Topic 1:

Analytical Chemistry

Introduction-I

- Study of methods for determining the composition of substances
    - qualitative (what?)
    - quantitative (how much?)
- Chemical analysis includes any aspect of the chemical characterization of a sample material.
- Analytical Chemistry is basically study of testing methods for determining composition of substances. This determination may be limited to qualitative results or quantitative estimation. Qualitative means what substances are present in composition.
- Whereas the percentage of components in a mixture is called quantitative estimation.
- Chemical analysis includes any aspect of chemical characterization, starting from collection of sample, extraction, sample preparation, instrumental analysis to statistical evaluation of collected data.

Detection / Qualitative:

Does the sample contain substance X?

Identification / Qualitative:

What is the identity of the substance in the sample?

Estimation / Quantitation:

How much of substance X is in the sample?

Separation:

- How can the species of interest (analyte) be separated from the sample matrix for better quantitation and identification? Quality control in the process industries
    - of starting materials
    - of intermediates
    - of products
- Environmental analysis
    - Monitoring and control of pollutants
- Clinical and biological studies
    - Measurement of nutrients
    - Measurement of drug levels in body fluids
- Geological assays
    - Measurement of metal concentrations in ores and minerals
    - Determination of oil/gas concentrations in rocks
- Fundamental and applied research
    - Chemical engineering: how much conversion (or separation) do we obtain under specific conditions?
    - Organic molecule synthesis: what compound have we made?

Topic 2

Analytical Chemistry

Introduction-II

In this module we will discuss about steps in analysis.

We must understand here the two terms; matrix and analyte

An analyte, component (in clinical chemistry) or chemical species, is a substance or chemical constituent that is of interest in an analytical procedure.

While in chemical analysis, matrix refers to the components of a sample other than the analyte of interest. The matrix can have a considerable effect on the way the analysis is conducted and the quality of the results obtained; such effects are called matrix effects.

- **Sampling**
    - Grab and composite
    - Types of sampling pattern
- Sample preparation
    - Dilution / concentration
    - Wet digestion
    - Dry ashing
- Selection of Analytical Methods
    - Standard analytical methods

Validated Method

First step in analysis is Sampling. The results of your analysis simply depend upon the sampling. Sampling technique, sampling type and sampling pattern depend upon the matrix, location, variability of constituents, bulk of bags or product etc.

Sample may collect at some particular time and location are called grab sample or many grab samples may combine to form composites.

From 100 of Kg, 1000 of litters or acres of land we collect the sample in grams. And to analyse we have to finalize just 2-3 gram of sample, or maximum 100 mL of liquid. Some time sample need dilution while some time we have to concentrate a sample. To analyse we have to digest or extract our analyte from the sample. This is called sample preparation.

Then we have to select an analytical method, that may be a standard method or a non-standard laboratory developed validated method. Selection of method depend upon variability of constituents in matrix, concentration of analyte in the sample, and availability of proper instrumentation.

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- **Analysis**
    - Wet analysis
    - Instrumental analysis
- Instrument analysis
    - calibration of apparatus and equipment,
    - SOPs, STMs,
    - IQ/OQ/PQ of equipment
- Evaluation of analytical data
    - Sample and Population,
    - Significant figures,
    - Mean, Mode, Median,
    - UoM, Std.Dev., Variance etc)
- Reporting of results
- We may use an instrumental method of analysis or wet analysis. Certain wet analysis methods are acid base titration, redox titration, complexometric titration or gravemetric analysis methods.

- If we choose instrumental method, the instrument should be calibrated. Should follow proper standard operating procedure and standard testing methods. Instrument should be installed, operated and performed according to standard specifications.
- And the last but not least is statistical evaluation of analytical data. We will learn in future modules about sample and population of analytical data. Significance of significant figures. Calculation of mean, median and mode of available data and measurement of uncertainty, standard deviation and variance etc.
- Finally we report our analytical results along with standard specifications, using proper units of measurements and all related informations or logos on report.

Topic 3:

Analytical Chemistry

Introduction-III

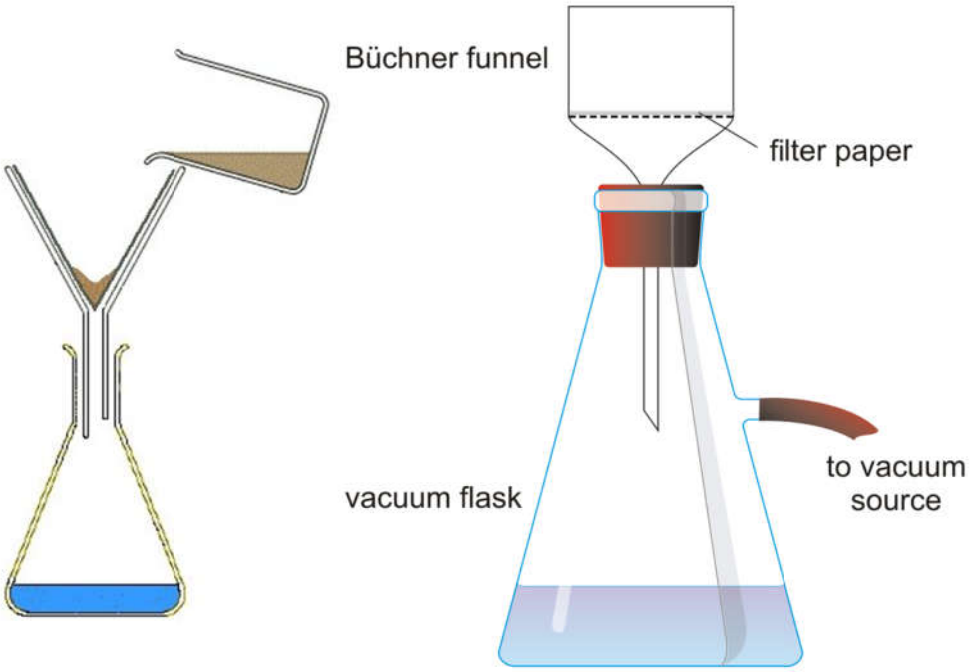
In current module we will discuss about separation techniques; a brief introduction.

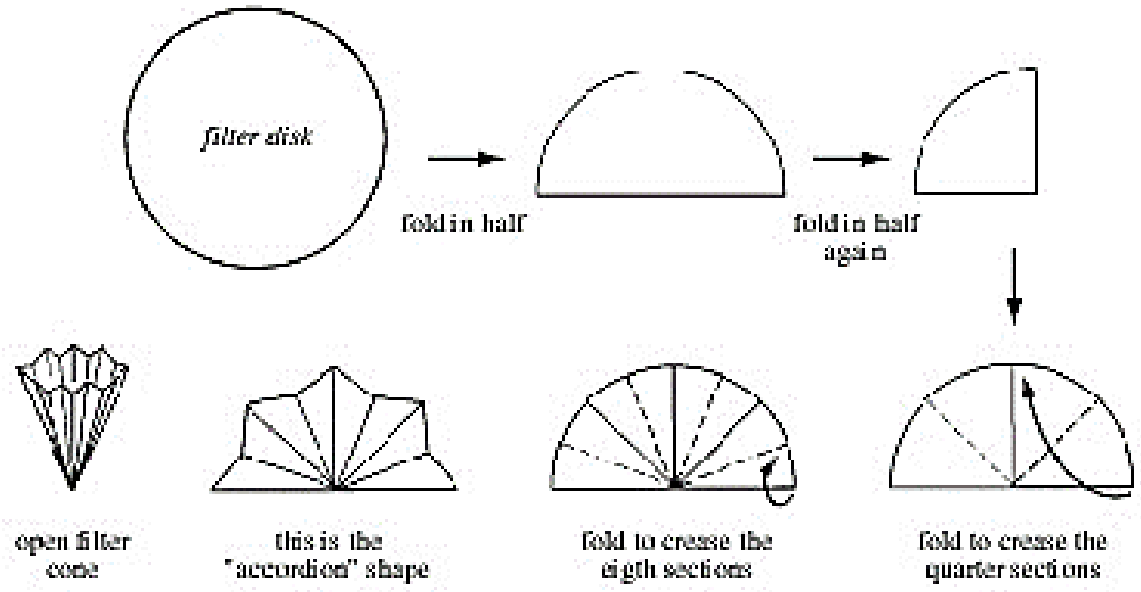
As a part of sample preparation we have to separate our analyte in first phase. Our matrix may be gas, solid, liquid or semi solid. Our analyte may be soluble or suspended in matrix. First we have to start with separation or semi purification.

- Filtration
    - To separate solid from liquid
- Sublimation
    - To separate solid from solids
- Solvent Extraction
    - To separate solvents between two immiscible liquids

- **Solid Phase Extraction**
    - **To separate soluble substances from liquid samples**

Separation Techniques

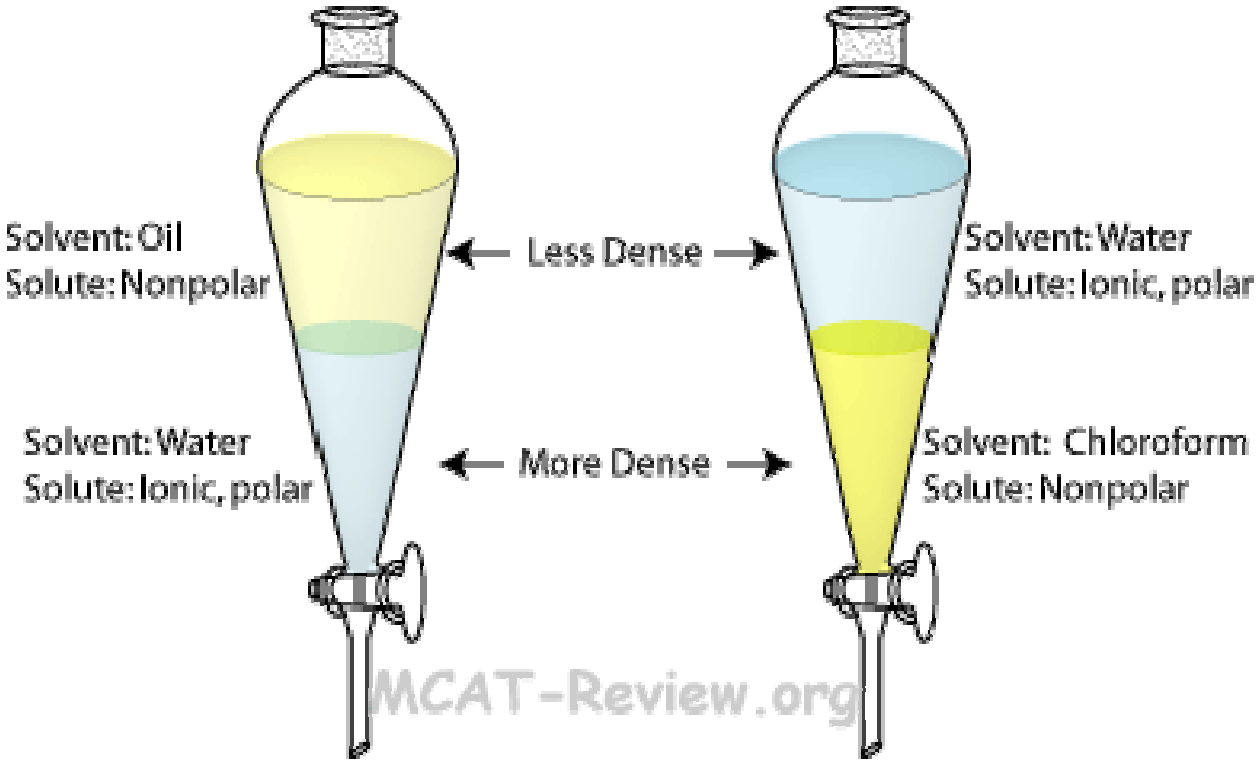


- 

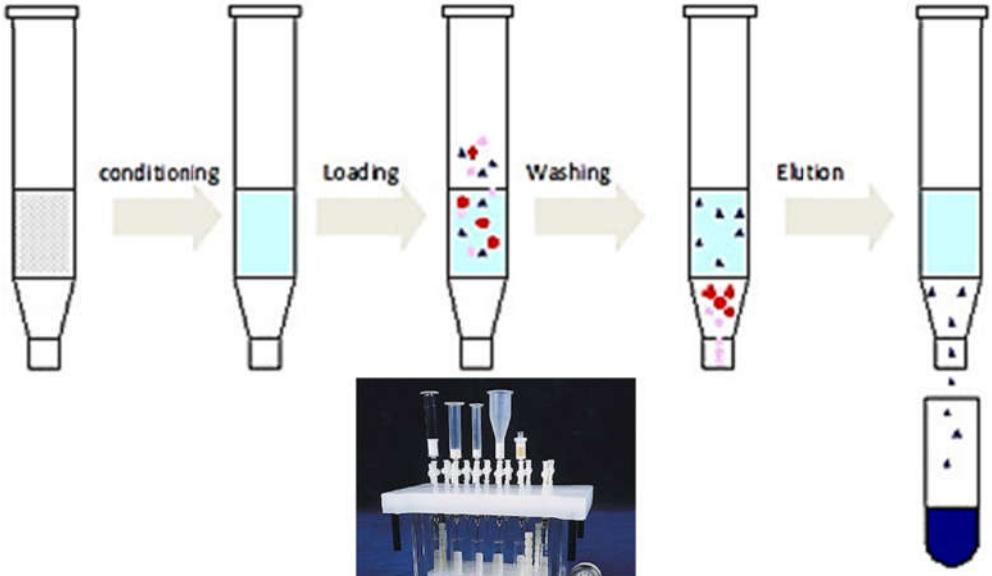
Filtration

- To separate solid from liquid

- Sublimation
    - To separate solid from solids
- Solvent Extraction
    - To separate solvents between two immiscible liquids
- Solid Phase Extraction
    - To separate soluble substances from liquid samples
- To separate solid from solid sublimation can be used as an analytical technique.



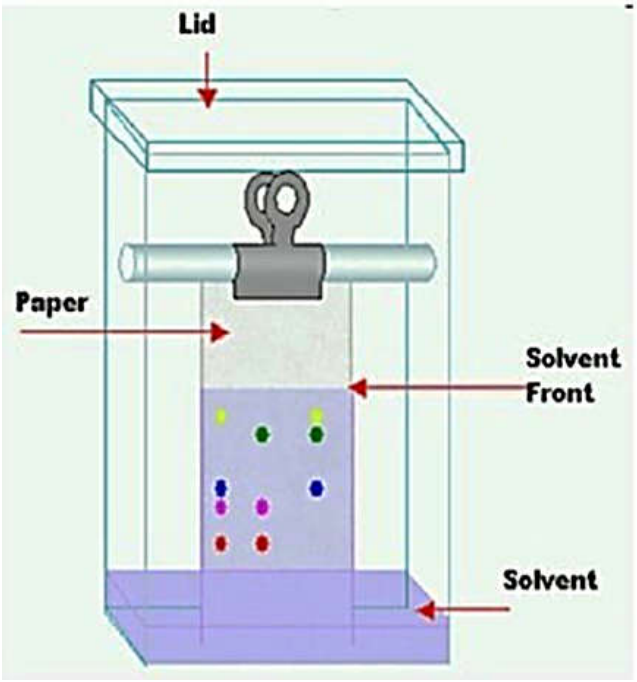
Separation Techniques

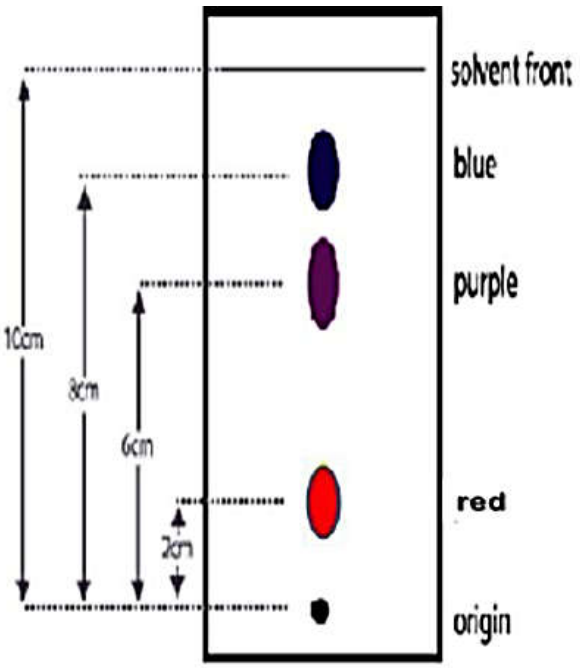


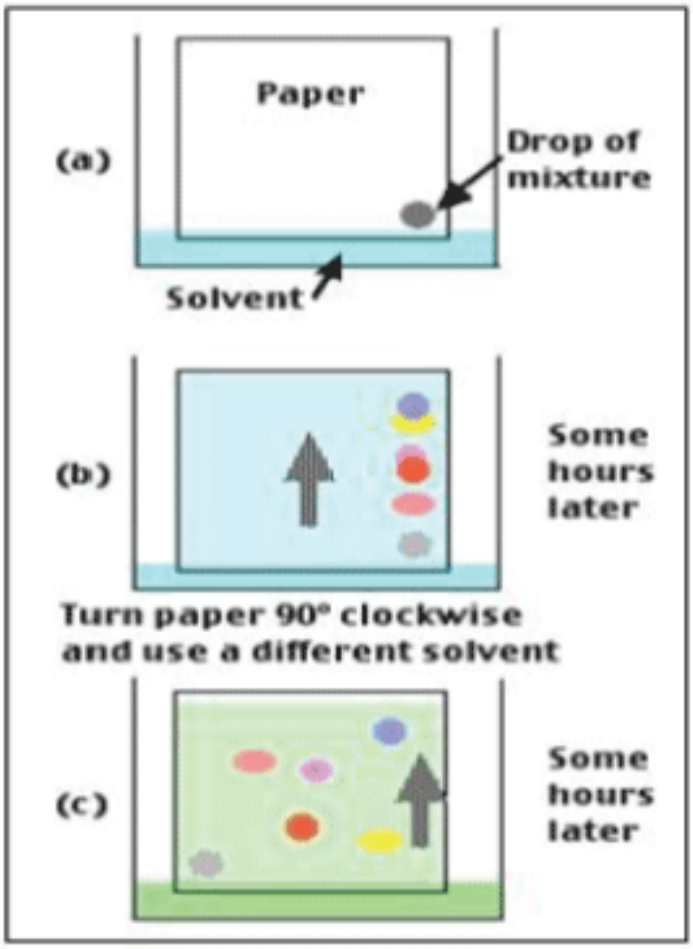
Chromatographic techniques

- Types of chromatography
- Paper chromatography (1 and 2D)
- Thin layer chromatography
- Column chromatography

- **Instrumental Techniques**
  - **HPLC (high performance liquid chromatography)**
  - **GC (Gas chromatography)**







Chromatographic techniques

- Types of chromatography
- Paper chromatography (1 and 2D)
- Thin layer chromatography
- Column chromatography

- **Instrumental Techniques**
  - HPLC (high performance liquid chromatography)
  - GC (Gas chromatography)

Topic 4:

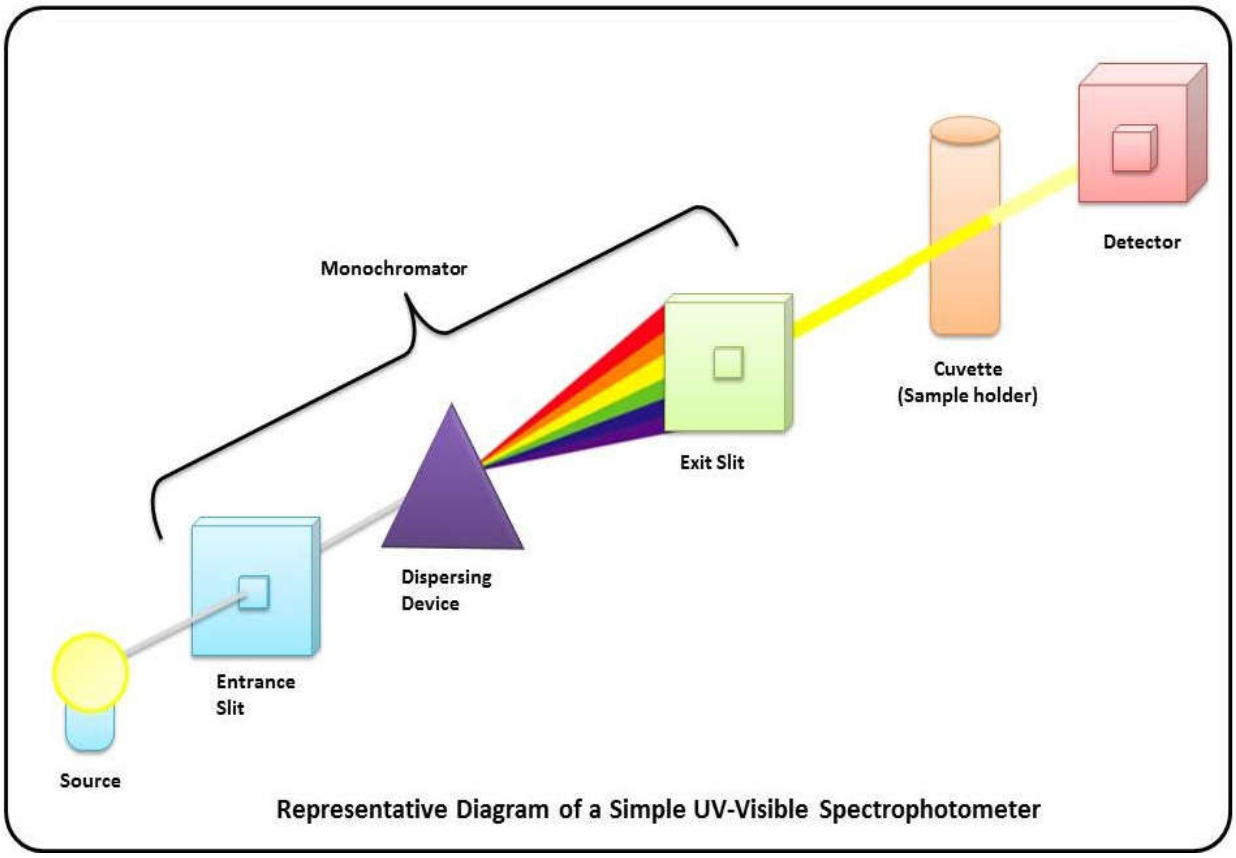
Analytical Chemistry

Introduction-IV

$$A = log_{10} \frac{I_o}{I} = \varepsilon lc$$

All the spectroscopic techniques use certain kind of electromagnetic radiations and are

based on Beer Lambert law. These are basically two laws; one connected to absorbance with Transmittance; the lambert law and second discuss relation of absorbance with concentration of sample; that is Beer's law.



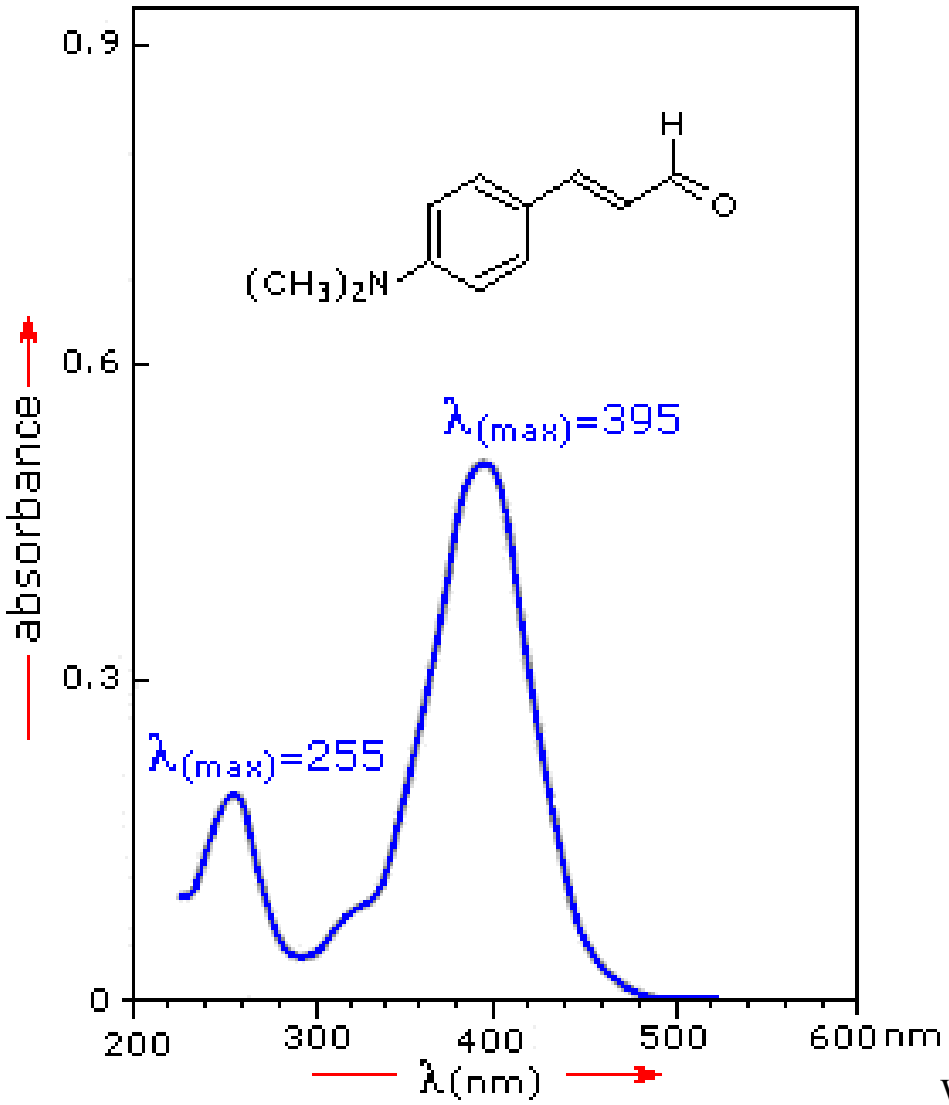
Representative Diagram of a Simple UV-Visible Spectrophotometer

A light beam of particular wavelength when passed through a sample decreased in intensity because it either absorb or distorted and don't reach to the detectors. The particular part of the radiation that absorbed reflect certain characteristics of our sample and molecule.

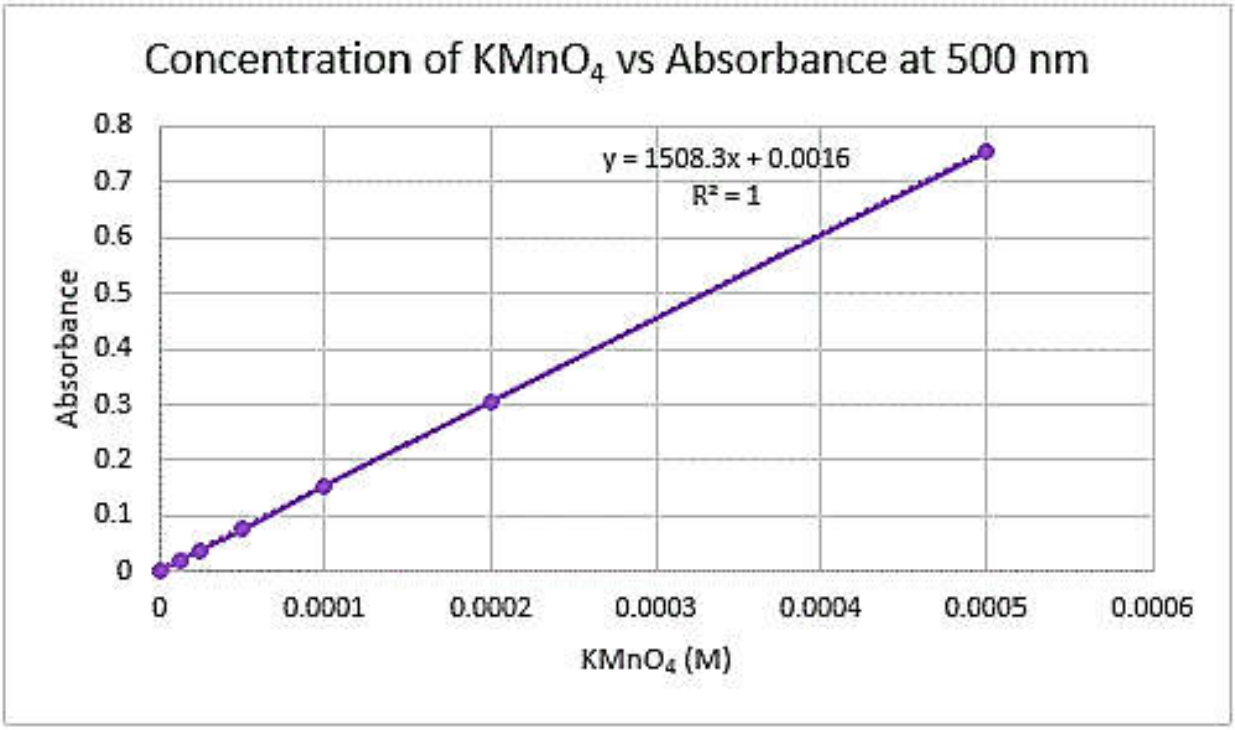
- **UV Spectroscopy**
    - **To find wavelength**
    - **To estimate concentration of unknown in sample**
- **IR Spectroscopy**
    - **Use to evaluate functionalities in an Organic molecule**
- **NMR spectroscopy**

- **On basis of magnetic properties define certain nuclei**

- There are different spectroscopic techniques available in market to solve our different analytical problems. The most widely used technique is UV Spectroscopy. That is basic instrument found in food and drug analysis laboratories.



We use this technique for either finding out wavelength maximum of any molecule or use it for evaluation of concentration. N,N-dimethyl cinnamaldehyde



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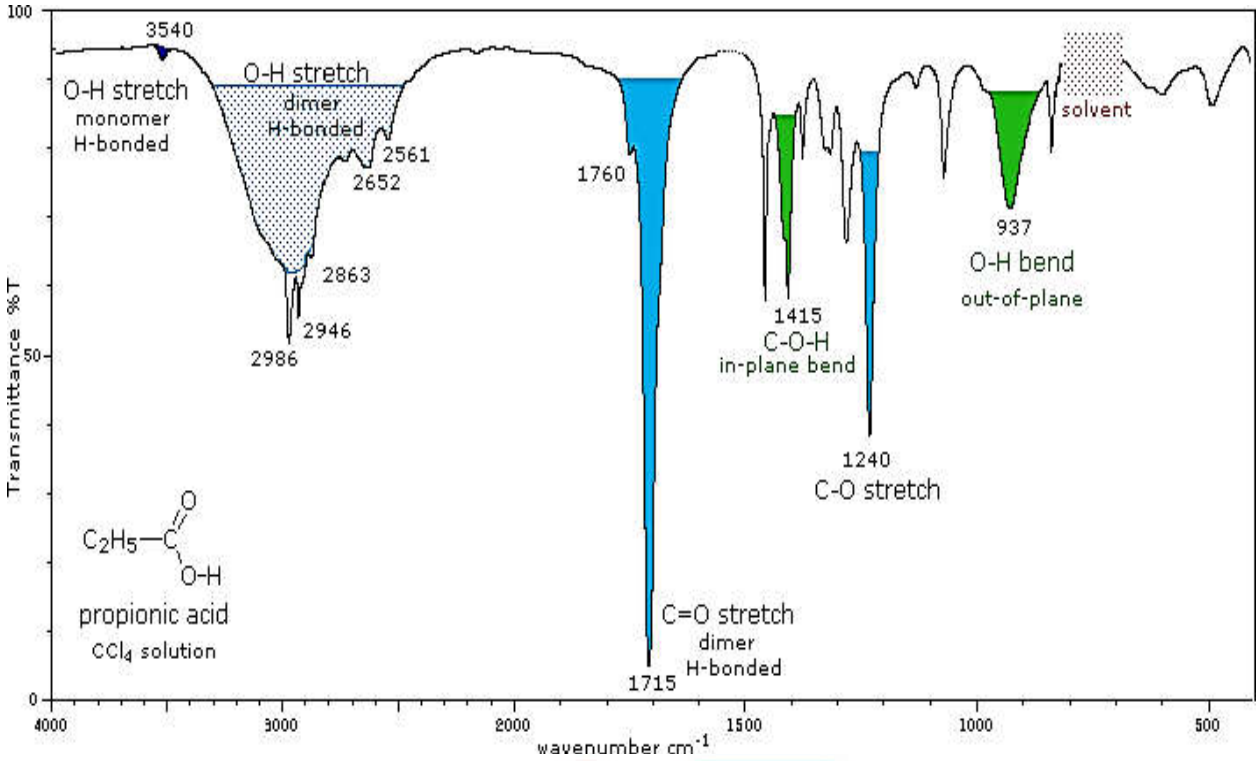
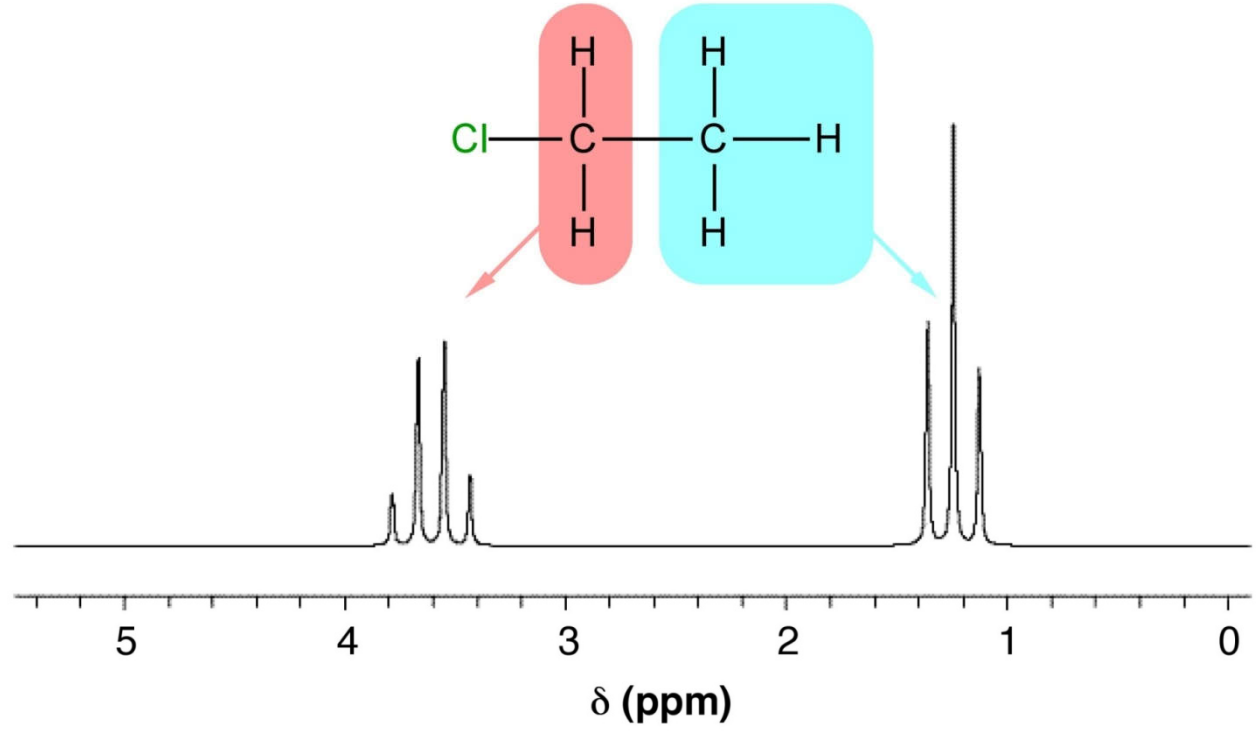
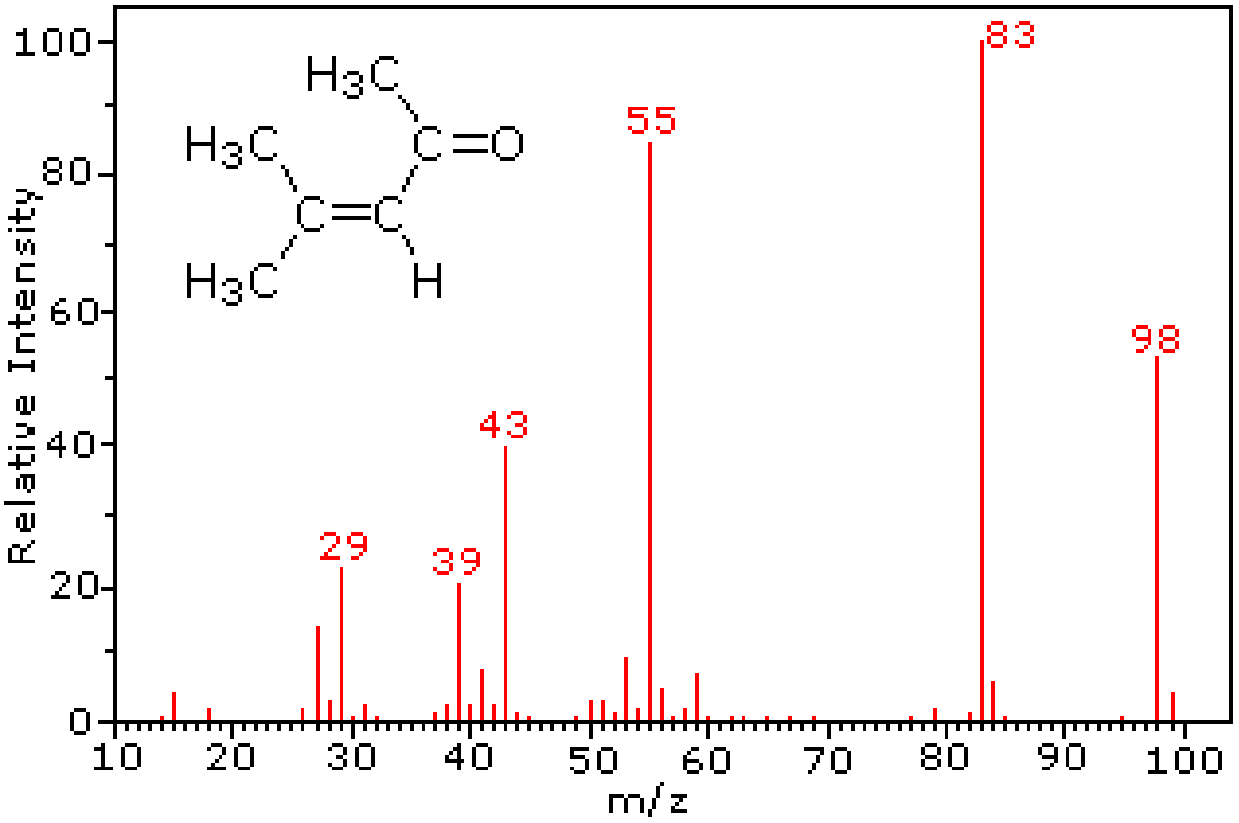
- Another spectroscopic technique is IR Spec.

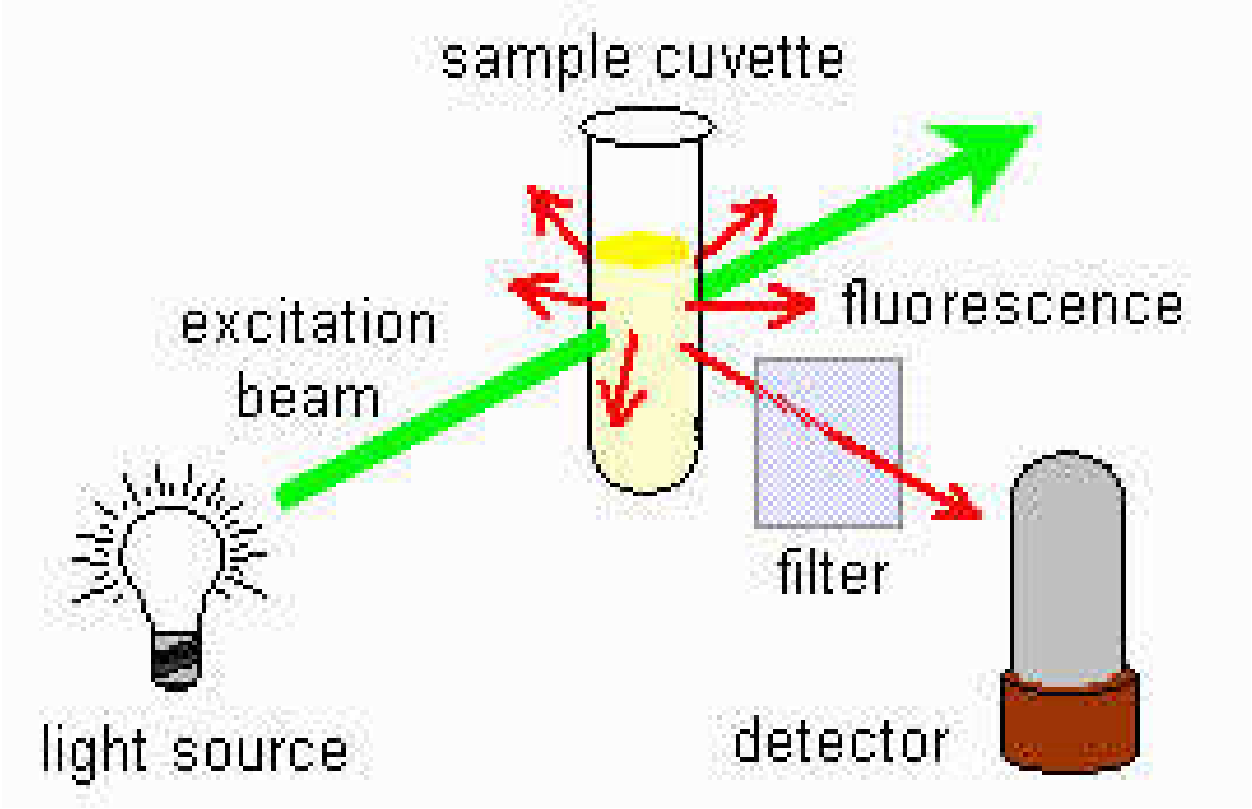






Mass Spectrometry

- **Used to evaluate mass of separated molecules**
- **Used as a detector**
- **Atomic Absorption spectroscopy**
- **FAAS, GFAAS**
- **Atomic fluorescence spectroscopy**
- **Evaluate certain organic molecules**
- **Atomic Emission spectroscopic**
- **ICP OES, ICP MS**



- Mass Spectrometry
- Used to evaluate mass of separated molecules
- Used as a detector
- Atomic Absorption spectroscopy
- FAAS, GFAAS
- Atomic fluorescence spectroscopy
- Evaluate certain organic molecules
- Atomic Emission spectroscopic
- ICP OES, ICP MS
-

Topic 5:

Analytical Chemistry

Introduction-IV

Spectroscopy

- Study of light is called Spectroscopy
    - UV Spectroscopy
    - IR Spectroscopy
    - NMR Spectroscopy
    - Mass Spectrometry
- There are different spectroscopic techniques available in market to solve our different analytical problems. The most widely used technique is UV Spectroscopy. That is basic instrument found in food and drug analysis laboratories.

Spectroscopic techniques

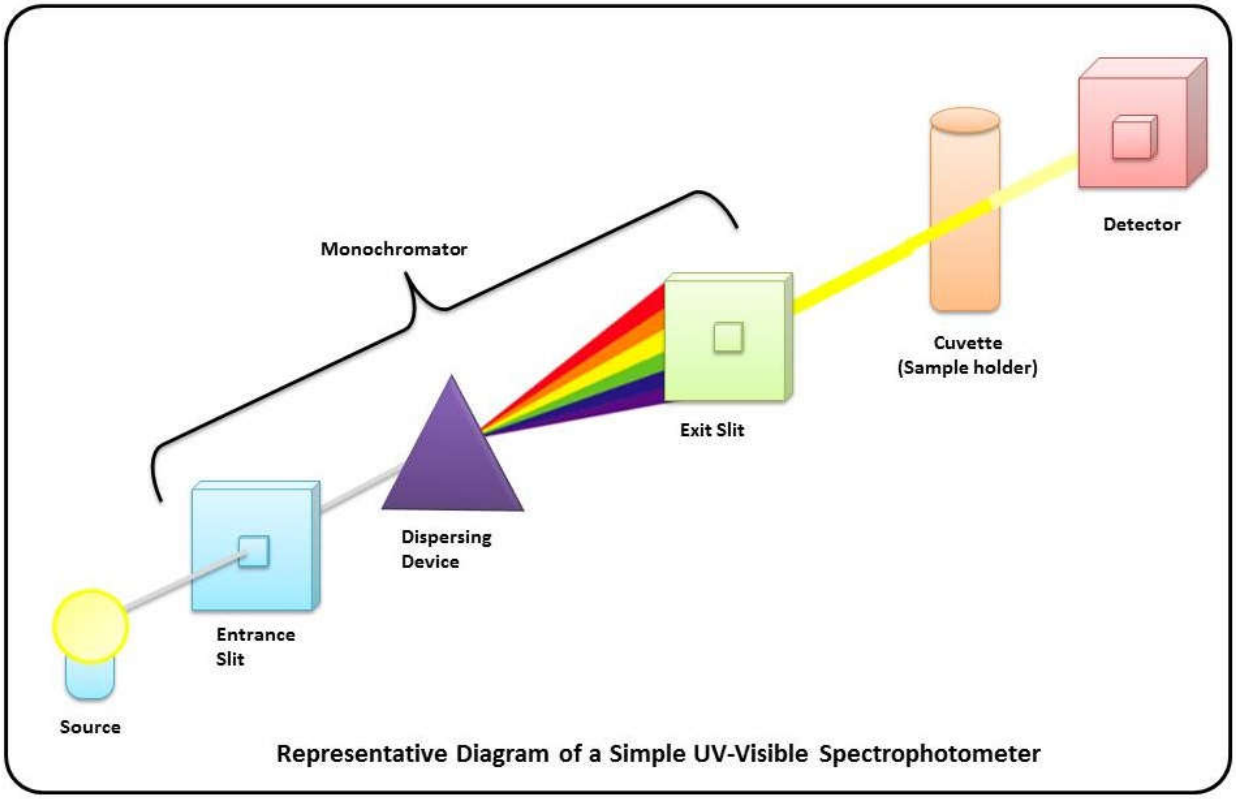
Beer Lambert Law

$$A = log_{10} \frac{I_o}{I} = \varepsilon lc$$

I_0 = Incident light
I = Transmitted light
l = path length
C = Concentration
ε = Molar Absorptivity Constant

All the spectroscopic techniques use certain kind of electromagnetic radiations and

are based on Beer Lambert law. These are basically two laws; one connected to absorbance with Transmittance; the lambert law and second discuss relation of absorbance with concentration of sample; that is Beer's law.



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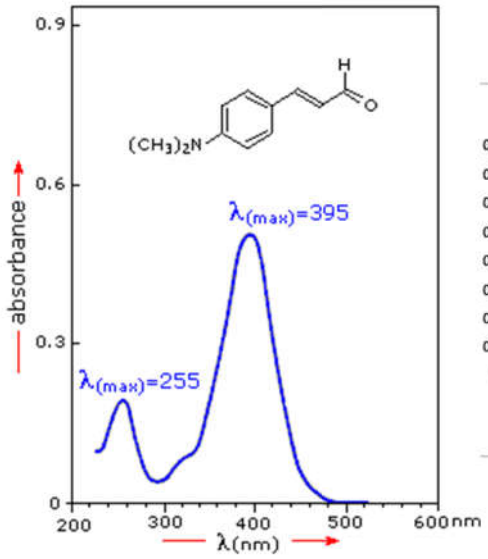
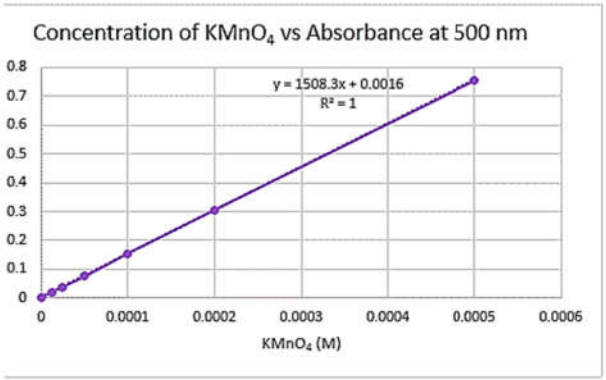
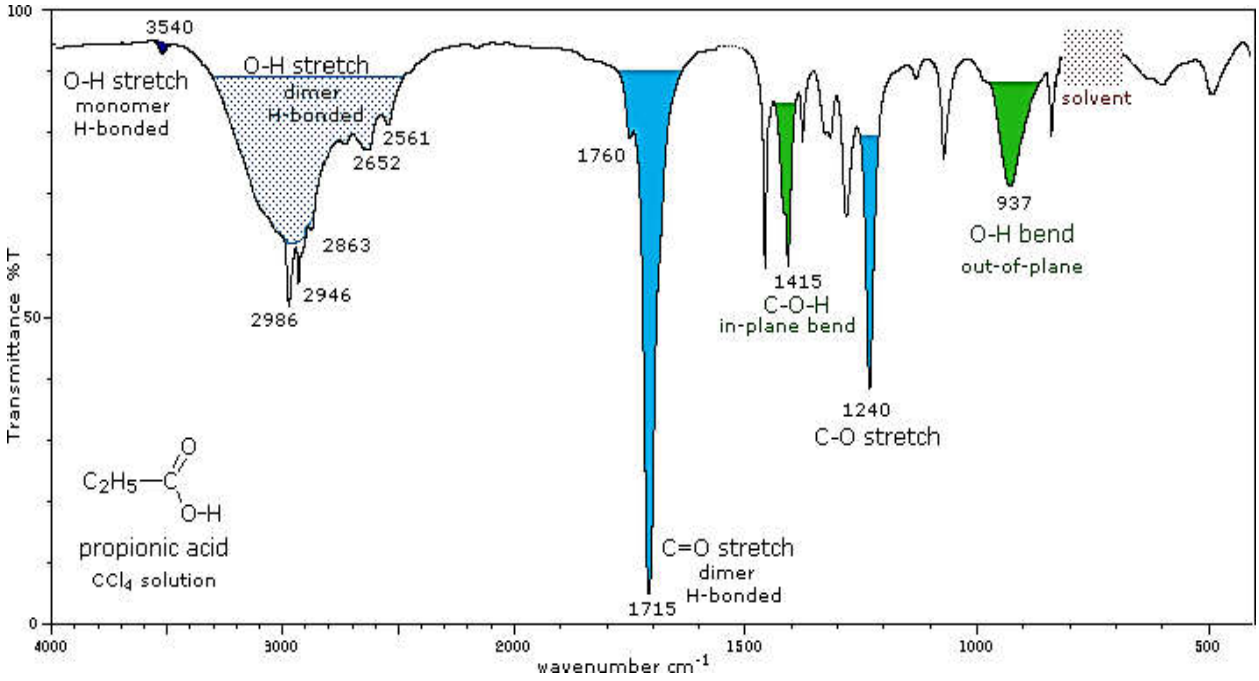
Spectroscopic techniques





We use this technique for either finding out wavelength maximum of any molecule or use it for evaluation of concentration. N,N-dimethyl cinnamaldehyde

- **IR Spectroscopy**
    - **Use to evaluate functionalities in an Organic molecule**



- **NMR Spectroscopy**
    - **Used for structure elucidation and not for quantitation**
- **Mass Spectrometry**
    - **Used as detector with both GC MS and ICP MS**
- Another spectroscopic technique is IR Spec. We

Topic 6:

Analytical Chemistry

Introduction-V

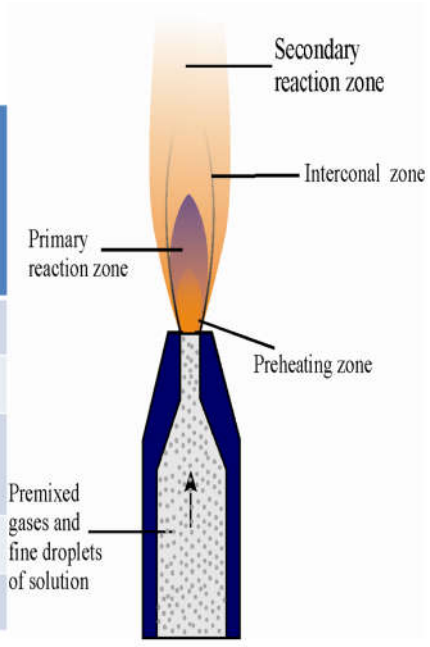
Atomic Spectroscopy

- **Atoms of different type absorb light of a certain wavelength**
- **They emit the same wavelength as they absorb**

Spectroscopic techniques

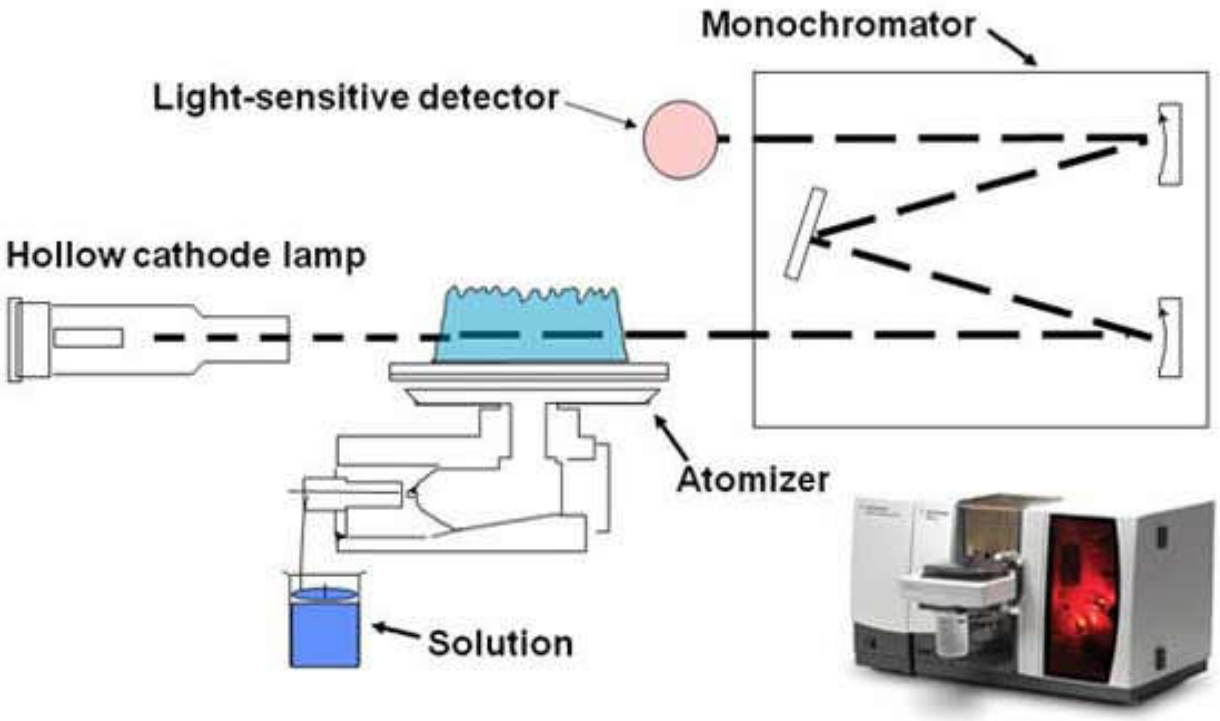
Flame photometry

Elements	Emission Wavel-ength (nm)	Flame Colour
Sodium (Na)	589	Yellow
Potassium (K)	766	Violet
Barium (Ba)	554	Lime green
Calcium (Ca)	662	Orange
Lithium (Li)	670	Red



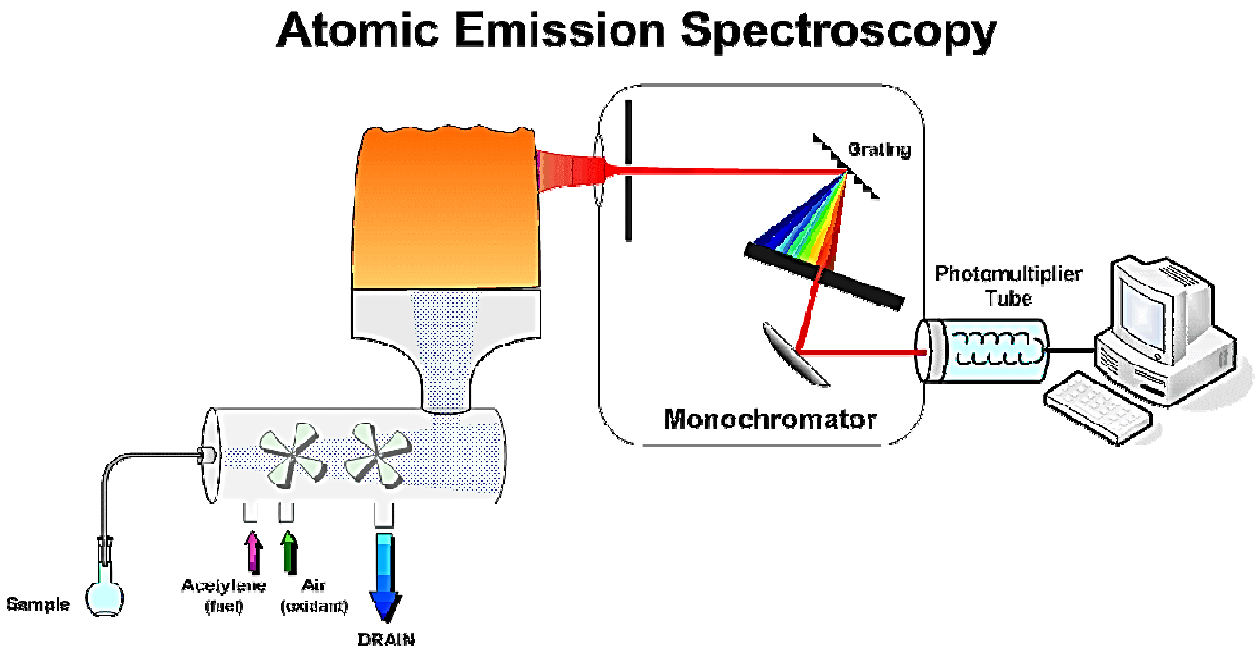
Atomic Absorption spectroscopy

- **Flame Atomic Absorption Spectroscopy (FAAS)**
- **Graphite Furnace Atomic Absorption Spectroscopy (GFAAS)**



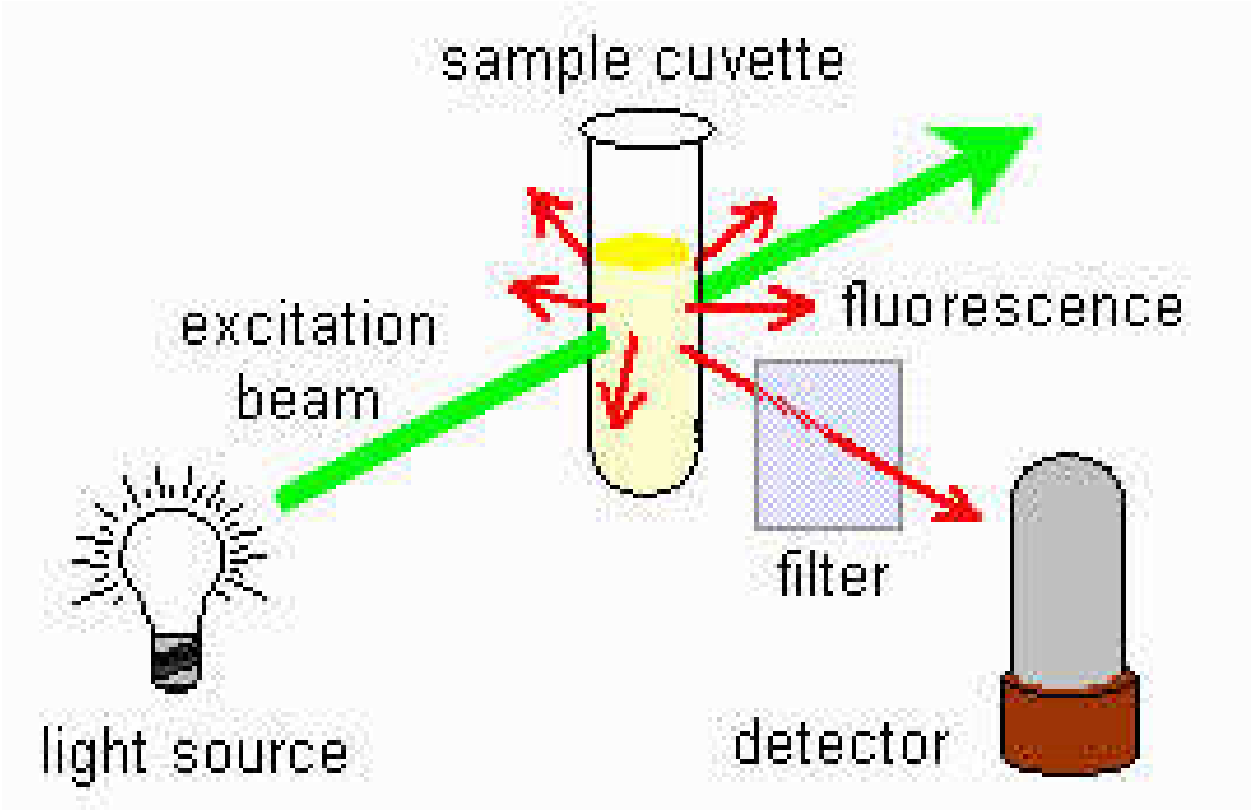
Atomic Emission spectroscopy

- **Inductive Coupled Plasma – Optical Emission Spectroscopy (ICP / OES)**
- **Inductive Coupled Plasma - Mass Spectrometry (ICP MS)**



Atomic fluorescence spectroscopy

- **Evaluate certain organic molecules and metals in different oxidation states**



Atomic Spectroscopy

- **Thus we can determine qualitatively the metal atom**
- **We can estimate concentration of particular metal atoms**

- Replicates
  - Same sized samples analyzed in same way
  - To improve reliability
  - To determine variability
- Mean
  - arithmetic mean, $\bar{x}$
  - $\bar{X} = \frac{\sum_{i=1}^{N} x_i}{N}$
- Median / Mode

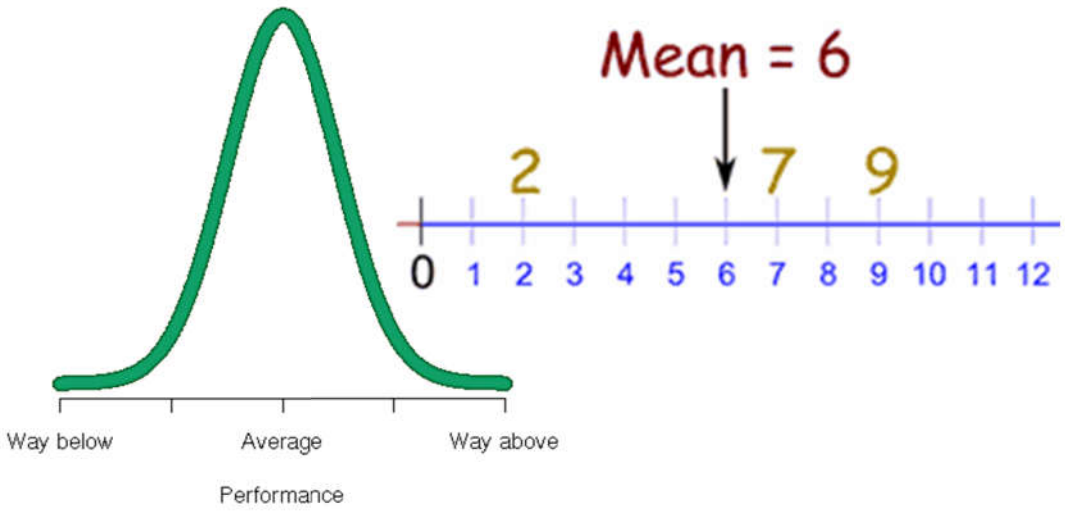
The replicates mean analysis of same size of sample under similar analytical conditions. Without changing reagents, analyst, environment etc. Only variable is the number of samples. This is done to improve reliability. Like we determine best tennis player in best of five games.

The second objective may be to determine variability in the samples. Like variability in land quality during soil analysis.

We analyse till concordant readings. Means with minimum variability in between of analytical results.

We may take average of all the readings. This average may also called arithmetic mean in statistics.

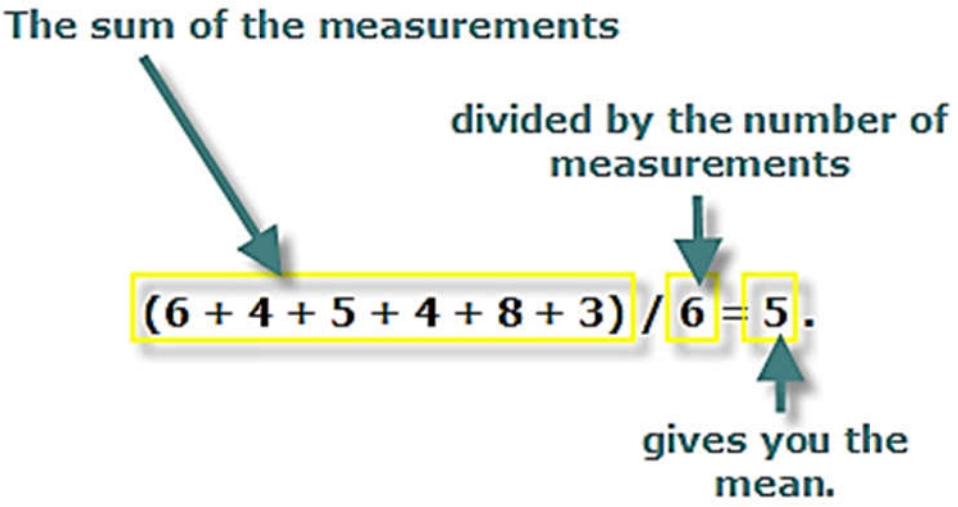
Chemometrics



Add the three readings and divide by three.

Average represents the peak of this gaussian curve.

Chemometrics



Add the number of replicates and divide by number of readings gives us mean of the data.

Chemometrics

- Replicates
  - Same sized samples analyzed in same way
  - To improve reliability
  - To determine variability
- Mean
  - arithmetic mean, $\bar{x}$
  - $\overline{X} = \frac{\sum_{i=1}^{N} x_i}{N}$
- Median
  - the middle result
- Mode
  - The most repeatable value

To calculate Median arrange the replicates or your data in ascending or descending order.

- Replicates
  - Same sized samples analyzed in same way
  - To improve reliability
  - To determine variability
- Mean
  - arithmetic mean, $\bar{x}$
  - $\bar{X} = \frac{\sum_{i=1}^{N} x_i}{N}$
- Median
  - the middle result
- Mode
  - The most repeatable value

Topic 9

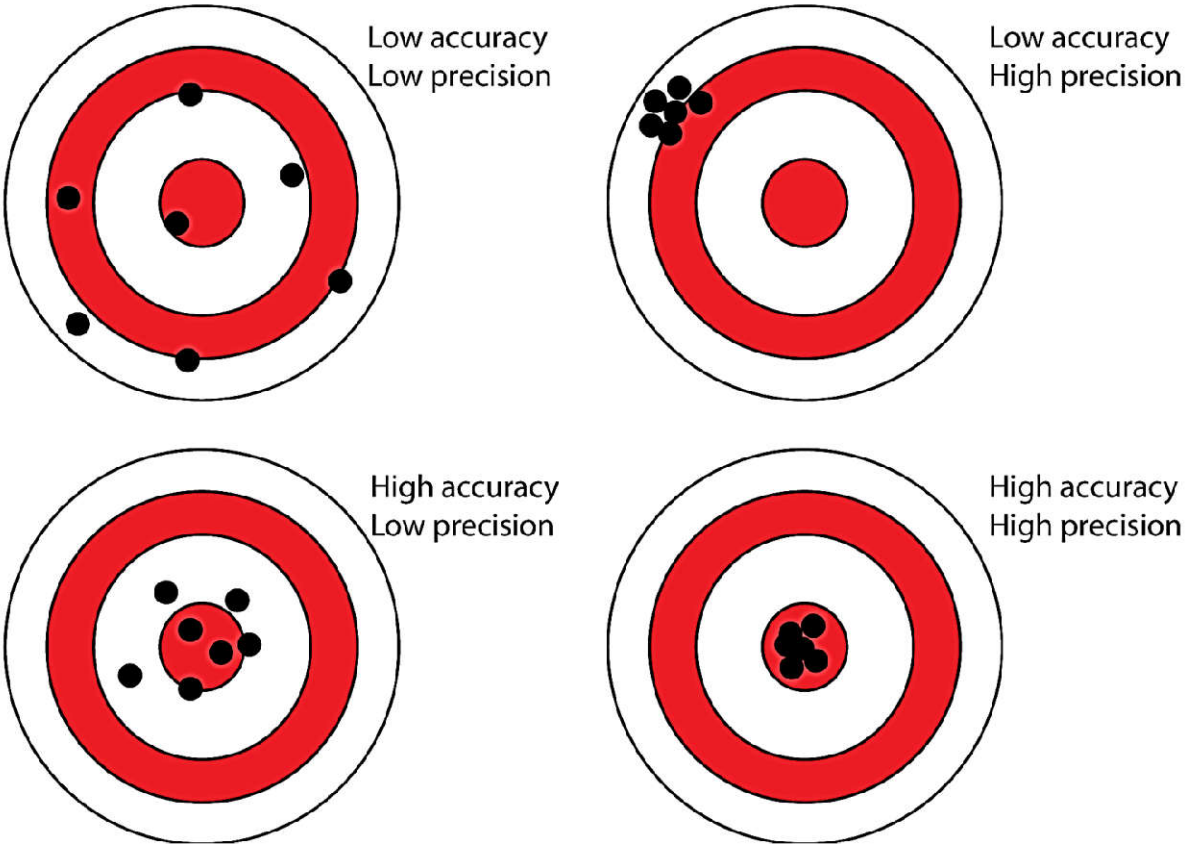
Analytical Chemistry

Chemometrics-II

- **Error and Uncertainty**
- **Types of error**
  - **Determinate error (Systematic error)**

    - **Indeterminate error (Random error)**

- **Accuracy and Precision**
- Normally during an analysis we can not have a single repeating reading. For example during an acid base titration we have 10.0 mL as titrant reading every time. It shows the careless behaviour of analyst or manufactured data. Otherwise it may be 10.5 mL or 9.5 mL etc.
- In dart board one can score maximum points if target the mid circle with plus minus on above and below and right to left
- **Error and Uncertainty**
- **Types of error**
    - **Determinate error (Systematic error)**
    - **Indeterminate error (Random error)**
- **Accuracy and Precision**
- Above type of uncertainty is called random error, that can be minimized but not eliminated. Therefore it is called indetrminate error, i.e. that can not be determined exactly
- The second type of error is determinate error.
- For example the fault in a weighing balance, whenever you place 1 g it read 1.1 g. Determinate error may be positive or negative while the indeterminate error always appeared to be above and below the average, therefore show + and – results.
- The third concept is accuracy and precision. Accuracy is closeness of data to the actual results. While precision is understood as closeness of data within itself. We can learn it in a better way with dart board analogy.



This dart board analogy representing the concept of accuracy and precision. The best suited posture is lower right bottom representing high accuracy and high precision. And the least one is above left corner with lowest accuracy and low precision.

- **Error and Uncertainty**
- **Types of error**
    - **Determinate error (Systematic error)**
    - **Indeterminate error (Random error)**
- **Accuracy and Precision**
- For good analytical result the best suited position is high precision, means least variation among the results. And close to the actual value

Analytical Chemistry

Chemometrics-III

- **Understanding systematic error**

- **Absolute error**
  - $E = x_i - x_t$
  - **It may be –ve or +ve**

- **Relative error**
  - $E_r = \frac{x_i - x_t}{x_t} \times 100$

- **Gross error**

Keep in my mind that systematic errors are those which could be estimated, therefore also called determinate error.

These error will be either in positive or negative side.

How to calculate these errors?

- **Consider we want to check the true value of our pipette.**
  - **First we have to generate data, fill the pipette and make it empty in a beaker placed on a balance and already tarred**
  - **Collect replicate data**

- **Calculate mean of that**
- **Difference in actual volume and observed volume may consider as an error**

Chemometrics

- Difference between experimental value and true value
- Shows whether the value is high or low
  - -ve error; measurement result is low
  - +ve error; measurement result is high
- no relation with sample size

For individual data:

$$\text{AbsoluteError } (E_a) = X_i - X_t$$

For average of data:

$$\text{AbsoluteError } (E_a) = \overline{X}_i - X_t$$

Chemometrics

- **Understanding systematic error**
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  - $E = x_i - x_t$
  - **It may be –ve or +ve**
- **Relative error**
  - $E_r = \frac{x_i - x_t}{x_t} \times 100$
- **Gross error**

Relative error give another aspect of errors.

Calculation of error relative to actual value is called relative error.

error may rise with sample volume, but relative error will remain same

Chemometrics

$$\text{Relative Error } (E_r) = \frac{(X_i - X_t)}{X_t} \times 100; \quad \text{In \%}$$

$$= \frac{(X_i - X_t)}{X_t} \times 1000; \text{ In PPT}$$

Problem

If 0.5mg of precipitate is lost as a result of washing and the precipitate actually weighs 500mg , what will be the relative error due to solubility.

It is calculated in percentage. Or part per thousands PPT.

0.5/5000*100= 0.1 % = 1 PPT

Chemometrics

- **Understanding systematic error**
- **Absolute error**
  - $E = x_i - x_t$
  - **It may be –ve or +ve**
- **Relative error**
  - $E_r = \frac{x_i - x_t}{x_t} \times 100$
- **Gross error**

END

Similarly in pipette if instead of 10 mL it shows 9.5 mL average or an error of 0.5 mL. So relative error may calculate 0.5/10*100 =5%

We can compare one pipette from other in accuracy.

Or we can compare and declare that a burette is more reliable than a pipette

Another term is used as Gross error

They are often the product of human errors. It may be single outliying value in data set

---

Topic 11

Analytical Chemistry Chemometrics-IV

- **Sources of error**
  - **Instrumental error**

- Method error
- Human error

Instrumental Error

- If a balance weigh 2 g as 2.1 g.
- If a 10 mL pipette draw a volume of 9.5 mL on average
- If a faulty pH meter read 4.0 pH buffer as 4.21 even after calibration
- Leakage in burette
- Sources of error
    - Instrumental Error
    - Method error
    - Human error

Method Error

- If a method say
    - heat it
    - stay at room temperature
    - use buffer of pH 10

Note: The meaning of such statements may be different for different analyst

Human Error (Personnel error)

- If a personnel
    - Problem in identifying colour / meniscus
    - Don’t follow procedure properly
    - Careless behavior in calibration
    - Note the meniscus above or below eye level

- Sources of error
    - Instrumental Error
    - Method error
    - Human error

Topic 12

Analytical Chemistry

Chemometrics-V

- **Removal of error**
    - **Calibration of Equipment**
    - **Validation of analytical method**
    - **Training of personnel**

Calibration of Equipment

- **Calibration of an analytical balance using standard weights**
- Calibration of pipette / micropipettes and other volumetric apparatus to SI units using a calibrated balance
- Calibration of pH meter with standard buffers

Validation of analytical methods

- Analysis of standard samples
    - Standard reference materials
    - Certified reference materials
- Independent analysis
    - By another analyst, by another equipment or by another method

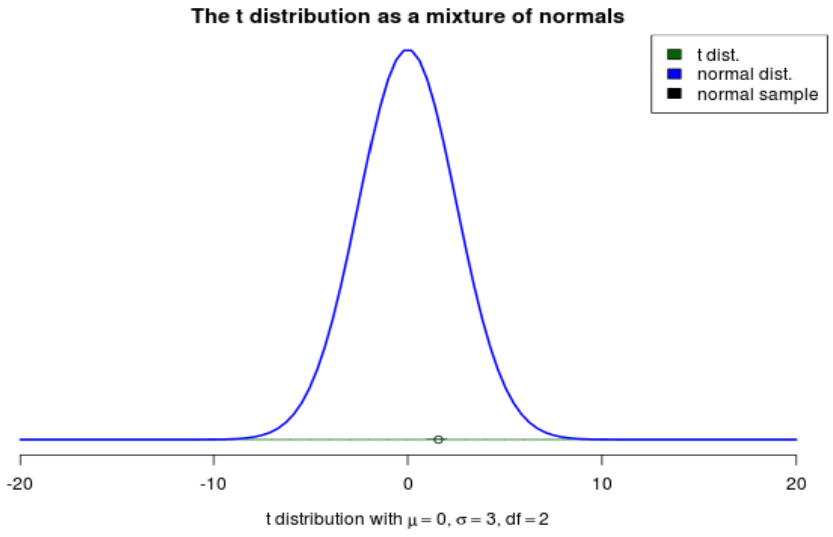
- Blank determination
- Variation in sample size

Topic 13

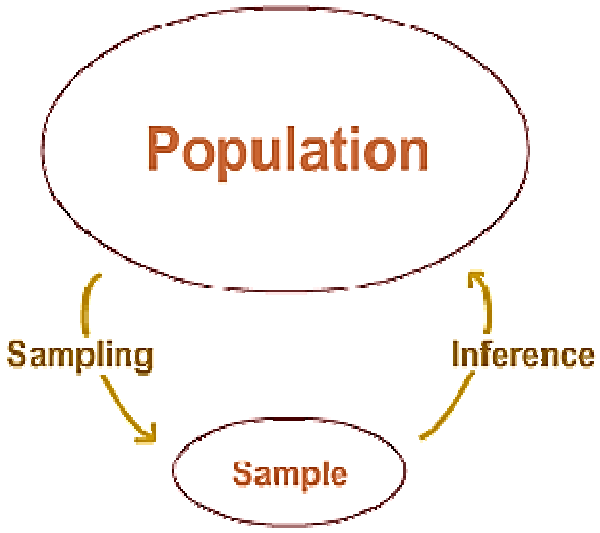
Analytical Chemistry

Chemometrics-VI

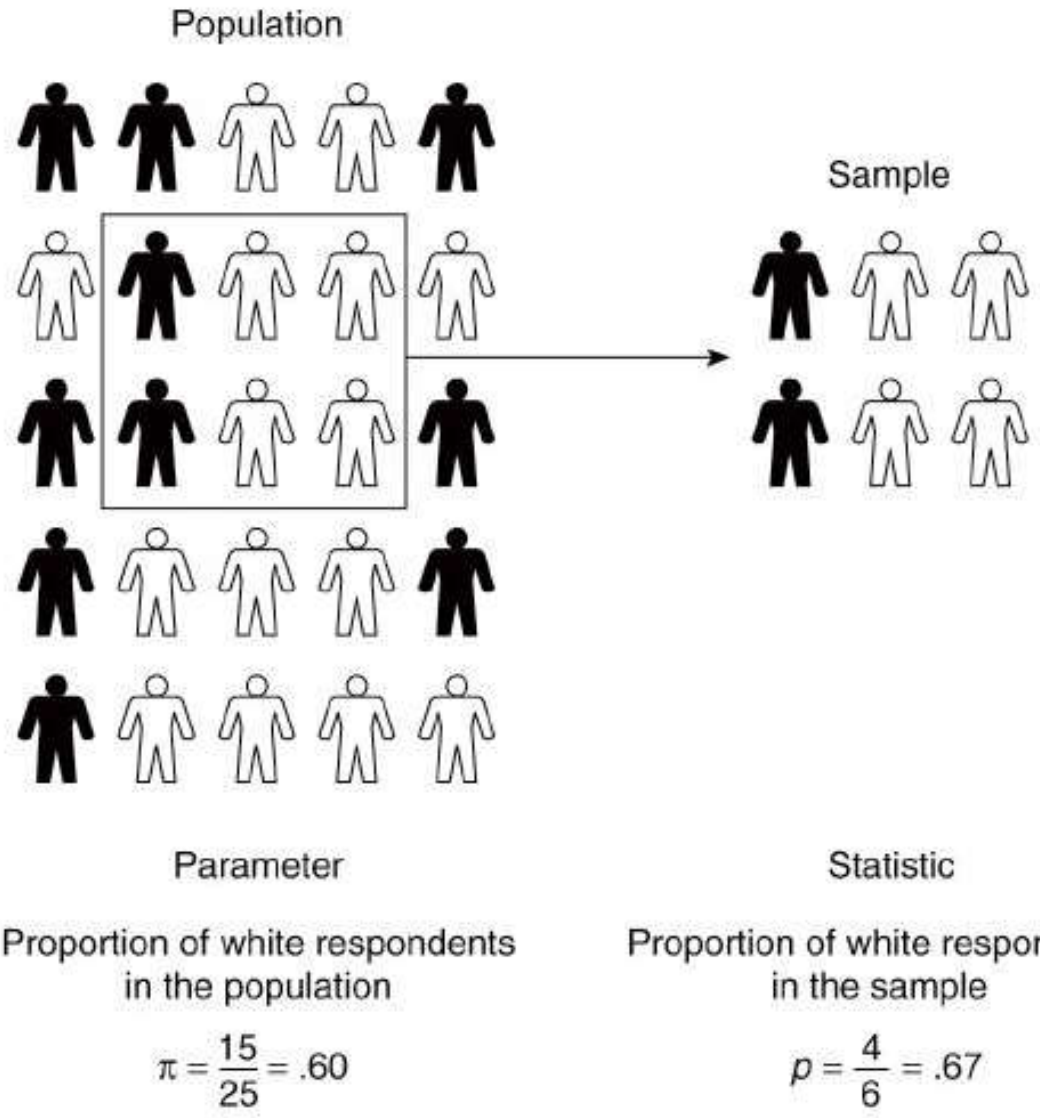
- **Sample and population**
- **Variance (the expand of analytical data)**
- But before starting this we must have an understanding of sample and population.
- Sample is a part of whole population. So gather analytical data with the sample may be close to actual one or may be different a little bit.
- It may vary a lot if sample is not correct.



Here we can see distribution of data and formation of normal distribution curve.



We draw a sample from population and infer our results to the population.



We can see that ratios in our sample can be close enough to population. However a sample from some other portion may miss guide, or biased. In a smaller sample size the chances of biased results increased.

Chemometrics

Sample and Population mean:

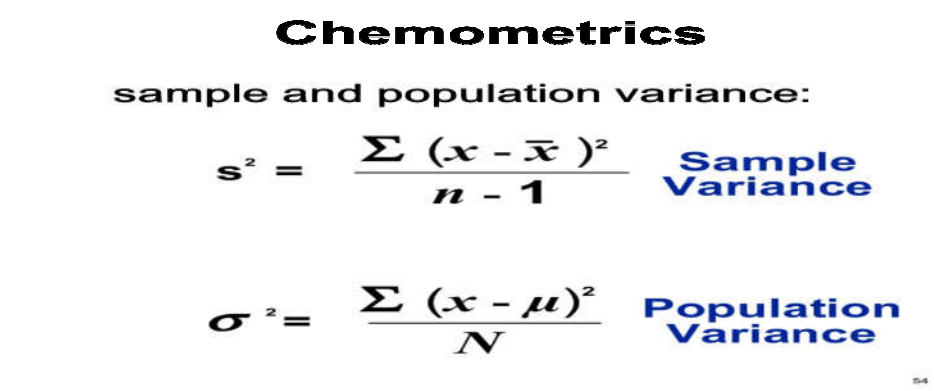
$$\bar{x} = \frac{\sum_{i=1}^{n} x_i}{n} \quad \mu = \frac{1}{N}\sum_{i=1}^{N} x_i$$

- **Sample and population**
- **Variance (the expand of analytical data)**
- Variance shows the expand of analytical data. The average of the **squared** differences from the Mean.

Chemometrics

Formula of sample variance:

$$s^2 = \frac{\sum (X - \bar{X})^2}{N - 1}$$

- 

Sample and population

- **Variance (the expand of analytical data)**

Topic 14:

Analytical Chemistry Chemometrics-VII

The standard deviation is square root of variance. We do some exercise to understand it in a better way

- **Standard deviation (the measure of precision)**

- **Confidence Interval**
- Std Dev is measure of precision. It shows how close is your data in a data set

Chemometrics

Standard Deviation formula:

$$\sigma = \sqrt{\frac{\sum_{i=1}^{N}(x_i - \mu)^2}{N}}$$

It denote with sigma.

Explain formula a bit

Chemometrics

How to calculate Std. Dev.?

X_i	Mean	$X_i - \bar{X}$	$(X_i - \bar{X})^2$
81	81	0	0
83	81	2	4
80	81	-1	1
83	81	2	4
79	81	-2	4
81	81	0	0
78	81	-3	9

Variance = 22/6
= 3.6
~ 4
Std. Dev. = 2

Reporting
of Results
= mean ± std dev

Mean = (81+83+80+83+79+81+78)/7

Here we show, how to calculate std dev?

- **Standard deviation (the measure of precision)**
- **Confidence Interval**

- And the next concept is confidence interval. That may be understood with following diagram

---

Topic 15

Analytical Chemistry

Chemometrics-VIII

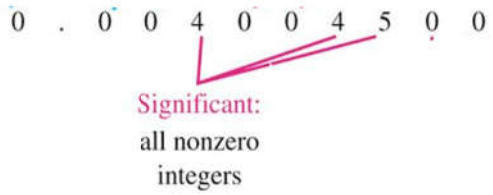
In previous slides we learn to calculate standard deviation. And to report them

But in reporting of results we must understand the significance of significant figures.

- **Reporting of data**
    - **Significant figures**
    - **Treating significant figures in calculations**
    - **Rounding off data**
- Significant figures should be placed with care. Just write a lengthy figure never make your analytical results precise.
- For example if you take titrant readings from a burette, and take an average of seven readings, you might end up with six digits but you must understand that the minimum readable point on burette was 0.1 mL so your result must show same number of digits.

Chemometrics

Significant Figures



- **Reporting of data**
  - **Significant figures**
  - **Treating significant figures in calculations**
  - **Rounding off data**
- So when ever add, subtract, multiply or divide the data we must follow certain rules

Mathematical Treatment of Significant figures

- **In addition or subtraction, the answer should have the least digits after decimal,**

  e.g., 3.4 + 0.020 + 7.31 = 10.7.

- **For multiplication and division answer should be rounded so that it contains the same number of significant digits as the original number with the smallest number of significant digits.**

Chemometrics

Exercise:

1. 37.76+3.907+226.4=?
2. 319.15 - 32.614 = ?
3. 2.02 × 2.5 = ?
4. 0.0032 × 273 = ?

END

Answers:

1. 268.067 ~ 268.1
2. 286.536 ~ 286.54
3. 5.05 ~ 5.1
4. 0.8736 ~ 8.7×10^{-1}

Topic 16

Analytical Chemistry

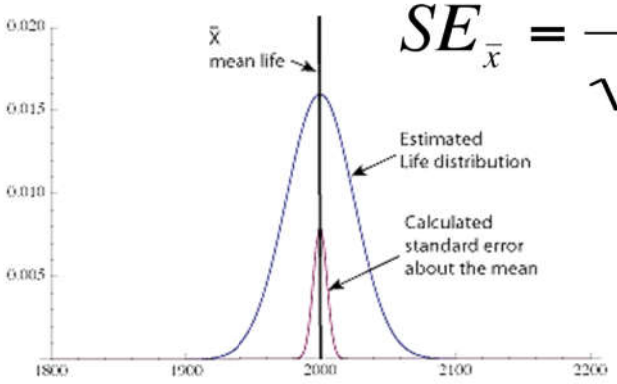
Chemometrics-IX

- **Reporting of data**
  - **Standard error of mean**
    - **standard deviation** of the **sampling distribution**
  - **Coefficient of variance**
  - **Relative standard deviation**
- A **standard error** is the **standard** deviation of the **sampling distribution** of a statistic. **Standard error** is a statistical term that measures the accuracy with which a sample represents a population. In statistics, a sample **mean** deviates from the actual **mean** of a population; this deviation is the **standard error**.

Chemometrics

Formula for SEM:

$$SE_{\bar{x}} = \frac{s}{\sqrt{n}}$$



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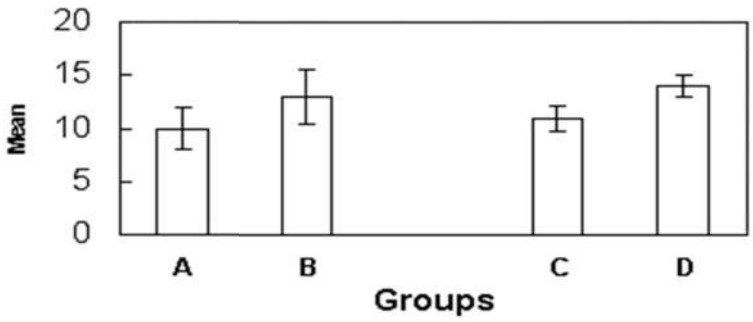
Chemometrics

Group mean and Standard errors:



Reporting of data

- **Standard error of mean**
- **Coefficient of variance**
  - measure of **spread** that describes the amount of **variability** relative to the mean
- **Relative standard deviation**

- The **coefficient of variation** is a measure of spread that describes the amount of **variability** relative to the mean. Because the **coefficient of**

variation is unitless, you can use it instead of the standard deviation to compare the spread of data sets that have different units or different means.

Chemometrics

Formula % CV:

Example:

$$CV = \frac{S}{\overline{x}} \times 100$$

- **Reporting of data**
  - **Standard error of mean**
  - **Coefficient of variance**
  - **Relative standard deviation**
    - **relative standard deviation (RSD)** is a special form of the **Std Dev** that is always positive**.**
- The **relative standard deviation** (RSD) is a special form of the **standard deviation** (std dev). It's generally reported to two decimal places (i.e. an RSD of 2.9587878 becomes 2.96). As the denominator is the absolute value of the mean, the RSD will always be positive

Formula RSD:

$$RSD = \frac{s}{\bar{x}} \cdot 100\%$$

However, the RSD cannot be negative while the **Coefficient of Variation** can be positive or negative. This is because the two formulas differ in a minor way: the **Coefficient of Variation** divides by the mean while the RSD divides by the absolute value of the mean

- **Reporting of data**
    - **Standard error of mean**
    - **Coefficient of variance**
    - **Relative standard deviation**

Topic 18

Analytical Chemistry

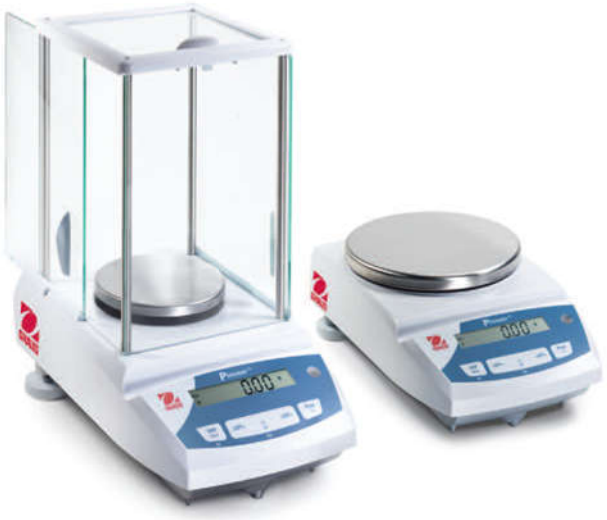
Chemometrics-XI

- **Standard preparations**
    - **Molarity**
    - **Molality**
    - **Normality**

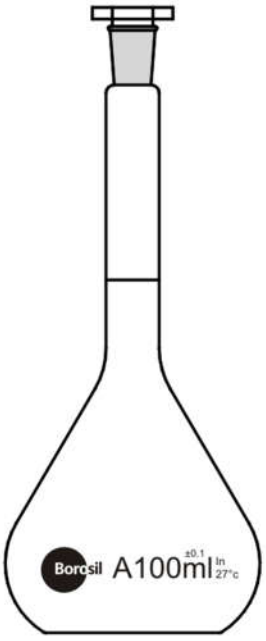
    - **Weight percent**
    - **Volume percent**
    - **Weight-Volume percent**
    - **Parts per million**
    - **Parts per billion**
- Molarity is the concentration of a particular chemical species. Formality, on the other hand, is a substance's total concentration without regard to its specific chemical form.

Chemometrics

Concept of mole:



Chemometrics



Not all the Volumetric apparatus used to take volumes.

Chemometrics

Molarity of solution:

$$\mathbf{M} = \frac{\textbf{moles solute}}{\textbf{Liters of solution}}$$

$$\text{Moles of unknown} = \frac{\text{mass of unknown}}{\text{molar mass}}$$

Molality is used in thermodynamic calculations where a temperature independent unit of concentration is needed. Molarity is based on the volume of solution containing the solute. Since density is a temperature dependent property a solution's volume, and thus its molar concentration, changes with temperature. By using the solvent's mass in place of the solution's volume, the resulting concentration becomes independent of temperature.

Chemometrics

$$Molality = m = \frac{moles\ of\ solute}{kg\ of\ solvent}$$

$$m = \frac{mol}{kg}$$

How to take Kg of solution….. May use balance or measuring cylinder

Chemometrics

$$\text{Normality} = \frac{\text{equivalents solute}}{\text{volume of solution in liters.}}$$

$$\underline{N} = \frac{Eq}{V}$$

Normality is a concentration unit that is no longer in common use. Because you may encounter normality in older handbooks of analytical methods, it can be helpful to understand its meaning. Normality defines concentration in terms of an equivalent, which is the amount of one chemical species reacting stoichiometrically with another chemical species.

Chemometrics

$$\text{Equivalent Weight} = \frac{\text{Molar Mass}}{H^+ \text{ ion per mole}}$$

$$\text{Eq. wt. of } \mathbf{O.A.} = \frac{\text{Molecular weight}}{\text{No. of electrons gained by one molecule}} = \frac{\text{Molecular weight}}{\text{Change in O.N. per mole}}$$

$$\text{Eq. wt. of } \mathbf{R.A.} = \frac{\text{Molecular weight}}{\text{No. of electrons lost by one molecule}} = \frac{\text{Molecular weight}}{\text{Change in O.N. per mole}}$$

Note that this definition makes an equivalent, and thus normality, a function of the chemical reaction in which the species participates. Although a solution of H2SO4 has a fixed molarity, its normality depends on how it reacts.

Chemometrics

weight percent	$\frac{\text{grams solute}}{\text{100 grams solution}}$	% w/w
volume percent	$\frac{\text{mL solute}}{\text{100 mL solution}}$	% v/v
weight-to-volume percent	$\frac{\text{grams solute}}{\text{100 mL solution}}$	% w/v

Weight percent (% w/w), volume percent (% v/v) and weight-to-volume percent (% w/v) express concentration as the units of solute present in 100 units of solution. A solution of 1.5% w/v NH4NO3, for example, contains 1.5 gram of NH4NO3 in 100 mL of solution.

Topic 19

Analytical Chemistry

Chemometrics-XII

- **Goals of sampling**
- **Sample Size**
- **Sampling types**
- **Sampling techniques**

- **Sample preparations**
- **Goals of Sampling**
    - **To obtain a mean analyte concentration**
    - **Unbiased estimate of the population mean.**
    - **Every possible sample is equally and likely to be drawn.**
- **Sampling types**
    - **Grab sample**
    - **Composite Samples**
    - **Gross samples**
- **Sampling techniques**
    - **Sampling Homogeneous Solutions (Liq. & Gases)**
    - **Sampling solids (sawing, milling, grinding)**
- **Sample preparations**
    - **Gross samples may be huge**
    - **Crushing, grinding, sieving, mixing, and dividing the sample (often into halves) to reduce its mass**
    - **Digestion and Extraction techniques**

Topic 20

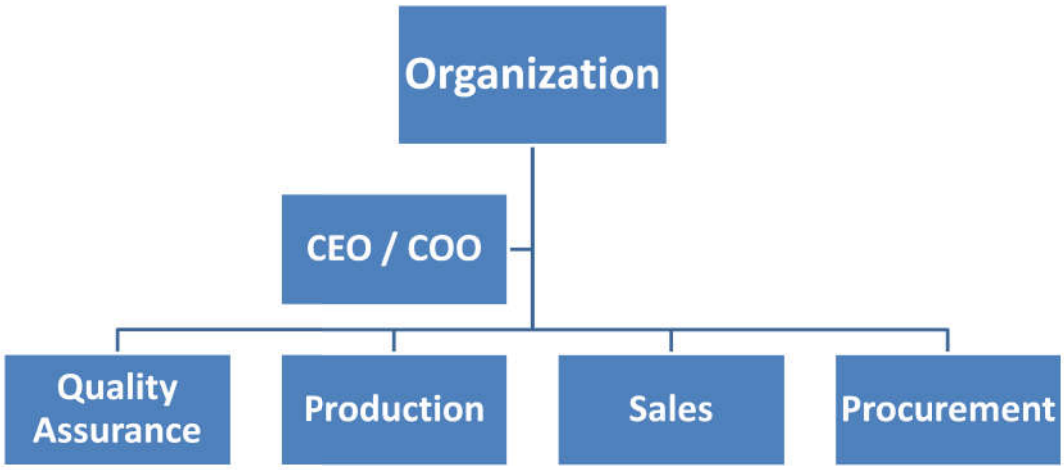
Analytical Chemistry

Quality Control

- **Quality**
    - **sum of the attributes or properties that describe a product**

- **Conformity to standards**
- **totality of features and characteristics**
- **fitness for purpose**
- **Customer satisfaction**

Quality Control



Quality is not residing in any particular field of an organization but it is at par and a part of every

Quality Control

Quality Control	Quality Assurance
• Internal View	• External view
• Everybody in the shop	• Independent person
• During the audit	• Can be after the audit
• Catching errors	• Confidence about the errors
• Focused on a product	• Focused on a process

Here we can understand the difference in QC and QA

- **Quality is blend of;**
    - **Fitness for purpose, adequacy of functioning and reliability, for the price paid**
    - **Design and manufacturing characteristics to meet customer's requirements**

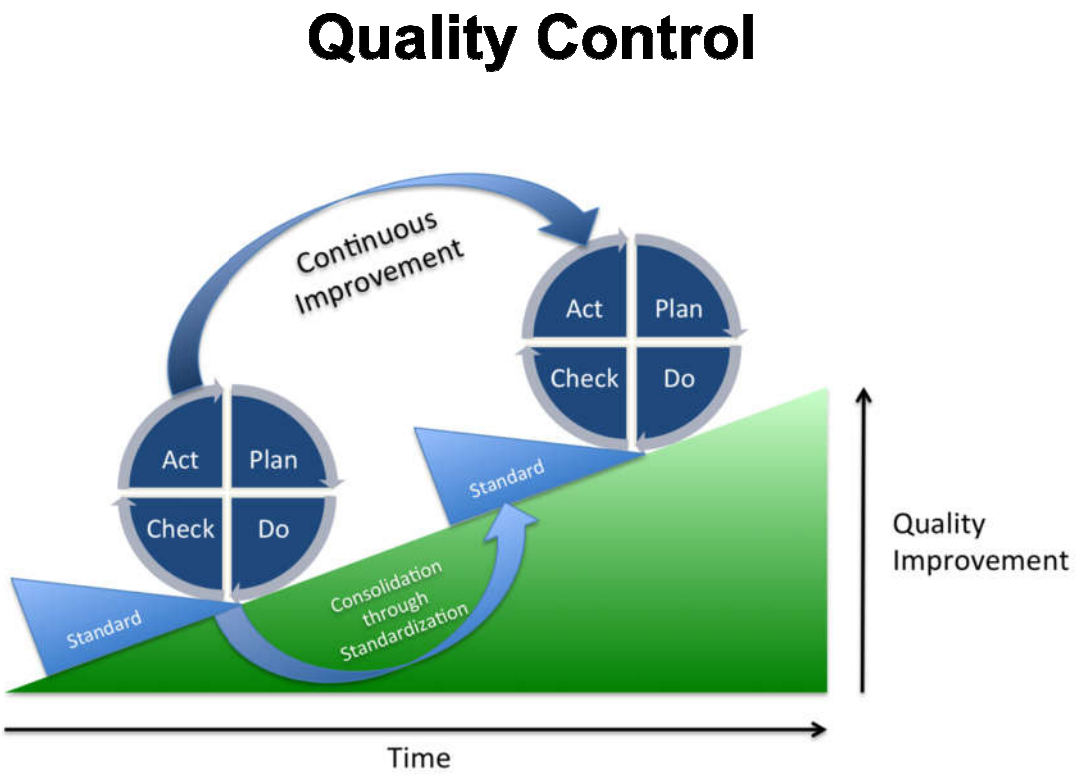
Topic 21

Analytical Chemistry

Quality Control Intro

- **Quality Control Tools**

- **QC tools are the means for Colleting data, analyzing data, identifying root causes and measuring the results.**
- **These tools are related to numerical data processing**



- **7 QC Tools**
  - **Scatter Diagram**
  - **Cause and Effect Diagram**
  - **Histogram**
  - **Check Sheet**
  - **Control Chart/Graph**
  - **Pareto Diagram**
  - **Stratification**

Quality Control

Application of QC tools in Problem Solving

	Graphs	Check sheet	Stratification	Pareto Diagram	Cause & Effect Diagram	Histogram	Scatter Diagram	Control Chart
Identification of problem	◎			◎				
Defining the problem	○	◎	◎	◎		○		
Record of facts		◎	◎			◎		◎
Detecting causes of problem			○		◎	◎	◎	
Develop Improvement method (Solution)								
Implementation								
Evaluation of result	○		○		◎	◎	◎	
Process control (Standardization)								◎

- **7 QC Tools**
  - **Scatter Diagram**
  - **Cause and Effect Diagram**
  - **Histogram**
  - **Check Sheet**
  - **Control Chart/Graph**
  - **Pareto Diagram**
  - **Stratification**
- In next presentation we will learn in detail the QC tools one by one.

Topic 22

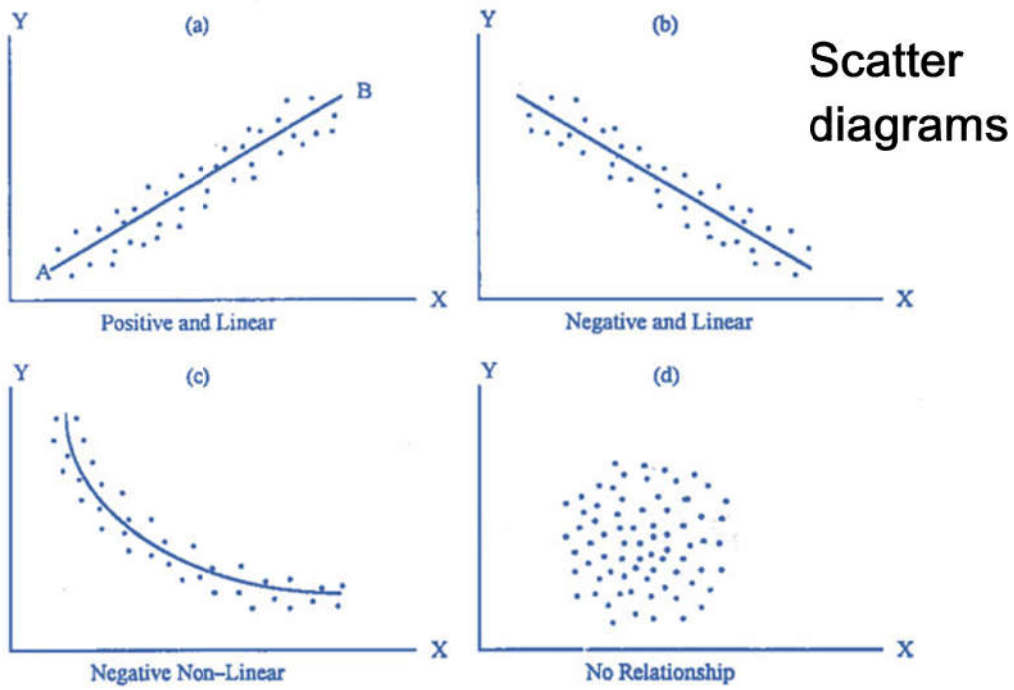
Analytical Chemistry

Quality Control Tools-I

- **Scatter Diagram**

- **To examine the relationship between the two, paired, interrelated data types**
- **To find whether or not these two data types are interrelated.**
- **To determine how closely they are related to identify a problem point.**
- **Examples of Scatter diagram**
- **Relationship between thermal treatment temperature of a steel material and its tensile strengths**
- **Relationship between visit made by a salesman and volume of sales**
- **Relationship between the number of persons visiting a department store and volume of sales**
- **Relationship between absorbance and concentration of a coloured sample (UV spectroscopy); calibration curve**
- **Relationship of volume to pressure or temperature**

Quality Control Tools



- **Scatter Diagram**
- **Can identify cause and effect relation.**
- **Can understand the relationship between two results.**

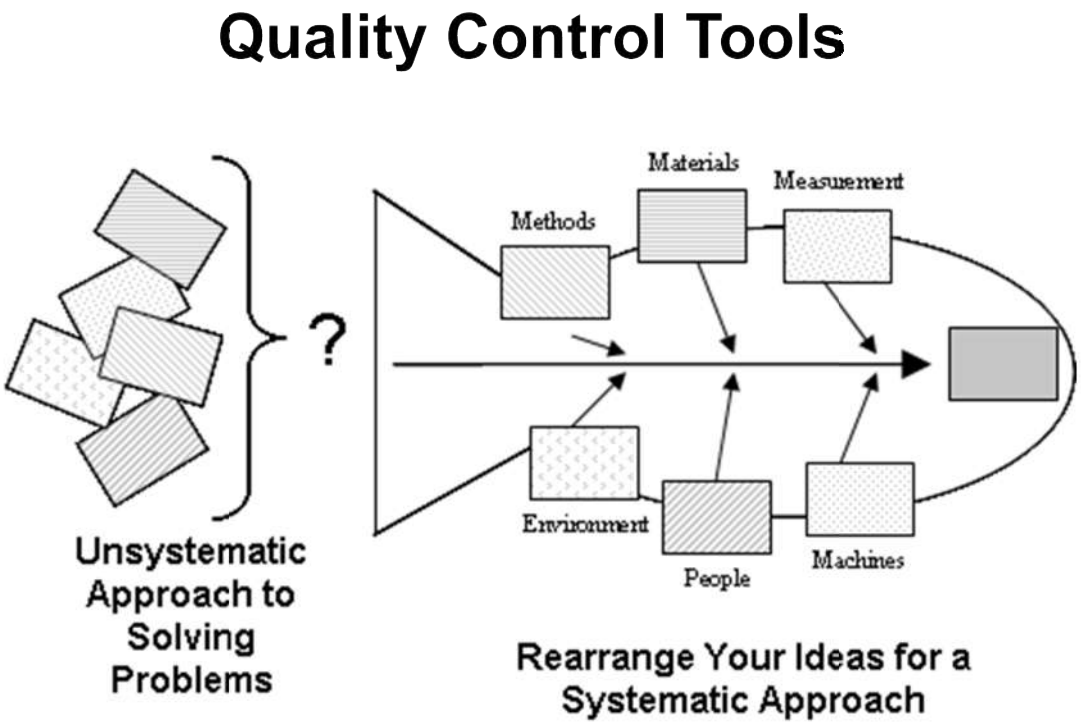
Topic 23

- **Analytical Chemistry**

  Quality Control Tools-II

  - **Cause & Effect Diagram**
    - **Also called fish-bone or Ishikawa diagram presents a systematic representation of the relationship between the effect (result) and affecting factors (causes).”**

- It is also called fish bone diagram, or Ishikawa diagram is a tool to identify the root cause that is responsible for an effect.
- **Cause & Effect Diagram**
    - **Solving a problem requires clarification of a cause and effect relationship, where the effect (e.g., the result of work) varies according to factors (e.g., facilities, machines used, method of work, workers, materials and parts used etc.).**
    - **To obtain a good work result, we must identify the effects of various factors and develop measures to improve the result accordingly.**



- **Cause & Effect Diagram**
    - **Can obtain a clear overall picture of causal relation. (A change in the cause triggers a variation in the result.)**

- **Can list up all causes to identify important causes.**
- **Can determine the direction of action (counter measure).**

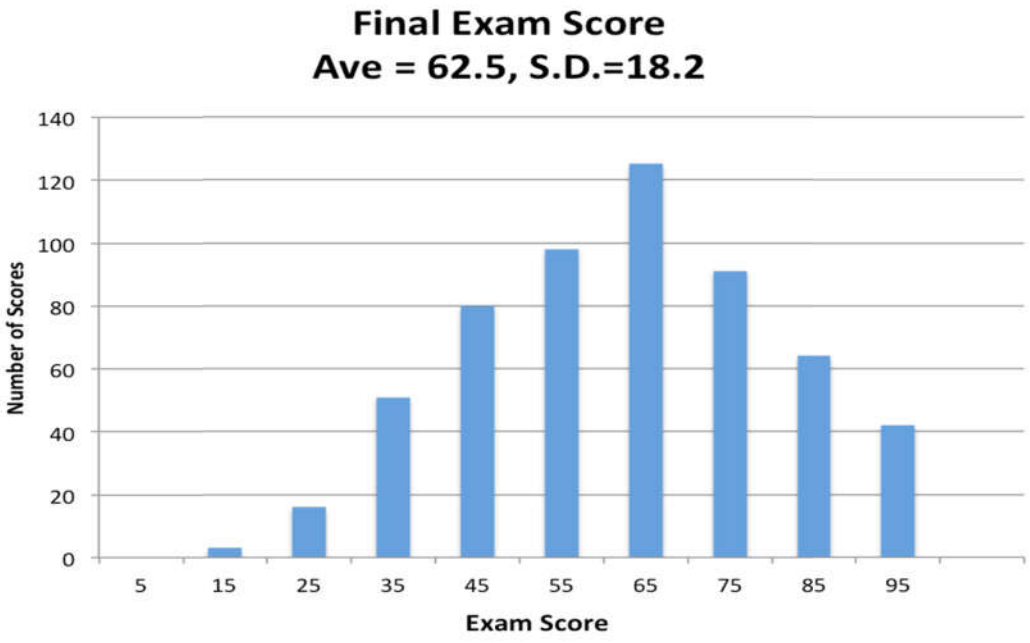
Topic 24

Analytical Chemistry

Quality Control Tools-III

- **Histogram**
    - **is mainly used to analyze a process by examining the location of the mean value in the graph or degree of variations, to find a problem point that needs to be improved.**
- **Histogram**
    - **When creating a histogram, "a range of data is divided into smaller sections having a uniform span and the number of data contained in each section (the number of occurrences) is counted to develop a frequency distribution table."**
    - **Then, "a graph is formed from this table by using vertical bars, each having the height proportional to the number of occurrences in each section."**
    - **Used to analyze a process to identify a problem point that needs to be improved by finding the location of the mean value or degree of variations in the graph.**

Quality Control Tools



- **Histogram**
    - **Can identify the location of the mean value or degree of variations.**
    - **Can find out the scope of a defect**
    - **Can identify the condition of distribution (e.g., whether there is an isolated, extreme value).**

Topic 25

Analytical Chemistry

Quality Control Tools-IV

- **Check Sheet**

A check sheet is "a sheet designed in advance to allow easy collection and aggregation of data."

- **Check Sheet**
    - **To check that procedure is followed effectively .**
    - **To eliminate possibility of skipping any of the required inspection items or step.**
    - **It is a self check.**
    - **Development of check sheet is effective QA tool, filling the data is Quality Control check**
    - **A check sheet is also effective in performing stratification (categorization).**

What a Clean Bathroom Looks Like	
Trash can is emptied.	
Toilet is scrubbed inside.	
Toilet is wiped down on the outside, including the base.	
The mirrors are shiny, no spots	
The sink is scrubbed clean.	
The counters are wiped down.	
The floor is swept and/or mopped.	
The soap container is at least half full.	
There are fresh towels.	
The shower or tub has been scrubbed.	
There is soap and shampoo in the shower or tub.	
The dirty laundry is where it belongs.	

A simplest form of check sheet to monitor cleaning of bathroom. Other possible examples……

- **Check Sheet**
    - **Ensures collection of required data.**

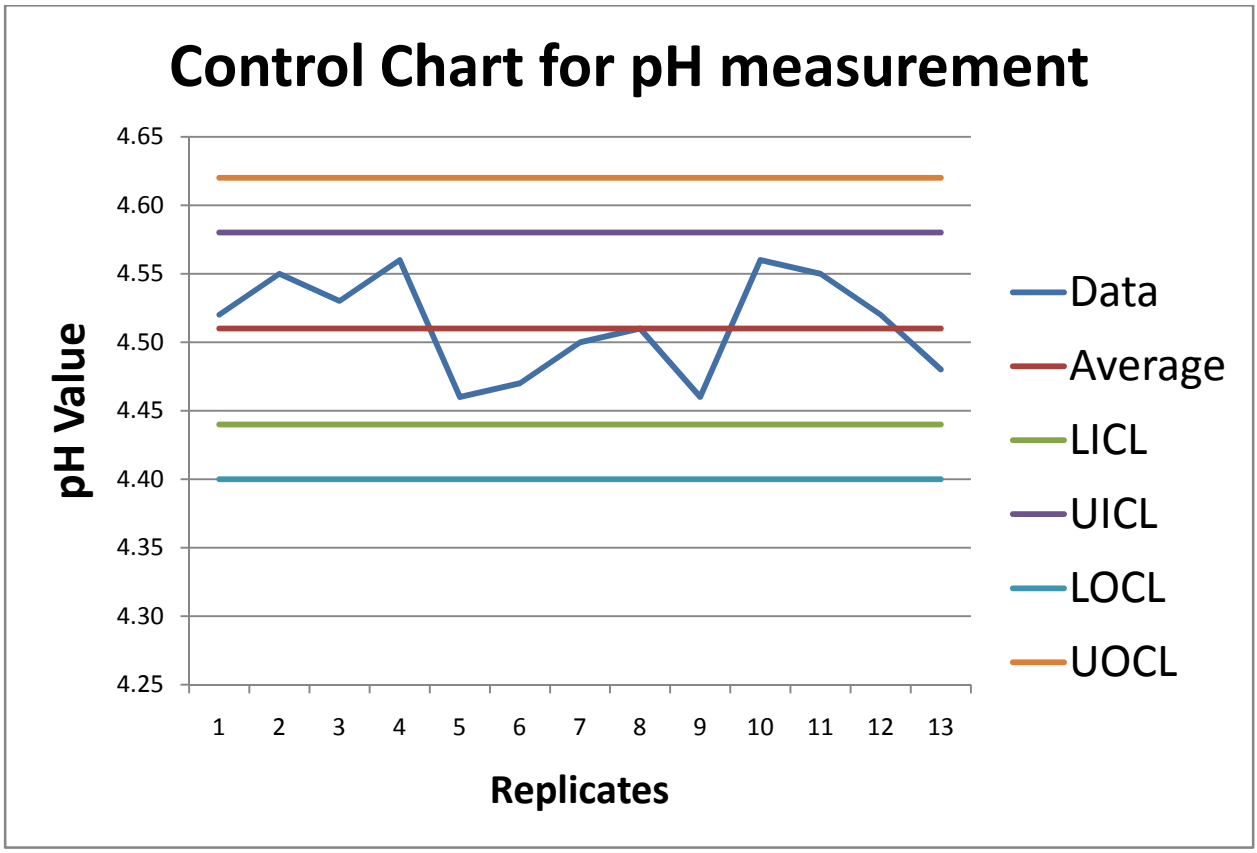
- **Allows a thorough inspection of all check items.**
- **Can understand tendencies and variations.**
- **Can record required data.**

Topic 26

- **Analytical Chemistry**
- **Quality Control Tools-V**
- **Control Chart**
    - **A control chart is used to examine a process to see if it is stable or to maintain the stability of a process.**
- **Control Chart**
        - **There are two types of control charts: one used for managerial purposes and the other for analytical purposes.**
        - **A control chart is used to identify dots that are outside the control limit, which indicate some anomalies in a process.**
        - **Seven consecutive dots below or above the mean (central) value, or an increment or a decline represented by seven consecutive dots also indicate "a problem in a process."**
        - **It needs to examine what has caused such a tendency or an increment/decline.**

	Data	Average	LICL	UICL	LOCL	
	4.52	4.51	4.44	4.58	4.40	
	4.55	4.51	4.44	4.58	4.40	
	4.53	4.51	4.44	4.58	4.40	

	4.56	4.51	4.44	4.58	4.40	
	4.46	4.51	4.44	4.58	4.40	
	4.47	4.51	4.44	4.58	4.40	
	4.50	4.51	4.44	4.58	4.40	
	4.51	4.51	4.44	4.58	4.40	
	4.46	4.51	4.44	4.58	4.40	
	4.56	4.51	4.44	4.58	4.40	
	4.55	4.51	4.44	4.58	4.40	
	4.52	4.51	4.44	4.58	4.40	
	4.48	4.51	4.44	4.58	4.40	
Mean	4.51		4.44	4.58	4.40	
Std Dev	0.04					



- **Control Chart**
    - **Can identify a change caused by elapse of time**

Can judge the process if it is in its normal state or there are some anomalies by examining the dots plotted on the chart.

Topic 27

Analytical Chemistry

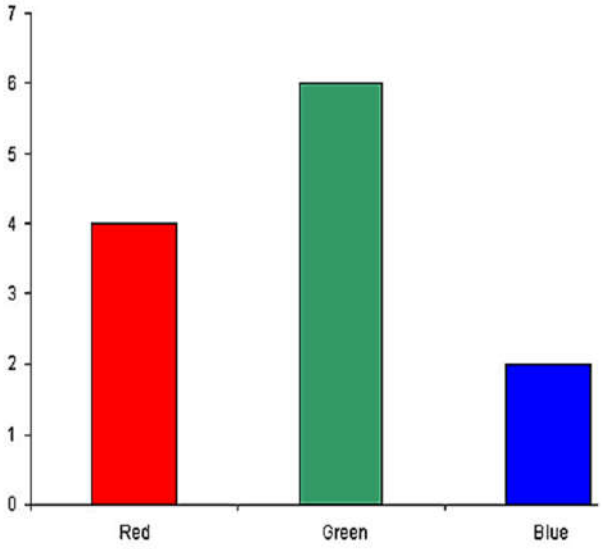
Quality Control Tools-V

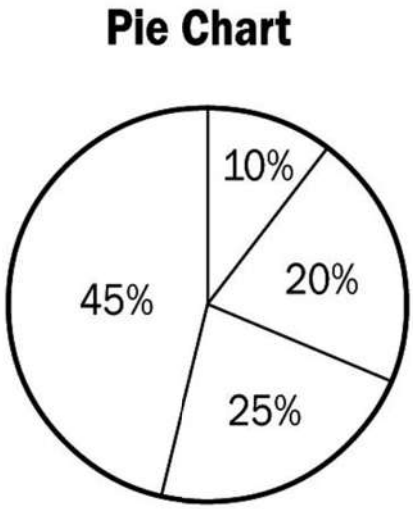
(Continued……)

- **Graphs**
    - **A graph is "a graphical representation of data, which allows a person to understand the meaning of these data at a glance."**
- **Graphs**

- **Unprocessed data simply represent a list of numbers, and finding certain tendencies or magnitude of situation from these numbers is difficult, sometimes resulting in an interpretational error.**
- **A graph is a effective means to monitor or judge the situation, allowing quick and precise understanding of the current or actual situation.**
- **A graph is a visual and summarized representation of data that need to be quickly and precisely conveyed to others.**

Quality Control Tools





- **Graphs**
  - **Can observe changes in a time-sequential order, ratios, and amounts.**
  - **For example**
    - **Changes in a time-sequential order – line graph**

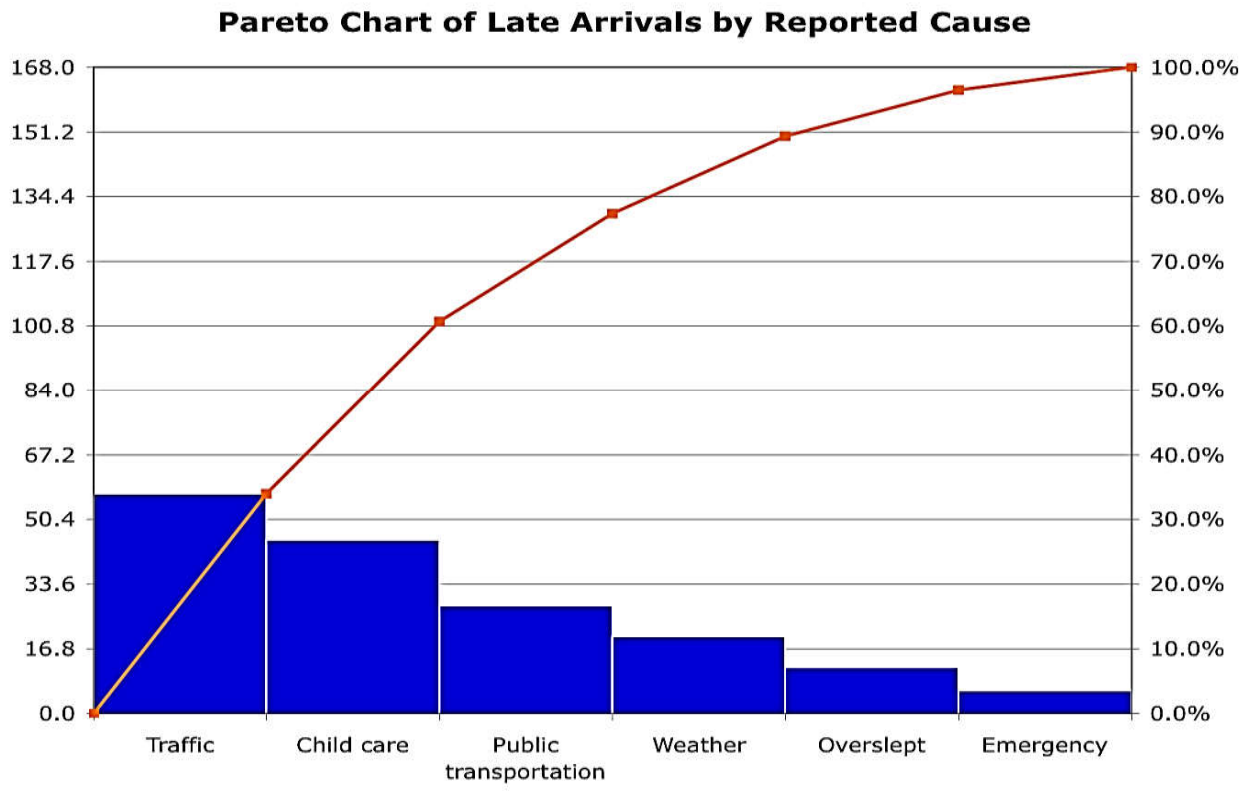
- **Amounts – bar graph, etc.**
- **Ratios – pie chart etc.**

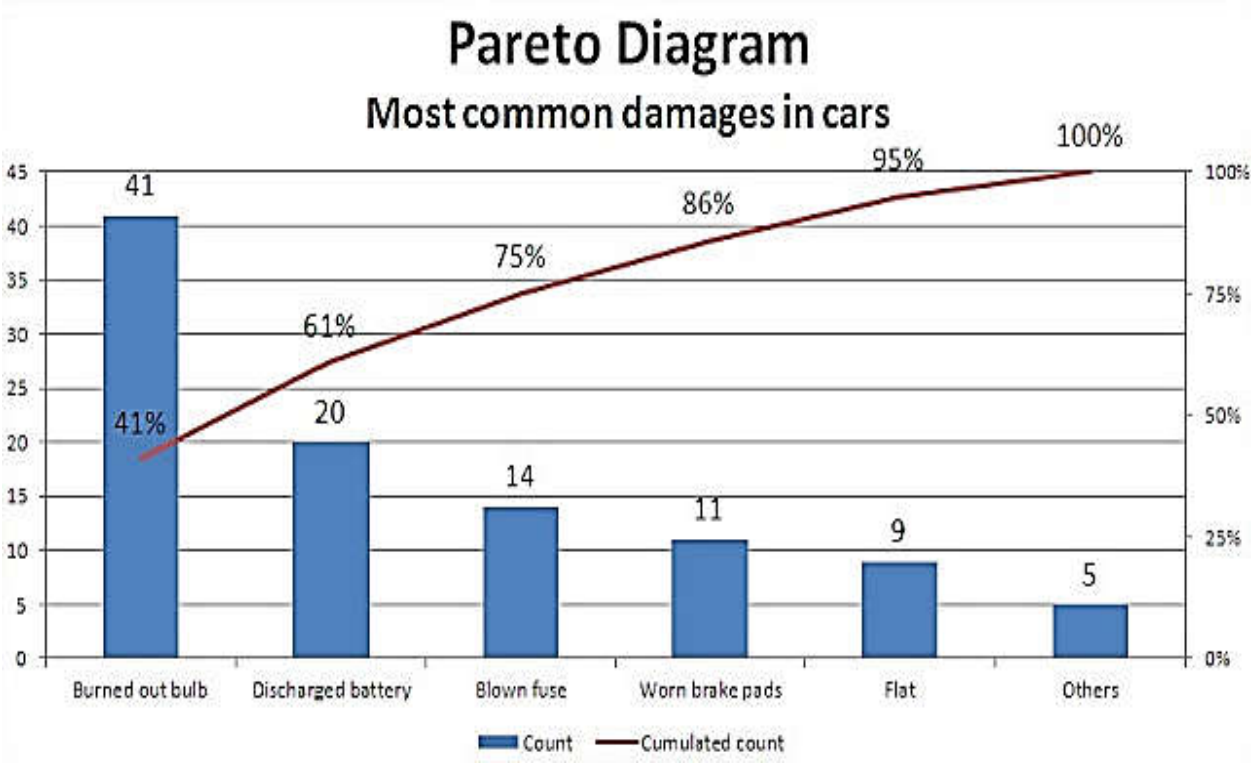
Topic 28

Analytical Chemistry

Quality Control Tools-VI

- **Pareto Diagram**
  - **is a combination of bar and line graphs of accumulated data,**
- **Pareto diagram**
  - **It is used where data associated with a problem e.g. a defect, or mechanical failure, or a complaint from a customer are divided into smaller groups by cause or by phenomenon and sorted by the number of occurrences or the amount of money involved. (The name "Pareto" came from an Italian mathematician who created the diagram.)**
  - **Bar chart arranged in descending order of height from left to right, bars on left relatively more important than those on right**
  - **Separates the "vital few" from the "trivial many" (Pareto Principle)**



- 

Benefits

- **Breaks big problem into smaller pieces**

- **Identifies most significant factors**
- **Shows where to focus efforts**
- **Allows better use of limited resources.**

Topic 29

Analytical Chemistry

Quality Control Tools-VII

- **Stratification**
  - **Stratification means to "divide the whole into smaller portions according to certain criteria."**
- **Stratification**
  - **In case of quality control, stratification generally means to divide data into several groups according to common factors or tendencies (e.g., type of defect and cause of defect).**
  - **Dividing into groups "fosters understanding of a situation." This represents the basic principle of quality control.**
  - **Stratification is a system or formation of layers, classes, or categories.**
  - **Stratification is used to describe a particular way of arranging seeds while planting, as well as the geological layers of rocks**

Item	Method of Stratification
Elapse of time	Hour, a.m., p.m., immediately after st work, shift, daytime, night time, day, v month

Variations among workers	Worker, age, male, female, years of experience, shift, team, newly emplo experience
Variations among work methods	Processing method, work method, w conditions (temperature, pressure, a speed), temperature
Variations among measurement/ inspection methods	Measurement tool, person performin measurement, method of measureme inspector, sampling, place of inspecti

- **Benefits**
  - **Allows observation of variations among strata.**
  - **By performing a cause analysis using the stratified data, the following can be accomplished.**

Topic 30

Analytical Chemistry

Quality Control Tools

(Use of Excel Worksheet)

- **Pareto Diagram: To identify the current status and issues**
- **Stratification: Basic processing during data collection**
- **Scatter Diagram: To identify the relationship between two variables**
- **Cause and Effect Diagram: To identify the cause and effect relationship**

- **Histogram:** **To see the distribution of data**
- **Check Sheet:** **To record data collection**
- **Control Chart/Graph: To find out abnormalities and identify the current status**

Quality Control Tools

Review QC tools in Problem Solving

	Graphs	Check sheet	Stratification	Pareto Diagram	Cause & Effect Diagram	Histogram	Scatter Diagram	Control Chart
Identification of problem	◎			◎				
Defining the problem	○	◎	◎	◎		○		
Record of facts		◎	◎			◎		◎
Detecting causes of problem			○		◎	◎	◎	
Develop Improvement method (Solution)								
Implementation								
Evaluation of result	○		○		◎	◎	◎	
Process control (Standardization)								◎

- **Use of Excel worksheet**
  - **These graphs can be constructed easily on Microsoft Excel worksheet**
  - **We may perform basic calculations (chemometrics) on that as well.**
  - **Switch to Excel**

Quality Control Tools

END

- Use of Microsoft Excel worksheet
  - Using these simple tools we can show the progress, the improvement, the problematic areas, possible starting options etc.

Topic 31

Analytical Chemistry

Quality Assurance-I

- **Validation of analytical methods**
  - **Analytical procedure is suitable for its intended purpose**
  - **Validate all non-standard analytical methods**
  - **Validated by R&D before being transferred to the QC**
- **Suitability of Instrument**
  - Status of Qualification and Calibration

- **Suitability of Materials**
    - Status of Reference Standards, Reagents, etc.
- **Suitability of Analyst**
    - Status of Training and Qualification Records
- **Suitability of Documentation**
    - Written analytical procedure and proper approved protocol with pre-established acceptance criteria.
- **Protocol: includes procedures and acceptance criteria**
- **Report: documented results**
- **Justification needed when non-pharmacopoeial methods are used (if pharmacopoeial methods are available). Justification to include data, e.g. comparisons with the pharmacopoeial or other methods**
- **Detailed standard test methods include:**
- **chromatographic conditions, reagents and others**
- **Method Validation includes**
    - **Specificity**
        - **Identification**
        - **Assay and Impurity Test**
    - **Linearity**
    - **Range**
    - **Accuracy**
        - **Assay**
        - **Impurities**
- **Method Validation includes (Cont….)**

- **Precision**
    - **Repeatability**
    - **Reproducibility**
- **Detection limit & Quantitation limit**
    - **Based on Visual Evaluation**
    - **Based on SNR**
    - **Based on Std Dev**
- **Robustness**

Topic 32

Analytical Chemistry

Quality Assurance-II

- **Specificity / Selectivity**
    - **ability to measure the desired analyte**
    - **determination of impurities and assay.**
    - **If analytical procedure is not specific a combination of two or more analytical procedures is recommended**
- **Suitable tests that should be able to discriminate compounds (may be of closely related structures)**
- **The discrimination of a procedure may be confirmed by obtaining positive results by comparison with a known reference material (positive control and negative control).**
- **The identification test may be applied to materials structurally similar to or closely related to the analyte.**

- **The choice of such potentially interfering materials should be based on sensible scientific judgment with a consideration of the interferences that could occur.**

Quality Assurance

Assay and Impurities

For chromatographic procedures, representative chromatograms should be used to demonstrate specificity, and individual components should be appropriately labeled.
Critical separations in chromatography should be investigated at an appropriate level.
In cases where a non-specific assay is used, other supporting analytical procedures should be used to demonstrate overall specificity. For example, where a titration is adopted to assay the drug substance for release, the combination of the assay and a suitable test for impurities can be used.

Examples

Total hardness test determined calcium and magnesium and reported as $CaCO_3$. For specifically Ca or Mg we may use atomic absorption spectroscopy.

Free Fatty acids / Acid value determine through acid base titration.

Crude protein estimated as Kjeldhal Nitrogen.

- **Specificity / Selectivity**

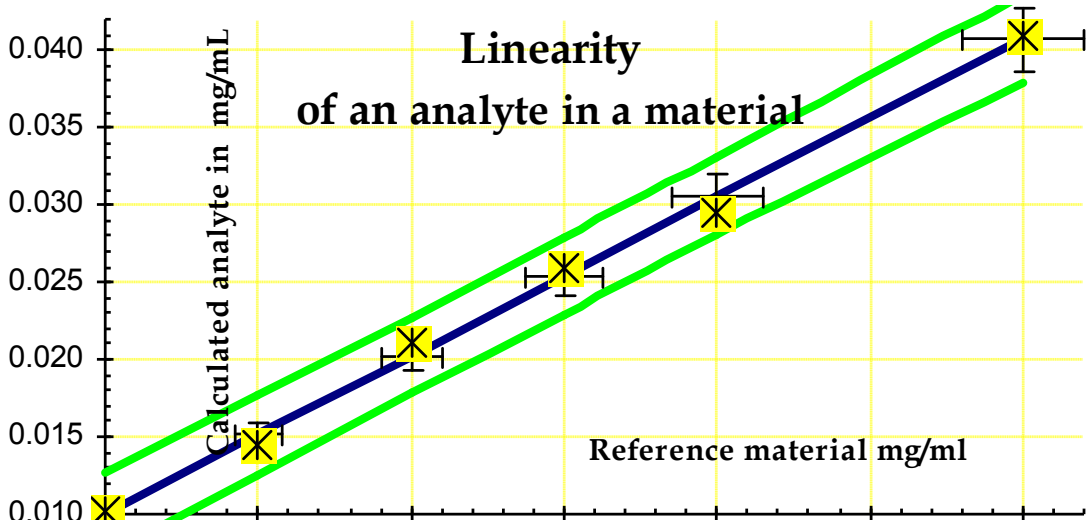
- **In this way we display ability to measure the desired analyte that may be active ingredient or may be the impurity or unwanted substance**

Topic 33

Analytical Chemistry

Quality Assurance-III

- **Linearity**
  - indicates the ability to produce results that are directly proportional to the concentration of the analyte in samples
  - **Linearity:**
  -
  - A series of samples should be prepared in which the analyte concentrations span the claimed range of the procedure. If there is a linear relationship, test results should be evaluated by appropriate statistical methods.
  - The correlation coefficient, y-intercept, slope of the regression line, and residual sum of squares should be submitted.
  - For the establishment of linearity, a minimum of five concentrations is recommended.



- **Linearity**
    - Different analytical techniques have different sensitivities and thus display linearity in variable ranges.
    - We have to choose the analytical method which matches the linearity of analyte with our matrix.

Topic 34

Analytical Chemistry

Quality Assurance-IV

- **Range:**

Range is an expression of the lowest and highest levels of analyte that have been demonstrated to be determinable for the product.

Range:

- The specified range is normally derived from linearity studies and depends on the intended application of the procedure.
- It is established by confirming that the analytical procedure provides an acceptable degree of linearity, accuracy, and precision when applied to samples containing amounts of analyte within or at the extremes of the specified range of the analytical procedure.
- Minimum specified ranges that should be considered:
- **For the assay of a drug substance or a finished (drug) product:** Normally from 80 to 120 percent of the test concentration.
- **For content uniformity:** Covering a minimum of 70 to 130 percent of the test concentration.
- **For dissolution testing:** +/-20 percent over the specified range; e.g., if the specifications for a controlled released product cover a region from 20

percent, after 1 hour, up to 90 percent, after 24 hours, the validated range would be 0-110 percent of the label claim.

- **For the determination of an impurity:** From the reporting level of an impurity to 120 percent of the specification.
- **Range:**
    - **Below or above detection limits the analyte can not be measured accurately.**

- **Topic 35**
- **Analytical Chemistry**
- **Quality Assurance-V**
- **Accuracy:**
    - Accuracy is the degree of agreement of test results with the true value, or the closeness of the results obtained by the procedure to the true value.
- Accuracy:
- It is normally established on samples of the material to be examined that have been prepared to quantitative accuracy.
- Accuracy should be established across the specified range of the analytical procedure.
- It is acceptable to use a “spiked” placebo where a known quantity or concentration of a reference material is used.
- Accuracy (Impurities)
- Accuracy should be assessed on samples (drug substance/drug product) spiked with known amounts of impurities.

- It should be clear how the individual or total impurities are to be determined, e.g., weight/weight or area percent, in all cases with respect to the major analyte.
- Accuracy may be inferred once precision, linearity, and specificity have been established.

Recommended Data:

- a minimum of 9 determinations over a 3 concentration levels covering the specified range (e.g., 3 concentrations/3 replicates).
- reported as percent recovery

Topic 36

Analytical Chemistry

Quality Assurance-VI

- **Precision:**
    - It is the degree of agreement among individual results.
    - The complete procedure should be applied repeatedly to separate and identical samples drawn from the same homogeneous batch of material. Reported as RSD.
- Precision:
- Repeatability: A minimum of nine determinations covering the specified range for the procedure, e.g. three concentrations/three replicates each, or a minimum of six determinations at 100% of the test concentration
- **Intermediate precision:** Within-laboratory variations
- usually on different days, analysts and equipment. (If reproducibility is assessed, a measure of intermediate precision is not required.)
- **Reproducibility:** Precision between laboratories

Reporting results:

- The standard deviation, relative standard deviation (coefficient of variation), and confidence interval should be reported for each type of precision investigated.

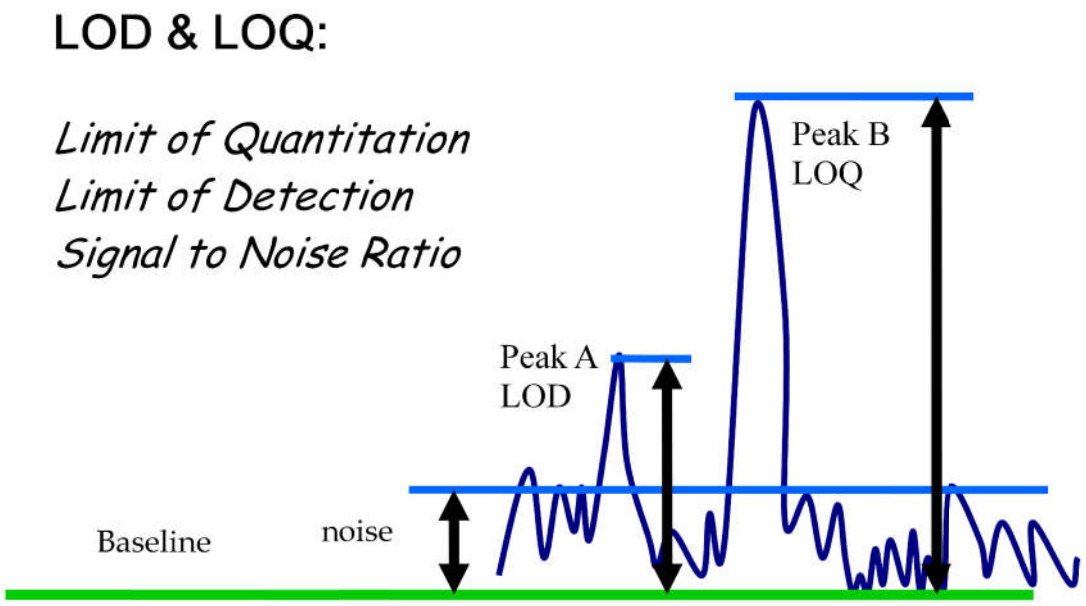
Topic 37

Analytical Chemistry

Quality Assurance-VII

- **Limit of Detection (LOD):**
    - It is the smallest quantity of an analyte that can be detected, and not necessarily determined in a quantitative fashion.
- Limit of Quantitation (LOQ):
    - It is the lowest concentration of an analyte in a sample that may be determined with acceptable accuracy and precision.

Quality Assurance



LOD & LOQ:

Approaches (instrumental or non-instrumental):

Visual Evaluation (mostly in non-instrumental methods)

Signal to Noise Ratio (3 or 2:1 is acceptable of LOD while 10:1 is generally acceptable for LOQ)

Standard Deviation of the Response and the Slope (3.3 σ/S for LOD & 10 σ/S for LOQ)

Standard Deviation of the Blank

Calibration Curve (The residual standard deviation of a regression line or the standard deviation of y-intercepts of regression lines may be used as the standard deviation).

LOD & LOQ:

- LOQ may be the least range of your measurement.

LOD mention the specificity measurement of analyte by your method.

Topic 38

Analytical Chemistry

Quality Assurance-VIII

- Robustness:
    - Robustness is the ability of the procedure to provide analytical results of acceptable accuracy and precision under a variety of conditions.
- Examples of typical variations:
- While performing chromatographic analysis:
- stability of test and standard samples and solutions
- reagents (e.g. different suppliers)
- different columns (e.g. different lots and/or suppliers)
- extraction time
- variations of pH of a mobile phase
- variations in mobile phase composition
- temperature
- flow rate

Method Validation Guidelines:

- VALIDATION OF ANALYTICAL PROCEDURES: TEXT AND METHODOLOGY Q2(R1)
- Developed by the appropriate ICH Expert Working Group

Topic 39

Analytical Chemistry

Quality Assurance-IX

- Measurement Uncertainty:
    - “A parameter associated with the result of a measurement, that characterizes the dispersion of the values that could reasonably be attributed to the measurand”.
- Sources of uncertainty:
- sampling,
- matrix effects and interferences,
- environmental conditions,
- uncertainties of masses
- volumetric equipment,
- reference values,
- approximations and assumptions incorporated in the measurement method and procedure,
- analyst

Type A and Type B UncertaintyUncertainty Type "A": Uncertainty component, evaluated experimentally from the dispersion of repeated measurements, using statistical methods.

Uncertainty Type "B": Uncertainties that are always expressed and evaluated as probability distributions like normal, rectangular and triangular distributions and are called Type B, uncertainties.

Normal Distribution: 95% confidence level.

Rectangular Distribution: without specifying a level

Triangular Distribution

Calculating Uncertainty:

Formula for evaluating Uncertainty, (Type "A")

$$U_A = \sigma / N \quad \text{(Standard error of the mean)}$$

Component of type B

Type B = (Component 1)^2 + (Component 2)^2 +……..

All the components added must have same units and distribution.

Formula for calculating the combined uncertainty (U_C)

$U_C = (U_A)^2 + (U_B)^2$ (Where U_A and U_B are the type "A" and type "B" Uncertainties)

Reporting Uncertainty:

- Expanded uncertainty

$U_e = U_C$ X k

(k = 2 Correspond to the confidence level of 95 %, in relation to the normal distribution curve).

- Uncertainty is reported as Y ± U_e with confidence level of 95% (Where, Y = measurand)

Topic 40:

Analytical Chemistry

Quality Assurance-X

ISO / IEC systems:

- ISO creates documents that provide requirements, specifications, guidelines or characteristics that can be used consistently to ensure that materials, products, processes and services are fit for their purpose.
- International organization for standardization creates documents to ensure quality of process, environment, testing activities, human performance etc.

Guidelines:

- A guideline aims to streamline particular processes according to a set routine or sound practice (GMP, GLP).

System:

- A set of policies and procedure to create consistent and valid results.

Certification:

- Certification refers to the confirmation of certain characteristics of an organization by some form of external review, assessment, or audit.

Accreditation:

- Accreditation is a process of validation set by a peer review board.
- Popular Standards:
- ISO 9001: Quality Management System
- Develop documentation (JD, SOP, WI, STM, SQA) to follow and create objective evidence (fill data and formats) that you have followed
- ISO 14001: Environmental Management System
- provides practical tools for organizations to manage their environmental responsibilities
- ISO 22000: Food Safety Management System
- ISO 45001: Occupation Health and Safety
- ISO 17025: Lab Management System

- General requirements for the competence of testing and calibration laboratories

ISO 17025:

- is an international accreditation system that prove the capability of a laboratory to produce reliable and valid analytical results.
- fulfills all requirements of ISO 9001 certification

Topic 41

Analytical Chemistry

Quality Assurance-XI

ISO 17025:

- **Contains 25 clauses**
- **15 management clauses**
- **10 Technical clauses**
- ISO 17025 comprises on 25 clauses ……Management clauses are to maintain management structure of an organization. You may understand it is the hardware. While the technical clauses are the software of the organization. The compliance of technical clauses mean that organization enhance technical competence of that lab or organization..
- Management Clauses:
- 4.1: Organization
- 4.2: Management system
- 4.3: Document control
- 4.4: Review of requests, tenders and contracts
- 4.5: Subcontracting of tests and services

- 4.6: Purchasing services and supplies
- 4.7: Services to customer
- **Management Clauses:**
- 4.8: Complaints
- 4.9: Control of non-conforming testing and/or calibration work
- 4.10: Improvement
- 4.11: Corrective action
- 4.12: Preventive action
- 4.13: Control of Records
- 4.14: Internal audits
- 4.15: Management Reviews
- Technical Clauses:
- 5.1: General
- 5.2: Personnel
- 5.3: Accommodation and environmental conditions
- 5.4: Test and calibration methods and method validation
- 5.5: Equipment
- Technical Clauses:
- 5.6: Measurement traceability
- 5.7: Sampling
- 5.8: Handling of test and calibration items
- 5.9: Assuring the quality of test and calibration results
- 5.10: Reporting of results

Topic 42

Analytical Chemistry

Quality Assurance-XII

4.1 Organization

Organization must be a legal entity

4.1 Organization

Legal entity

Conflict of interest defined (Part of larger org.)

Impartiality and freedom from commercial / financial pressures

Have policies in place to manage impartiality, judgement or operational integrity

Have Management and Technical staff.

Technical Manager and Technical Management

Organization must be a legal entity.

Policies must be to reduce conflict of interest…

Organization must have

- Technical and management staff
- Technical manager and Technical Management
- Organization must have technical manager and technical management

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Topic 43

Analytical Chemistry

Quality Assurance-XIII

4.2 Management system

- Organizational chart

- Policies
- Scope must be defined
- Organization
    - CEO / COO
    - Quality Assurance
        - Quality Manager / Technical Manager
    - Production
    - Sales
    - Procurement
- Organogram show hierarchy of an organization…. How big or small, what kind of variety it is producing, how many workers are there….
- **4.2 Management System**
- Must have implemented a MS appropriate for its scope and activities (documented to extent necessary to assure quality of result)
- Understood by all in organization and communicated to all
- System must be documented
- Top management must demonstrate commitment

Management System

- Top management must demonstrate commitment (lead by example)
- Must show commitment in Quality Policy

Topic 44

Analytical Chemistry

Quality Assurance-XIV

4.3 Document control

- The implementation of proper document control system ensure access to the latest version of related document to each one in the shop.
- Quality
- Manual
- Policies and Procedure
- WI, SOP, STM
- Formats and records
- 4.3 Document control
- Documents must be uniquely identified
- Approval and issue – Reviewed and approved (uniquely identified)
- Document changes – by original function. Altered text highlighted
- Computerized data must be controlled

4.3 Document Control

- Must have procedure for Document control
- Document of external origin must be listed
- List of all documents, issuance and retrieval record must be available

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Topic 45

Analytical Chemistry

Quality Assurance-XV

4.4: Review of request tenders and contracts

Request:

- Sampling, Testing and calibration requests

Tenders:

- For purchase of supplies

Contracts:

- Procurement
- Hiring
- 4.4 Review of requests, tenders and contracts
- Have procedures in place for this (Records of review must be available)
- Have necessary resources
- Differences resolved before acceptance
- Can be oral or documented (contract)
- Review of simple or routine results
- Repetitive tests – Review at initial stage only as long as unchanged
- Customer shall be informed of any deviation

4.5 Subcontracting of test and calibration:

- If a lab already accredited for certain test or calibration
- Temporary loss of capabilities

Personnel or equipment failure

Topic 46

Analytical Chemistry

Quality Assurance-XVI

4.6 Purchasing Services and Supplies:

- Reagents
- Apparatus and equipment
- Equipment maintenance

Calibration4.6 Purchasing of services and supplies

Must have procedure

Supplier quality assurance (SQA)

Maintain a register of suppliers

Purchased items must be quarantine for inspection

Properly segregated areas for accepted and rejected supplies

4.7 Customer service

- The laboratory shall obtain feedback from customers and analyze for possible improvement.

4.8 Complaints

- May be from internal or external customers or from own employees

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Topic 47**Analytical Chemistry**

Quality Assurance-XVII

4.9 Control of non-conforming testing and calibration work:

- Non-conformance?
- Procedure
    - What to do?
    - Who to do?

    - How to proceed?
- 4.9 Control of nonconforming testing/calibration work
- Policies – procedures implemented shall include
- Responsibilities and authority
- Evaluation
- Correction taken "immediately". Where necessary the customer is notified and work is recalled
- **Responsibility for authorizing resumption of work is defined**

4.10 Improvement

- **Shall continually improve effectiveness of MS through analysis**
- 4.10 clause is improvement. ISO 9001 have concepts of quality circles, discussion forum, participation from workers to suggest improvement. Similarly incorporated in ISO 17025

Topic 48

Analytical Chemistry

Quality Assurance-XVIII

4.11 Corrective action

- Reactive approach

and

4.12 Preventive action:

- Proactive approach
- 4.11 Corrective action
- Shall designate and give authority for implementing Corrective Action

- Shall start with a cause analysis (analysis of all potential causes)
- Identify all potential corrective actions (select and implement)
- Shall monitor corrective actions effectiveness
- 4.12 Preventative Actions
- Needed improvements and potential sources of NC shall be identified
- Action plans developed when identifiedCorrective and Preventive action:
- Prevention is better than cure
- Procedure must be there for both

Topic 49**Analytical Chemistry**

Quality Assurance-XIX

4.13 Control of records:

- What are records?
- Readily retrievable
- Protection and back up needed
- 4.13 Control of records
- Procedure for identification, storage, maintenance and disposal of records
- Quality records shall includes;
- **Test reports**
- Internal audit reports
- Management reviews (meeting minutes)
- Corrective and preventive action
- Supplier Quality assurance
- Sub contractors record

4.13 Control of records:

Records must be:

- Legible and retrievable,
- Retention time established
- Observation, data and calculations recorded
- Mistakes crossed out and signed not erased

Topic 50

Analytical Chemistry

Quality Assurance-XX

4.14 Internal Audits:

- **Type of audits**
- Purpose of audit
- Procedure
  - Who will do that?
  - What to audit?

4.15 Management review:

- Who to convene?
- Agenda of meeting
- 4.14 Internal audits
- Done periodical – All elements of system annually
- Done by trained and qualified staff - by persons independent of activities to be audited
- 4.15 Management reviews

- Suitability of policies and procedure
- Reports from laboratory personnel
- Outcome of Internal audit
- Assessment of external bodies
- Sub contractors and SQA record
- Results of ILC and PT
- Change in volume and type of work
- Customer complaints and feedback

Frequency:

- Every clause must be audited once in an year
- Horizontal and Vertical audits
- Management review meetings of laboratory's technical management with higher authorities once in an year

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