

ERRORS AND TYPES OF ERRORS

An inverse indicator of a result's correctness is its error. The outcome is more accurate the less inaccuracy there is. The difference between the correct value and the observed value is the mathematical definition of error:

Absolute Error = Observed Value – True Value

It may be negative or positive. But it is more convenient to express the error as relative error.

Relative Error = $\frac{\text{Observed value} - \text{True Value}}{\text{True Value}} \times 100$

I. TYPES OF ERRORS

Errors can be divided into two groups for practical purposes: (i) determinate errors and (ii) indeterminate errors.

1. Determinate Errors: As indicated by their name, determinate errors are those whose size can be established once a specific cause is assigned, enabling them to be rectified. For instance, consider the weighing of a hygroscopic salt such as calcium chloride. If it were weighed in an open environment, its weight would fluctuate due to the absorption of moisture from the atmosphere. The error resulting from the salt's moisture absorption can be rectified by weighing the salt after it has been dried and stored in a desiccator.

2. Sources of Determinate Errors: Determinate errors can be attributed to a variety of sources. While it's not necessary to list them all, the most significant ones are outlined below:

- **Errors due to Equipment:** Such errors stem from defective or uncalibrated equipment, such as imbalances in the arms of the scale, inadequate precision of the balance, uncalibrated measuring containers, or uncalibrated weights, among others.
- **Errors due to Reagents:** The quality of reagents plays a pivotal role in quantitative analysis. In specific cases, reagents may contain impurities that could disrupt the accuracy of a particular quantitative analysis. Additionally, errors can occur when incorrectly standardized solutions are used for titration.
- **Personal Errors:** These errors arise from inherent limitations in an analyst's ability to make precise observations, which is to say, they stem from the innate weaknesses of the analyst. For instance, certain individuals consistently identify the endpoint of a titration as slightly beyond the actual point due to their inability to accurately discern color changes.
- **Operational Errors:** Operational errors pertain to the procedures employed during an analysis. These errors remain unrelated to the instrument, equipment used, or the chemical characteristics of the system under investigation. They primarily stem from the operator's lack of attentiveness in quantitative work. Examples include the unintentional loss of solution due to splashing during heating, incomplete removal of precipitate from vessels, and insufficient or excessive washing of precipitates.

- **Methodic Errors:** Occasionally, the accuracy of a specific method for quantifying a particular component in a given sample may be compromised due to an inappropriate selection of the procedure within the required range, leading to inaccurate results. For instance, when determining trace amounts of iron in water, the gravimetric method would yield an incorrect result, necessitating the selection of a method suitable for trace-level concentrations, such as a spectrophotometric method. Methodical errors are intrinsic to the chosen method and cannot be rectified unless the appropriate method is employed.
3. **Indeterminate Errors:** Indeterminate errors are errors for which an exact cause cannot be identified, making them uncorrectable. These errors may have sources similar to those of determinate errors, but specific causes cannot be pinpointed for indeterminate errors. Even after applying all available corrections for potential determinate errors, the repeated observations may still exhibit variation, which is attributed to indeterminate errors. Indeterminate errors cannot be entirely prevented or eliminated through corrections; however, they can be significantly minimized through heightened diligence in the work process and an increase in the number of replicate determinations.

II. MINIMIZATION OF ERRORS

1. **Calibration of Equipment and Purification of Reagents etc:** To mitigate determinate errors arising from equipment and reagents during quantitative estimations, several self-evident measures can be adopted. These include: (i) weight calibration, (ii) calibration of volumetric glassware, (iii) utilization of purified reagents, and (iv) appropriate sample sizes. Following the calibration of devices, corrections should be applied accurately, and equipment should be subject to periodic recalibration. Reagents with the desired level of purity should be chosen, and purification should be carried out when necessary. A useful comparison can be made by referencing high-purity labeled reagents, such as AR reagents.
2. **Use of Blanks:** Errors resulting from specific sources such as reagents, containers, or the solubility of precipitates can be minimized through the judicious use of blanks. In precise work, a blank run is typically the preferred approach. A blank includes all the other reagents necessary for a particular analysis, excluding the material being examined, and a blank run encompasses all the procedural steps involved in the actual analysis, mirroring the sample analysis. The correction is then applied to the results, referred to as a blank correction. For example, in a volumetric determination, the titrant reading is often adjusted for the volume of titrant needed to induce a change in color for an indicator (known as an indicator blank).
3. **Independent Analysis:** Identifying methodic errors can be quite challenging, as there can be multiple pathways through which these errors occur. One approach to detecting determinate methodic errors involves analyzing a synthetic sample with a well-defined composition that closely mimics that of the analyte. Another method to mitigate methodic errors often involves analyzing the sample using a well-established, reliable method. In this case, the results obtained from one method can be compared to those obtained from an entirely different method. If the results from these two fundamentally distinct methods align, there is a high likelihood that the values are correct with only minimal margins of error.

III. SIGNIFICANT FIGURES

You know that a number is a mathematical expression of a quantity. A figure, or digit, is any one of the characters 0, 1, 2, ..., 9 which, alone or in combination, serves to express a number. The digits of a number which are needed to express the precision of the measurement from which the number was derived are known as significant figures.

Numbers from 1 to 9 are consistently considered significant figures, while the inclusion of 0 as a significant figure depends on the context. A digit within a number represents the quantity associated with its respective place value. In the case of the number 542, each of the figures represents its respective place value, signifying five hundreds, four tens, and two units, making all of them significant.

There are certain rules which need to be followed to measure the significant figures of a calculated measurement.

- All non-zero digits are significant.
- Zeroes between non-zero digits are significant.
- A trailing zero or final zero in the decimal portion only are significant.

Following are the significant figures rules that govern the determination of significant figures:

1. Significant digits include all non-zero digits. For instance, in 6575 cm, there are four significant figures, and in 0.543, there are three significant figures.
2. If a zero appears before a non-zero digit, it is not considered significant. This initial zero is indicative of the decimal point's position. For example, in 0.005, there is only one significant figure, and the number 0.00232 has three significant figures.
3. Zeros situated between two non-zero digits are also considered significant figures. For example, the number 4.5006 has five significant figures.
4. Trailing zeros on the right side of a number are also counted as significant figures. For instance, 0.500 has three significant figures.

IV. CONTROL CHARTS

An essential statistical tool for the analysis and management of repeated operations is the control chart. W.A. Shewart created the control chart, which is predicated on the idea that all repetitive operations contain some degree of unpredictability.

It is hard to find two really identical things in nature. If anything, we encounter precisely the same items. This also applies to the processes involved in production. There isn't a production method that can generate identical things every time.

A control chart is a picture that shows the data that has been gathered. The data might be applicable to sample quality characteristics that are measured or assessed. A common tool for observing and analyzing industrial processes are control charts. To ascertain whether a process is under control or not, one can utilize a control chart. The primary goal of a control chart is to distinguish between random or common causes of variation and specific or

assignable causes of variation. Control charts, which are based on normal distribution theory, typically include a centerline (CL), lower control limit (LCL), and upper control limit (UCL). The control limits show the range of typical variability, whereas the centerline is an approximation of the process average. Finding a production process's inherent capability with the aid of a control chart enables more informed decisions regarding reliability and more accurate comparisons between various designs and production techniques.

There are many types of control charts used in analytical quality assurance:

- Shewhart charts.
- X-charts
- Recovery rate control charts (RR charts)
- Range control charts (R-charts)
- X-R combination charts
- Standard deviation charts...

1. Shewart Quality Control Chart: For industrial product control, Shewart invented the quality control chart. The product, which needs to have consistent features within the specified bounds, is the problem. Let's talk about the screw production process as an example. You can spot-check any number of objects for length during the manufacturing process. namely, it is possible to measure the screw length. Once a production step has been monitored for a few days with many random samples, divide the samples into N subgroups according to the day. Perform analysis on N subgroups and corresponding mean is calculated. It is a graph with time, day, series number etc.. on the x-axis and the concentration of the variable in the reference material on the y-axis. Target, warning and action lines are marked parallel to the x-axis.

The graph clearly shows significant abrupt changes in the production process that result in a drop in quality. The likelihood of producing scrap and receiving complaints from customers is reduced when production process errors are fixed quickly.

Calculation Process:

Calculate the Average(X) and Range(R) for each subgroup

$$X = \sum x/N \quad R = \sum R/N$$

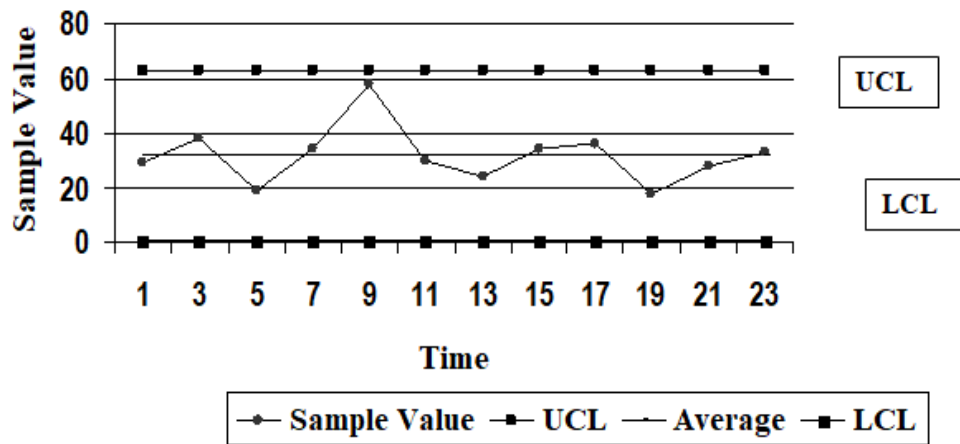
$$UCL = X + A_2R \quad \text{or} \quad UCL = X + 3S \quad (A_2 = 3/d_2\sqrt{n})$$

$$LCL = X - A_2R \quad \text{or} \quad LCL = X - 3S \quad (S = \text{Standard deviation})$$

- X-chart shows the variation in the averages in the samples.
- R-chart shows consistency of the process i.e. it shows the variation in the ranges of the samples.
- σ chart shows the variation in the process.

The typical control chart(X) is given by...

Plot of Sample Data Over Time



2. Basic Concepts of Environmental Management: Human-induced alterations to the environment have persisted throughout various historical periods. Nevertheless, the past two centuries, particularly in the aftermath of the industrial revolution, have experienced a rapid escalation in environmental transformations, primarily driven by the widespread utilization of natural resources on an unprecedented level. The extensive combustion of fossil fuels, the emission of diverse chemical contaminants into the atmosphere, water, and soil, deforestation for agricultural purposes, and the intensive exploitation of all available natural resources now pose a significant threat to the very environment upon which human survival hinges.

Top of Form

Happily, there is a growing recognition of environmental issues in the majority of countries worldwide. Many individuals believe that persisting with unsustainable development practices is a path leading to potential disaster. Governments are becoming more attentive to the counsel provided by environmental advocates and are progressively implementing laws aimed at safeguarding the environment from the adverse effects of economic endeavors. Nevertheless, the effective enforcement of environmental regulations is proving to be a challenge in most instances.

3. AIMS OF ISO-14000

- Minimize how their operations (processes, etc.) negatively affect the environment.i.e,Cause adverse changes to air,water,or land.
 - It is a process for managing company activities that impact the environment.
 - Observe with applicable laws,regulations,and other environmentally oriented requirements, and Continually improve in the above.
- ISO-14000 is a management system standards developed by the technical committee TC-207.this mainly concentrates on environment management.
 - ISO-14004: Environmental management system specification with guidance for use.
 - ISO-14004: Environmental management system general guidelines on principles, systems and supporting techniques.

- ISO-14010: Guidelines on environmental auditing-general principles.
- ISO-14011: Guidelines on environmental auditing-audit procedures,auditing of environmental system.
- ISO-14012: Guidelines on environmental auditing-qualification criteria for environmental auditors.

4. ISO 14000 is a group of standards covering the following areas

- Environmental Management Systems (14001, 14002, 14004)
- Environmental Auditing (14010, 14011, 14012)
- Evaluation of Environmental Performance (14031)
- Environmental Labeling (14020, 14021, 14022, 14023, 14024, 14025)
- Life-Cycle Assessment (14040, 14041, 14042, 14043)

5. The Environmental Management System contains the following elements

- An environmental policy supported by top management.
- Identification of environmental aspects and significant impacts.
- Identification of legal and other requirements.
- Environmental goals, objectives, and targets that support the policy.
- An environmental management program.
- Definition of roles, responsibilities, and authorities.
- Training and awareness procedures.
- Process for communication of the EMS to all interested parties.
- Document and operational control procedures.
- Procedures for emergency response.
- Procedures for monitoring and measuring operations that can have a significant impact on the environment.
- Procedures to correct nonconformance.
- Record management procedures.
- A program for auditing and corrective action.

6. Benefits of Implementing ISO 14000 EMS: Environmental Management Systems (EMS) serve as the cornerstone of the ISO 14000 series of global environmental management standards. An EMS can attain registration as compliant with the ISO 14001 EMS standard. Given that the ISO 14001 EMS encompasses the entire organization and all its facets impacting the environment, it can enhance an organization's environmental performance across various dimensions. This enhanced performance entails a cost for the organization, but these costs can be recouped through proactive pursuit of associated benefits.

The following categories describe the advantages of an EMS and how to register the EMS with ISO 14000:

- Increased Profits
- Operations
- Marketing

- Regulatory Compliance
- Social

7. Increased Profits

- Adopting ISO 14001 today serves as a foundation for the implementation of other ISO 14000 series standards. This step-by-step approach has the potential to lower the overall costs of ISO 14000 implementation, thanks to the insights gained in each phase.
- Decreasing the quantity of materials and energy needed for product manufacturing can lead to reduced product costs, material handling expenses, and waste disposal outlays.
- Some companies have discovered that running an Environmental Management System (EMS) is more cost-effective than a compliance-focused system.
- An EMS can contribute to a decline in pollution incidents and the associated recovery costs.
- Recycling manufacturing waste and unused resources can boost revenues, even if the recycling is done in a separate facility that can utilize the waste as input in their production.
- Enhancing employee health and safety not only improves productivity but also reduces sick days and lowers insurable risks.
- A reduction in insurance claims can result in reduced coverage costs and settlements.
- Meeting the diverse standards of different countries can be a costly endeavor, but ISO 14000 offers a singular standard that can streamline these efforts.

V. ISO-9000

1. What is ISO

I – International
O – Organization For
S – Standardisation

2. What is ISO 9000 : 2000

It outlines the principles of the Quality Management System and provides a glossary of its terms.

9000 – 90 Countries & 100 acceptable Products Standards

2000 – Year of Publication / Revision

3. Birth of ISO

1945 – While Second World War, there was no belief in International Market.

1967 – Realisation of the need of Worldwide Global business

1987 – Formation of ISO and release of ISO Standard (Rev No – 00)

1994 – Revision in Original Standard (Rev No. – 01)

2000 – Revision in 2nd edition of 1987

4. Features of ISO standards

- These are standards of system of production
- These are generic standards
- These are practical standards
- These are not product standards
- These ensure consistency of product quality
- In this, mistakes are corrected in a systematic way so that chances of repetition are reduced.

5. Benefits that will be derived from Working to ISO 9000-2000

- Improved communication at all levels
- Decreasing trend in rejections, reworks, customer complaints
- Decreasing trend in inventories
- Lead time reduction
- Customer relation improvement.
- Trust/confidence enhancement.
- Sub-contractor relation improvement.
- Long term association.
- Improved housekeeping
- Improved contacts with overseas buyers.
- People development
- Improved health of people.
- Passport to international market
- Adopting the ISO-9000 standards by the Indian industry will improve foreign exchange and allow it to compete on the global stage.
- Membership of exclusive club
- Change in culture
- Right at first time to reduce rework / cost
- Higher productivity and economical production
- Quality as a way of life – Highly disciplined
- Best use of resources
- Customer confidence – consistent quality
- Top management commitment and employee involvement
- More business – more profit
- Saves time (Effective system which is established is known to all)
- It increases morale of the company
- It ensures Quality and after sales service to customers
- It improves team work
- It saves cost by :
 - Avoiding repetition of work
 - Avoiding unnecessary records
 - Monitoring processes

- Opportunities for export market
- Due to increased confidence of customers in you, you get more & more orders
- It improves discipline in the organization
- It increases credit in the market

6. Disadvantages

- The ISO-9000 series of standards requires a significant resource commitment for implementation. The system's creation and documentation take a lot of time.
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7. **What is ISO 9001: 2000:**It lays forth the specifications for a Quality Management System, while the organization must show that it can produce goods that meet customer demands, relevant legal requirements, and customer satisfaction standards.

8. **What is ISO 9004: 2000:** It offers recommendations that take into account the Quality Management System's efficacy and efficiency.

9. **What is ISO 19011: 2002:** It provides Guidance on Auditing Quality and Environmental Management System.

10. **What is ISO 14000: 1996:** It is Environmental Management System Standard.

11. **What is ISO 20000:** IT Services Management

12. **What is ISO 27001:** Security Management System

13. Where & whom can Applicable for ISO?

All Small Scale, Medium Scale, Large Scale Engineering, Automobile Industries, Service Sectors like Banks, Institutes, Hospitals, Construction, Software industries, Pharmaceutical, Agricultural, Chemical, Electrical, Electronics, Telecommunications, Traders Shop Keepers, Housing Societies etc. Government Sectors.

14. Why ISO Certificate is required?

- To Achieve Customer Delightness
- To increase Profit margin in the business
- To get more customers & more business
- To continual improve in Quality, Cost Reduction, Services & Safety
- To retain good people in the organization
- To diversify it into the related field
- To increase export
- To compete with the competitors
- To increase productivity of the Organisation

15. When ISO 9000 Certificate required?

As per customer Demand As per Own Management requirements of Quality Improvement & Cost Reduction. To enable the organisation to compete with competitors. Need of Improvement in the business profit. Need to streamlining and smoothening the organisation working.

16. How we can get ISO Certificate?

- Through the decision made by top management to pursue ISO certification.
- By selecting a certified lead auditor, consultant, and trainer to provide guidance during the implementation process.
- By establishing, documenting, implementing, and maintaining a Quality Management System in accordance with the ISO 9001:2000 standard.
- By finalizing and approving Process Flow Diagrams, Raw Material Quality Plans, In-Process Quality Plans, Bought-Out Quality Plans, and Final Product Quality Plans for each product within every operation.
- By maintaining records in alignment with product, process, and system requirements and their associated documentation.
- By continually working to enhance the quality objectives established by top management.
- By reducing the occurrence of customer complaints.

17. ISO 9000-1, Quality management and quality assurance standards: Guidelines for selection and use: Provides a foundation for comprehending and choosing the standards that are suitable for your needs. provides advice on how to allocate, manage, and plan resources to create dependable and long-lasting products.

18. ISO 9001: Model for Quality Assurance in design/development, production, installation: A product or a service has to pass through several stages before it is supplied to the customers. Even after it is supplied to the user, a necessity may arise to keep a follow up action. So that user does not face any problems or difficulties in using the product. ISO-9001 standard gives a model for quality assurance from designing the product and continuing even after the product is delivered to the customer.

ISO-9001 applies to industries that design, produce, install product and provide service after sales as per requirements of the customer. some specific examples are heat exchangers, coolers, filters, extraction columns...for process industries.

After product is manufactured, and inspected for conformance with specifications it should be installed by the supplier at the customer's premises and trail run should be conducted.

19. ISO-9002: Model for Quality Assurance in Production, Installation and Servicing: Some products require quality assurance only during production and till they are delivered to the customer or installed in his premises. In such cases the manufacturer gives his own design to meet the customer requirements and has to only prove the production process is capable of producing the product as per the requirements of the customer. Civil structures, Construction of bridge etc...are the examples. So the model is

applicable where the assurance on quality is required only during production and up to satisfactory installation.

20. ISO-9003: Model for Quality Assurance in final inspection and test: Certain products require quality assurance only after they are manufactured i.e. at the time of supply. The customer is not concerned with how they are manufactured. He is interested only in getting the product of desired quality as stated by the supplier. Examples of such cases are: Domestic appliances, petroleum products, components used in the assembly of manufacturer of bigger items such as automobiles etc....Most of the consumer items also fall in this category.

21. ISO-9004: Quality management and quality system elements Guidelines: ISO-9001, ISO-9002 and ISO-9003 apply where a contract between supplier and contractor exists. In non-contractual situations companies may adopt ISO-9004 which gives guidelines for quality management.

It is essential to build confidence of the customer that the organization can supply the desired quality of the products or service. The organization has to take several integrated steps in managing all matters which have direct or indirect effect on its image to deliver the products of desired quality.

This standard is not obligatory in nature; rather, it furnishes you with directives for establishing a quality system that caters to the requirements of both your customers and your organization. It offers quality management recommendations that are pertinent to producers of processed materials, particularly those distributed in bulk. These guidelines facilitate the implementation of ongoing quality enhancement practices within your organization, leveraging data collection and analysis tools and techniques.

22. ISO 10005, Quality management– Guidelines for quality plans: You can use this standard as a guide to create quality plans for managing certain projects, contracts, or goods.

23. ISO 10011, Guidelines for auditing quality auditing systems: The quality system has to be checked from time to time for its proper functioning. It has to be updated or modified to meet the demand of the time. Otherwise the systems will lose their effectiveness or fail to meet the requirements of time.

24. ISO-10011-1: This standard outlines the role of auditors, delineates their responsibilities, and covers various aspects of auditing, including the execution of the audit and reporting. It can be employed for internal purposes within your organization or for auditing your suppliers.

25. ISO-10011-2: This standard addresses the qualification requirements for auditors responsible for quality systems, specifying their competencies essential for conducting audits. It offers guidance on the necessary education, training, experience, personal qualities, and management skills required to effectively execute an audit.

26. ISO-10011-3: Deals with establishment of audit function. Provides basic guidelines for managing quality system audit programmes.

VI. PARAMETERS FOR METHOD VALIDATION

The method needs to fulfill specific validation requirements in order to be suitable for the intended use. The following typical validation features should be taken into account: range, accuracy, precision, limit of detection, linearity, selectivity (specificity), and quantitation.

- 1. Selectivity (Specificity):** A method's selectivity is defined as its ability to identify a specific analyte or analytes in a complex mixture without interference from other mixture constituents. It is common to use the phrases selectivity and specificity interchangeably. In general, a method is said to be specific if it yields a result for just one analyte; on the other hand, a method that yields results for several chemical entities that may or may not be distinguished from one another is said to be selective. A selective method is one in which the response stands out from all other responses. The term selectivity is more applicable than specificity because relatively few analytical techniques respond to only one analyte. "Specificity is the ultimate of Selectivity," according to the International Union of Pure and Applied Chemistry (IUPAC). The term "selectivity" is encouraged by the IUPAC, but "specificity" is discouraged.

Data demonstrating the lack of interference peaks with respect to degradation products, artificial contaminants, and the matrix (excipients present in the formed product at expected quantities) must be presented in order to prove the analytical method's selectivity.

In order to demonstrate that the analyte chromatographic peak cannot be attributed to more than one component, peak homogeneity or peak purity tests (such as diode array or mass spectrometry) can be used to evaluate the selectivity of chromatographic procedures.

- 2. Linearity:** The capacity of an analytical method to yield test findings that, either directly or through the use of a well-defined mathematical transformation, are proportionate to the concentration (amount) of analyte in samples within a particular concentration range is known as linearity. A minimum of six standards with concentrations ranging from 80 to 120 percent of the anticipated concentration range should be used to assess linearity.

Analyzing a plot of the analytical response as a function of analyte concentration visually will establish the linearity of a technique. If a linear relationship is found, test findings should be analyzed using the proper statistical techniques, such as least squares regression line computation. Regression analysis may occasionally require the test data to undergo a mathematical modification first.

Data on the slope of the line, intercept, and correlation coefficient must all be included in reports that are filed. Analyte concentrations and response should be clearly correlated, as shown by the measured slope. It is assumed that the absence of a significant departure from linearity in the findings indicates that the correlation coefficient, $r > 0.99$, is present throughout the working range of 80–120 percent. In the event where r is less than 0.99, the submitter is required to explain how precise calibration is going to be kept up to date. When a non-linear reaction is intentionally employed, it needs to be explained.

- 3. Range:** Usually, the linearity investigations yield the specified range. The range of an analytical technique is the range of the analyte concentration (amounts) in the sample for which the analytical method's precision, accuracy, and linearity have been shown to be appropriate.

The ensuing minimum defined ranges must to be taken into account:

- For the purpose of assaying an agricultural or veterinary chemical product's active constituent: typically between 80 and 120 percent of the label or test concentration; and
 - To determine an impurity, use a range of 120% of the specification to the impurity's specification level.
- 4. Accuracy:** The degree to which the determined value of an analyte in a sample matches to the true value is known as the analytical method's accuracy. There are various techniques to quantify accuracy, and the approach chosen should make sense for the matrix. Any of the following methods can be used to assess an analytical method's accuracy: reevaluating a known-concentration sample and contrasting the measured and "true" values. But it's necessary to use a well-characterized sample, such a reference standard.
- The product matrix - spiked recovery approach. In the spiked-placebo recovery approach, a formulation blank (sample containing all other ingredients save the active(s)) is mixed with a known amount of pure active constituent. The mixture is then tested, and the outcomes are compared to the predicted outcome.
 - Regular addition technique. The standard addition method involves the analysis of a sample, followed by the addition of a known quantity of pure active ingredient and another assay. The predicted response is compared with the variations in the two assays' results.

Recovery in both cases (spiked-placebo recovery and standard addition approach) is defined as the percentage difference between the observed and expected results.

It is necessary to assess a method's accuracy at multiple fortification levels since it can differ along the range of potential assay values. At least three concentrations (80, 100, and 120%) in the anticipated range should be covered by the accuracy.

Comparing test results with those from another verified test method is another way to assess accuracy.

Acceptance Criteria: The analyte concentration, sample matrix, and sample processing technique all affect the anticipated recovery. The following ranges should have the mean percentage recovery:

| % Active/impurity content | Acceptable mean recovery |
|---------------------------|--------------------------|
| ≥ 10 | 98 – 102% |
| ≥ 1 | 90 – 110% |
| 0.1 – 1 | 80 – 120% |
| < 0.1 | 75 – 125% |

5. Precision: The precision of an analytical procedure signifies how closely measurements from multiple samplings of a uniform sample, conducted under specified conditions, agree with each other (indicating the degree of dispersion). Precision can be evaluated on three levels: repeatability, intermediate precision, and reproducibility. For the purposes of these guidelines, a straightforward assessment of repeatability is deemed sufficient. Typically, the precision of an analytical procedure is quantified using measures such as variance, standard deviation, or coefficient of variation based on a series of measurements. It is recommended to perform a minimum of five replicate sample determinations and conduct a basic statistical evaluation of the results, which should include the percent relative standard deviation. If deemed appropriate, outlier tests such as Dixon's or Grubbs Test may be applied to the data. Any excluded outliers should be clearly noted, and an attempt to explain the reasons behind individual outliers is advisable.

The following levels of precision are recommended.

| Component measured in sample | Precision |
|------------------------------|-------------|
| $>10.0\%$ | $\leq 2\%$ |
| 1.0 up to 10.0% | $\leq 5\%$ |
| 0.1 up to 1.0% | $\leq 10\%$ |
| $< 0.1\%$ | $\leq 20\%$ |

6. Limit of Detection (LOD): The limit of detection (LOD) for an analytical procedure represents the minimum amount of an analyte in a sample that can be detected, although not necessarily quantified with precision. To determine the LOD, samples with known analyte concentrations are analyzed, and the minimum level (lowest calibration standard) at which the analyte can be consistently detected is established. The lowest calibration standard that yields a peak response corresponding to the analyte is analyzed multiple times (typically 6-10). The average response (\bar{X}) and standard deviation (SD) are calculated, and the LOD is calculated as $\bar{X} + (3 \times \text{SD})$.

7. Limit of Quantitation (LOQ): The limit of quantitation (LOQ) refers to the minimum quantity of the analyte in a sample that can be accurately determined with a specified level of precision, following the given experimental conditions. The LOQ serves as a critical parameter in quantitative assays, particularly for analyzing low levels of compounds within sample matrices. It is notably employed in the assessment of impurities, degradation products, or low concentrations of active ingredients in a product.

To determine the limit of quantitation (LOQ), standard solutions are prepared at an estimated LOQ concentration, typically derived from preliminary investigations. The solution is then injected and analyzed multiple times (usually 6-10). The average response and standard deviation (SD) are calculated from the obtained results, with the SD ideally being less than 20%. If the SD surpasses 20%, a new standard solution with a higher

concentration is prepared, and the same procedure is repeated. The LOQ is calculated as $X + (10 \times SD)$.

8. **Specificity:** The analytical method's capacity to quantify the analyte without influence from external factors
9. **Robustness:** Ability to stay unaffected by slight but purposeful changes in procedure parameters
Changes could be in the analytical solution's stability, the mobile phase's pH, the column (lot/supplier), the temperature, or the flow rate.
10. **Determination:** Comparison results under differing conditions with precision under normal conditions¹³

VII. YAUDEN PLOTS

1. Constructing a Youden Plot

- X and y axes are drawn on the same scale spanning the range of data.
- Each point corresponds to the results of one lab. So the intersection of the
- x value (the first response on the horizontal axis) and y-value (the
- second response on the vertical axis) forms a coordinate pair.
- Draw a 45-degree line to help spot large, systematic errors
- Remove obvious outliers (Remove M and E).
- A circle is drawn to predict the data variation.
- The center of the circle is the intersection of replicate medians.
- The radius of the circle is based on a multiple of the pooled, within-lab standard deviation
- depending on the desired percentage expected to fall within a bivariate normal distribution.
- Youden recommend a multiple of 2.5 to 3 be used to contain most of the plotted points.

2. Youden's Experiment

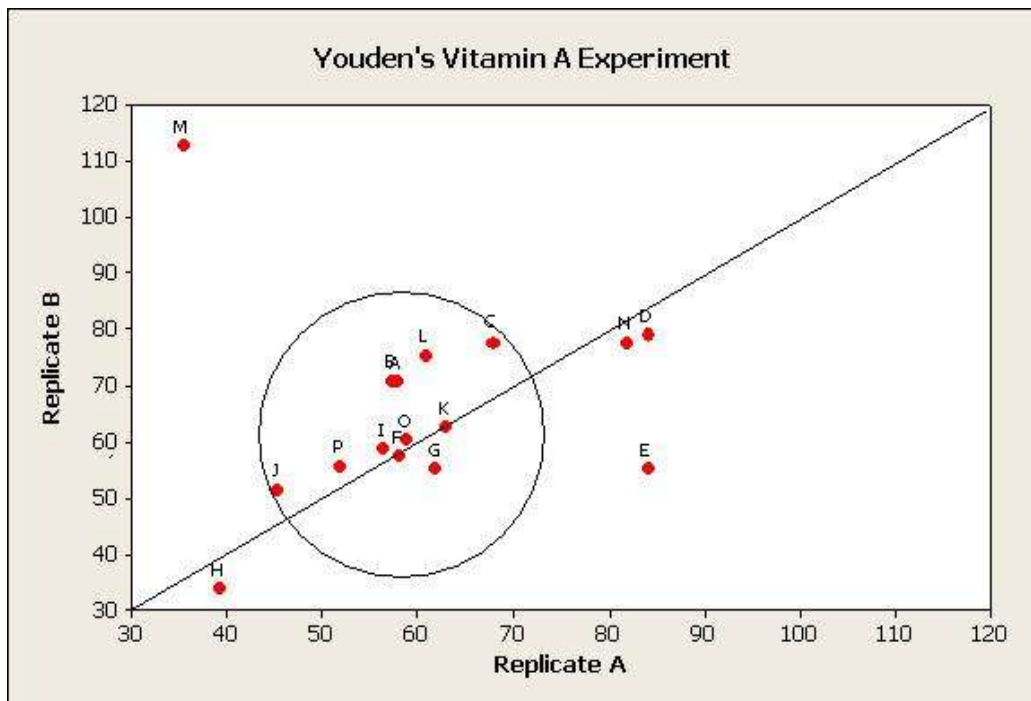
- One sample of Vitamin A was divided
- into 16 equal samples. Each lab was
- asked to test their sample twice
- (duplicate testing). Data was collected
- from each lab and recorded in this chart.

| Lab | Replicate 1 | Replicate 2 |
|-----|-------------|-------------|
| A | 57.9 | 70.9 |
| B | 57.3 | 71.1 |
| C | 67.9 | 77.9 |
| D | 84 | 78.9 |

| | | |
|----------|------|-------|
| E | 84 | 55.3 |
| F | 58.1 | 57.6 |
| G | 61.9 | 55.3 |
| H | 39.2 | 33.9 |
| I | 56.4 | 58.8 |
| J | 45.3 | 51.6 |
| K | 63 | 62.7 |
| L | 60.9 | 75.6 |
| M | 35.4 | 112.7 |
| N | 81.7 | 77.6 |
| O | 58.9 | 60.5 |
| P | 51.9 | 55.8 |

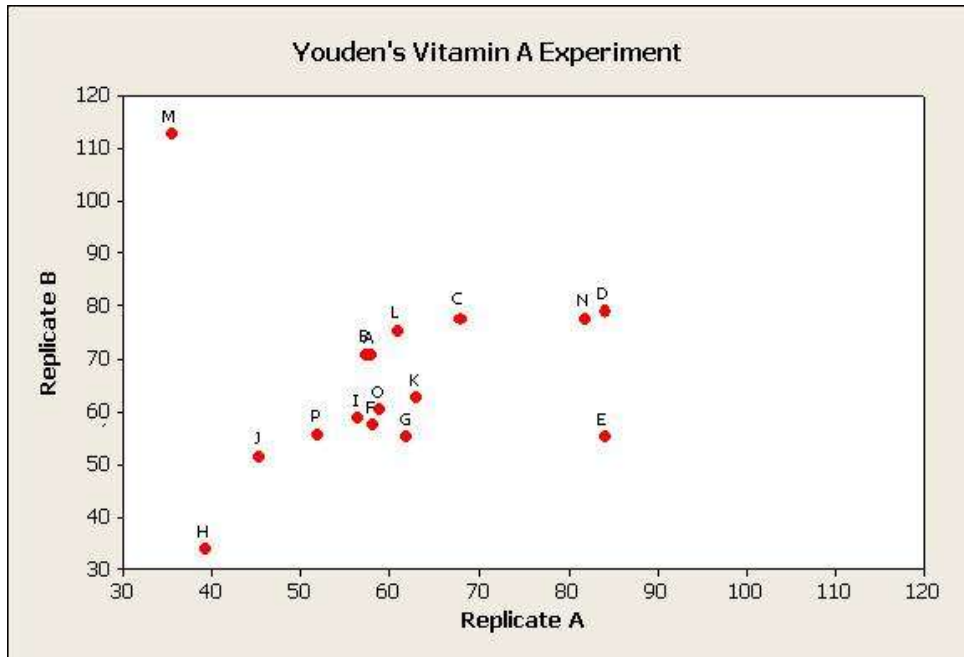
A Youden Plot quickly tells you:

- Which labs provided the most repeatable data (precision)
- Which labs have lab technique problems (bias and systematic error)

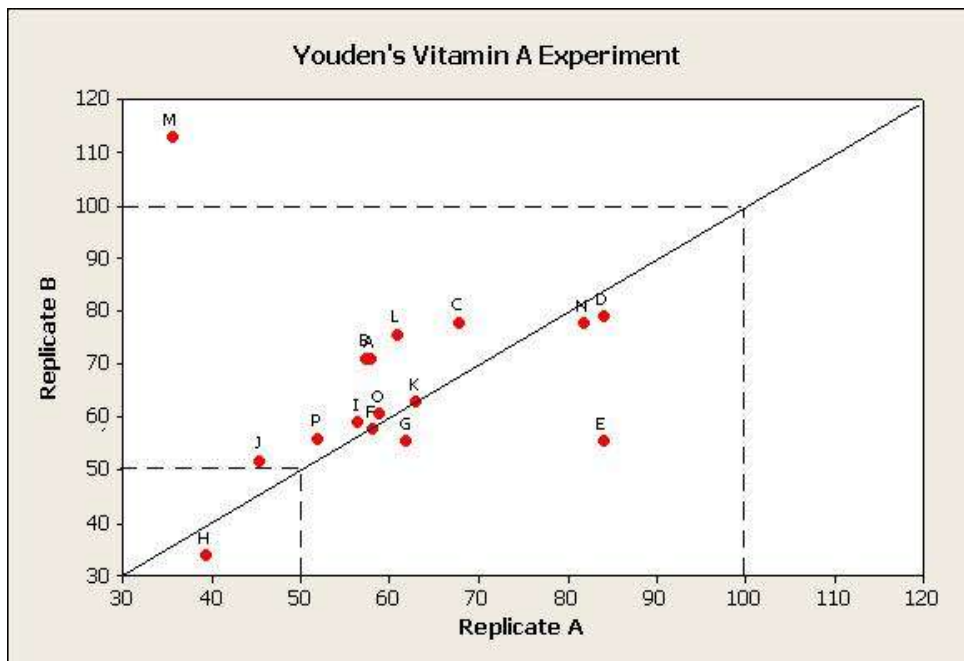


3. How to construct a Youden Plot:

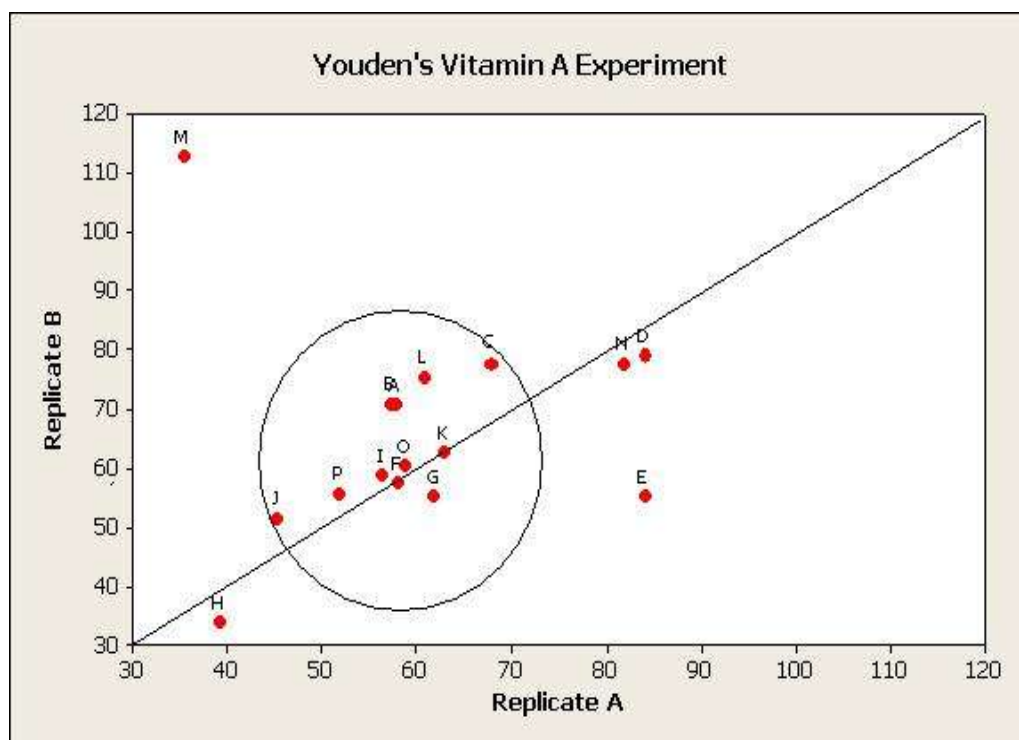
- Plot each pair of data points as x,y coordinates.
- Make sure the axes scales are the same.



Draw a 45 degree reference line to help you look for data precision.



- Draw a circle whose center is the intersection of the replicate medians after removing obvious outliers.
- The radius of the circle is calculated by using a multiple of 2.5 to 3.0 times the standard deviation of the within-lab data.



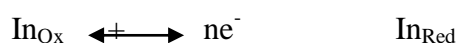
VIII. THEORY OF REDOX INDICATORS

There are mainly three types of indicators used to detect the end point in redox titrations.

- Self Indicators.
- Internal Indicators.
- External Indicators.

1. Self Indicators: If the titrant is highly colored, this may be used to detect the end point. For example, a 0.02M potassium permanganate has a deep purple color. A dilute solution of potassium permanganate is pink. The product of its reduction, Mn^{+2} , is nearly colorless. During a titration with KMnO_4 , the purple color of the MnO_4^- is removed as soon as it is added because it is reduced to Mn^{+2} . As the titration completes, if an excess drop of KMnO_4 imparts a pink color to the solution, indicating the completion of the reaction.

2. Internal Indicator: Highly colored dyes that have the ability to be reduced or oxidized and are weak reducing or oxidizing agents are known as redox indicators. The reduced and oxidized versions have distinct hues. The voltage at a certain titration point will determine the indicator's color and oxidation state. The best redox indicators will show a clear, noticeable color shift and have an oxidation potential that is halfway between the titrated solution and the titrant.



$$E_{\text{ind}} = E^{\circ}_{\text{ind}} + \frac{0.0591}{n} \log \frac{[\text{Ox}_{\text{ind}}]}{[\text{Red}_{\text{ind}}]}$$

Where E_{ind}° is the standard electrode potential of the indicator. For a sharp color change at the end point, E_{ind}° should differ by about at least 0.15V from the standard potential of the other system involved in the reaction.

Examples:

Ferriin Indicator {1,10-Phenanthroline Iron(II) complex}:

Ferriin is one of the best redox indicators. The base 1,10-Phenanthroline combines readily in a solution with Iron(II) salt in the molecular ratio 3:1 forming the intensively red 1,10-Phenanthroline Iron(II) complex ion (Ferriin). With strong oxidizing agents, the Iron (II) is oxidized to form Iron (III) complex (Ferrin) which has a pale blue color.



Standard redox potential for this indicator is +1.14V. Formal potential is +1.06V in 1M HCl solution. The color change occurs at 1.12V because, the color of the reduced form is so much more intense than that of oxidized form.

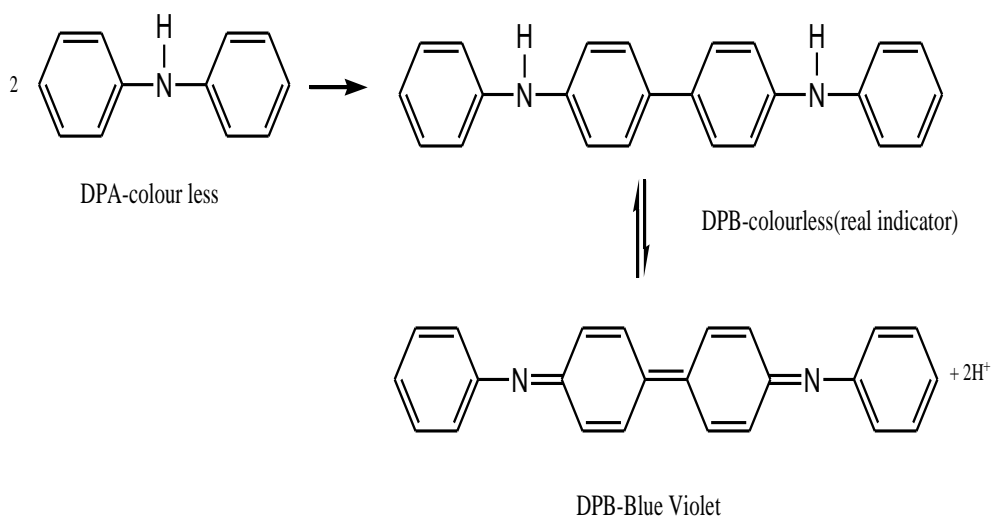
- 3. Importance:** The indicator has great value in the titration of Iron (II) salts and other substances with Ce(IV) Sulphate solutions.

Example: Consider the titration of the 0.1M Iron (II) ion with 0.1M Ce(IV) solution and the equivalence point is at 1.10V. Ferriin changes from deep red to pale blue at the redox potential of 1.12V. The indicator will therefore be present in reduced form after the addition of 0.1% excess of Ce(IV) Sulphate solution. The potential rises to 1.24V and the indicator is oxidized to pale blue form.

The standard potential of the ferriin can be modified considerably by the introduction of various substituents in the 1,10-Phenanthroline nucleus. The most important substituted ferriin is,

- 5-Nitro,1,10-Phenanthroline Iron(II) Sulphate (Nitro Ferriin) $E^{\circ}=1.25\text{V}$
- 4,7-dimethyl-1,10-Phenanthroline Iron(II) Sulphate (Dimethyl Ferriin) $E^{\circ}=0.85\text{V}$

- 4. Diphenyl Amine Indicator:** Diphenyl amine in the presence of H_3PO_4 is the most important widely used internal indicator. It is colorless in the reduced form and violet blue in the oxidized form.



When dichromate solution is added to acidic ferrous salt solution containing phosphoric acid and DPA the ferrous ions are oxidized to ferric ions which are then complexed with H_3PO_4 .

If ferrous ions are free, they would have oxidized DPA before the end point, imparting blue colour to the solution. When all the Iron (II) ions are oxidized to Iron (III) ions which are complexed with H_3PO_4 , addition of a drop of $\text{K}_2\text{Cr}_2\text{O}_7$ will oxidize DPA producing a distinct violet blue colour. The reduction potential of the DPA and DPB system is +0.76V.

Disadvantages: The disadvantage of DPA and DPB is its solubility, it is slightly soluble in water and hence it can be employed as 1% solution in conc. H_2SO_4 . This has been overcome by the use of salt as Ba or Na Diphenyl Amine Sulphonate, which is employed in 0.2% aqueous solution. The redox potential is slightly higher (0.85V) in 0.5M H_2SO_4 and the oxidized form has a reddish violet colour.

| Indicator | Colour change | | Formal potential |
|-------------------------|---------------|--------------|------------------|
| | Oxidised form | Reduced form | |
| Ferrouin | Pale blue | Red | 1.06v |
| Nitro Ferrouin | Pale blue | Red | 1.25v |
| 5,6 dimethyl Ferrouin | Pale blue | Red | 0.97v |
| 4,7 dimethyl ferrouin | Pale blue | Red | 0.88v |
| Diphenyl Amine(DPA) | Violet | Colour less | 0.76v |
| Diphenyl Benzidine(DPB) | Violet | Colour less | 0.76v |
| Starch | Blue | Colour less | 0.53v |
| Methylene Blue | Blue | Colour less | 0.52v |

5. **External Indicator:** Highly colored dyes that have the ability to be reduced or oxidized and are weak reducing or oxidizing agents are known as redox indicators. The reduced and oxidized versions have distinct hues. The voltage at a certain titration point will determine the indicator's color and oxidation state. The best redox indicators will show a

clear, noticeable color shift and have an oxidation potential that is halfway between the titrated solution and the titrant.

- 6. Starch Indicator:** For the iodine titrations, this indicator is utilized. When starch and I_2 combine, they create a reversible complex with a deep blue color. Up to the equivalency point, the solution in titrations of reducing agents with iodine is colorless. The complex formed between starch and iodine causes the solution to become blue when an excess titrant drop is added.