.1.1 Green Analytical Methods Business Rules and Their Application in NEMI

- **Greenness profiles were developed from "greenness" acceptance criteria**
- **Four US EPA profile acceptance criteria used:**
  1. **PBT (persistent, bioacculumative, & toxic)**
  2. **Hazardous**
  3. **Corrosive**
  4. **Waste**

- **Profiles were developed by 25 experts**
- **Energy criterion was desired but was too difficult to rate within method protocols**

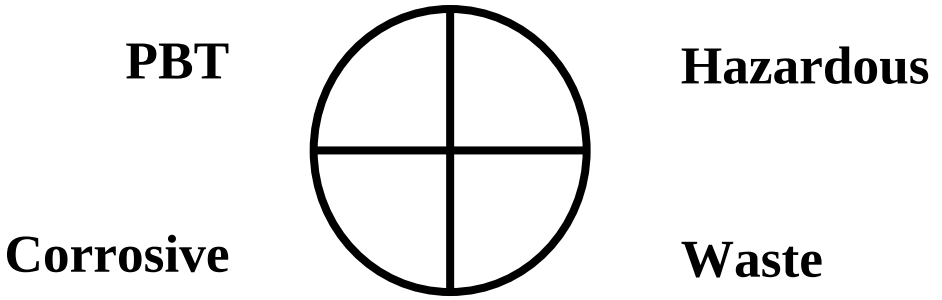
3.1.1 Green Analytical Methods Business Rules and Their Application in NEMI – (Continued)

- **Instead of "more green" a "less green" system was used**
- **A method is defined as "less green" if**

1. **a chemical used in the method is listed as a persistent, bioacculumative, & toxic chemical, as defined by US EPA,**
2. **a chemical used in the method is listed on US EPA's hazardous waste lists,**
3. **pH during the analysis is <2 or >12, (*corrosive*) or**
4. **the amount of waste generated is >50 g with a sample's analysis.**

3.1.1 Green Analytical Methods Business Rules and Their Application in NEMI – (Continued)

- A Four-quadrant circle developed for easily recognized summary of greenness profile



- If a method is NOT "less green" (i.e., is "more green") then a quadrant is filled in with green.

3.1.2 Examples of Green Analytical Methods Searches and Uses in NEMI

- **Data for methods in NEMI was used to generate greenness profiles. Data included:**
  - **the sample size that is worked up for analysis,**
  - **chemicals used and amounts (to which the persistent, bioaccumulative, & toxic chemical and hazardous acceptance criteria Rules #1 and #2 are applied),**
  - **pH (to which the corrosive acceptance Rule #3 is applied), and**
  - **waste amount generated (to which the waste acceptance Rule #4 is applied)**

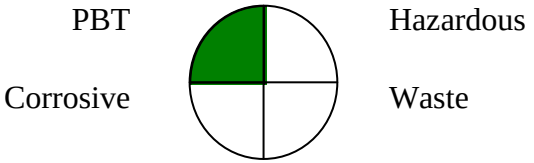
3.1.2 Examples of Green Analytical Methods Searches and Uses in NEMI – (Continued)

- **Example – find a method with US EPA regulatory acceptance for the insecticide Aldrin in water with detection level < 0.2 ug/L (ppb) and relative standard Deviation (RSD) < 20%**
  - **Search of NEMI finds two acceptable methods:**
    - **EPA Method 525**
    - **EPA Method 505**

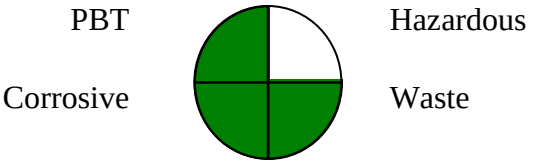
3.1.2 Examples of Green Analytical Methods Searches and Uses in NEMI – (Continued)

- Method 525.2 has only the PBT quadrant filled-in green while Method 505 has the corrosive, PBT, and Waste quadrants filled-in green
  - **Method 505 is the "greener" of the two.**

(EPA Method 525.2)



(EPA Method 505)



3.1.2 Examples of Green Analytical Methods Searches and Uses in NEMI – (Continued)

- **Why is Method 505 "Greener" than 525.2?**
  - **Method 525.2 uses ethyl acetate, methylene chloride, and methanol to extract 1L of water to which HCl is added to reduce pH to < 2 so more than 50 g waste is generated**
  - **Method 505 uses only 2 mL of hexane to extract 35 mL of water with no pH adjustment so < 50 g is generated**
    - **Therefore, only the hazardous quadrant is left uncolored green (hexane is on US EPA's TRI pollutant list)**

3.1.3 Green Analytical Methods Greenness Profile Failures Causes and Examples

- **More than 2/3 of methods in NEMI had sufficient information to be evaluated (560 of them)**
  - **Three most common reasons why greenness of methods could NOT be evaluated were:**

    1. No information on sample size or chemicals used in a method

    2. Full method was not available to be used for greenness profile evaluations

    3. Incomplete information in a method – parts were referenced as being in another method

3.1.4.1 – Waste Criterion Examples

- **The most frequent cause of a method to be "less green" was a failure to meet the requirements of the Waste greenness rule; that is, the method generated more than 50 g of waste for every sample analyzed.**

- **Two-thirds of the evaluated methods failed the waste greenness rule.**

  - **Of these methods, the ones testing for organic compounds frequently used large sample sizes and used relatively large amounts of solvents for extraction.**

3.1.4.1 – Waste Criterion – 3 Examples of Methods for Organics That Fail

- EPA Method 625 – uses 430 mL of methylene chloride to extract 1 L of water
- USGS Method O-1104 uses 75 mL of hexane to extract 1 L of water
- ASTM Method D5475 uses 22 mL of methyl tert-butyl ether and 441 mL of methylene chloride to extract 1 L of water

Water is contaminated and exceeds 50 g of waste plus the solvents in each case exceed 50 g

3.1.4.1 – Waste Criterion – 3 Examples of Methods for Organics That Pass

- Standard Methods 6610B injects 1 mL of a 25 mL aliquot of water for HPLC analysis
- EPA Method 502.2 purges 5 mL of water with inert gas which is analyzed by GC
- Strategic Diagnostics Method 73310 uses less than 0.1 mL water analyzed by the ELISA immunoassay technique

In each case < 50 g waste is generated

3.1.4.1 – Waste Criterion – 3 Examples of Methods for Inorganics That Fail

- Standard Method 3120B where 8 mL of HNO_3 and 10 mL of 50% HCl are added to 100 mL of water for ICP analysis
- DOE (Department of Energy) Method MM800 where 118 mL of various acids are added to 100 mL of water for uranium analysis by ICP-MS
- USGS (US Geological Survey) I-3840 where HCl and other reagents are added to 100 mL of water for sulfide analysis by iodiometric titration

Water is contaminated and exceeds 50 g of waste plus the solvents in each case exceed 50 g

3.1.4.1 – Waste Criterion – 3 Examples of Methods for Inorganics That Pass

- EPA Method 200.8 which uses only 20 mL of acidified water for analysis of metals by ICP-MS (although 1 L of water is collected)
- EPA Method 326.0 which uses 0.25 mL of a 10 mL water sample for bromide analysis
- USGS Method I-3239 which uses a 10 mL water sample to which 1 mL of 20% ammonium chloride is added for cobalt analysis by FAA spectrometry

In each case < 50 g waste is generated

3.1.4.2 – Hazardous Chemicals Criterion Examples of Methods that Fail

- Second most frequent reason for greenness profile failure is use of hazardous chemicals in a method
  - EPA Method 410.1 for COD (Carbon Oxygen Demand) uses a 50 mL water sample with $HgSO_4$ solution, potassium dichromate, and other chemicals
  - USGS Method I-1232 for Cr VI uses a 100 mL water sample with ammonium pyrrolidine dithiocarbamate and Methyl Isobutyl Ketone extraction
  - EPA Method 605 for benzidines uses a 1 L water sample, 270 mL of chloroform and other chemicals

These are all hazardous chemicals used in the method

3.1.4.2 – Hazardous Chemicals Criterion Examples of Methods That Pass

- **In contrast, examples of** methods that pass the hazardous chemicals greenness criterion **include the following:**
  - **USGS Method I-3152 for calcium uses a 10 mL water sample with 1 mL of lanthanum chloride solution that is analyzed by flame Atomic Absorbtion (AA)**
  - **IDEXX Method SimPlate for heterotrophic bacteria uses a 10 mL water sample and incubation of the bacteria**
  - **EPA Method 524.2 for volatile organic compounds uses 40 mL of water that is purged with an inert gas to trap the analytes on a solid sorbent material for GC-MS analysis.**

Non-hazardous chemicals are used with these methods

3.1.4.3 – PBT Criterion Examples of Methods that Fail

- **Only 5% of NEMI methods failed PBT greenness criterion and 100% of those also failed the hazardous chemical criterion (only tiny amounts of Hg used in last 2 examples)**
  - **EPA Method 335.2 for cyanide in which sulfide is removed from the water sample with a scrubber containing 25 mL of 3% lead acetate solution**
  - **ASTM Method D1252B for COD in which 1.5 mL of a digestion solution that contains mercuric sulfate is added to a 2.5 mL sample of water in a microscale analysis**
  - **Standard Methods Method 3500-VB, where vanadium is measured spectroscopically after 1 mL each of ammonium persulfate-phosphoric acid, gallic acid, and mercuric nitrate solutions are added to 10 mL of a water sample.**

Persistent, bioaccumulative, & toxic chemicals are in red

3.1.4.4 – Corrosive Criterion Examples of Methods That Fail

- ~20% of NEMI methods fail this criterion
- Sample pH adjusted to either < 2 or > 12
  - EPA Method 200.8 for metals in water analysis by ICP-MS, where the pH of the 20 mL sample prepared for analysis is reduced by nitric acid to pH <2
  - EPA Method 604 for phenols in water by GC where pH of a 1 L sample of water is raised to >12 using sodium hydroxide prior to extraction with methylene chloride and then lowered to <2 using sulfuric acid solution for a second extraction
  - Standard Methods Method 6251B for haloacetic acids and trichlorophenol by GC-ECD, in which the pH of a 30 mL water sample is adjusted to <0.5 using 98% sulfuric acid

Corrosive chemicals are in red

3.2 Other Sources of Information on Green Analytical Methods

- Relatively few other sources currently available
  - Many sources of information on “green chemistry” but few yet on “green analytical methodology”

- This is an emerging sub-discipline of green chemistry
- This curriculum is devoted to helping define and grow green analytical methodology

3.2.1 Application of the Principles of Green Chemistry in Analytical Chemistry

- **Institute of Chemistry, Tallinn University, Estonia**

http://old.iupac.org/publications/pac/2006/pdf/7811x1993.pdf

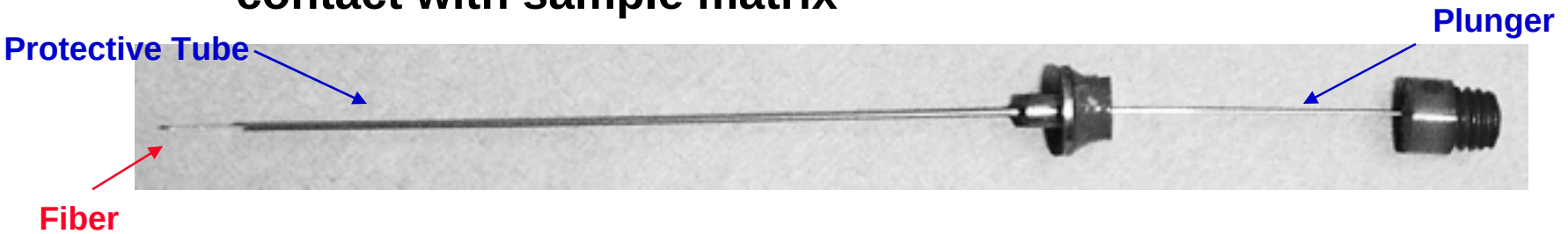
  - **Review article provides an overview of green analytical methodology techniques**

- **Relation between green chemistry and green analytical chemistry**
- **Review of separation methods**
- **Advantages of Electrophoresis**
- **Micronization in Separation Methods**
- **Alternative solvents**

3.2.2 – Green Analytical Chemistry – Solid Phase Microextraction

http://alpha.chem.umb.edu/chemistry/ch471/documents/GreenAnalyticalChemistry.pdf

- PowerPoint Slide Presentation
  - Summarizes principles, advantages and techniques for solid-phase microextraction (SPME)
  - Fibers coated with an extracting phase are placed in contact with sample matrix



  - After equilibrium is established the fiber is transferred to an injection port of a GC or HPLC instrument for desorption and analysis

3.2.3 GC Challenges and Green Analytical Chemistry

http://www.pjoes.com/pdf/11.2/185-187.pdf

- Polish Journal of Environmental Studies
  - Summarizes ways to advance green analytical methodology when using gas chromatography
    - No solvent used for sample preparation for water samples
    - Sorption and thermal desorption for air samples
    - High Speed (Fast) gas chromatography
  - Advantages of each of these techniques are discussed

4.0 Live Real-time Green Analytical Methods Using the Internet

- Principles of searching and applying green analytical methodology in a laboratory are demonstrated in the following slide using NEMI
- To accomplish this demonstration you must be connected to the Internet and be connected to http://www.nemi.gov
- Example uses a search for green analytical methods for phosphorus in water
- These same principles can be applied to any analyte that has methods included in the NEMI database.
- Remember, the first principal is that no matter how "green" a method is, if it doesn't satisfy the analytical performance criteria that are needed, then it is not a useful method and should not be selected.

4.1 Example - Phosphate in Water

Objective: Select a Green Analytical Method with MQOs (Measurement Qualitative Objectives) of:

- **Detection Level of 0.01 mg/L or less**
  - **0.01 mg/L is also the same as 0.01 parts per million (ppm) or 10 parts per billion (ppb)**
- **Precision with RSD of 10% or less**
  - **Standard Deviation (SD) and Relative Standard Deviation (RSD) are used to express precision and NEMI uses RSD for consistency**
- **Bias (as % Recovery) of 10% or less**
  - **Recovery would be + or – 10% or from 90 to 110%**

4.1 Phosphate in Water – (Continued)

- **From www.nemi.gov enter "phosphate"**
  - **Select "WATER" as medium and then Search**
  - **Evaluate table of methods first for sensitivity and greenness profiles**
    - **Note several methods have acceptable detection levels but insufficient information for greenness profiles**
  - **Next evaluate methods for precision & bias**
    - **EPA 300.0 and Hach 9048 methods qualify best**
  - **Finally consider cost and instrument availability**

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