Errors in ppharmaceuticalsal aanalysis

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What is Error…?

- Error is the difference between the true result (or accepted true result) and the measured result.
- If the error in an analysis is large, serious consequences may result. As reliability, reproducibility and accuracy are the basis of analytical chemistry.
- A patient may undergo expensive & even dangerous medical treatment based on an incorrect laboratory result because of an analytical error.

$$\text{Error} = \frac{\text{measured mean value} - \text{true value}}{\text{true value}}$$

- And the difference between the experimental value and true value is termed as absolute error.
- Absolute error may be negative or positive.

Types of errors :

There are two principle types of error in analysis :

- Determinate or systematic error
- Indeterminate or random error

DETERMINATE ERROR

- They are caused by faults in the analytical procedure or the instruments used in the analysis.
- Determinate errors are systemic errors i.e. they are not random.
- As the name indicates that the cause of this type of error may be found out & then either avoided or corrected.

- A particular determinate error may cause the analytical results produced by the method to be always too high.
- Another determinate error may render all results too low.
- Sometimes the error remains constant;
- All results are too high or too low by the same amount.

- Determinate error can be additive or they can be multiplicative . It depends on the error & how it enters into the calculation of the final result.

- This determinate error could be the result of an incorrectly calibrated balance.

- If the balance is set so that the zero point is actually 0.5 mg too high, all masses determined with this balance will be 0.5mg too high.

- If this balance was used to weigh any std. sol. Used in the laboratory, the std. concentration will be erroneously high,and all of the results obtained using this std. will be erroneously high.

- The error is reported as the absolute error, the absolute value is the difference between the true and measured value.

Measured mean value – True value =

Absolute error

- Determinate errors may arise from some faulty step in the analytical process.

- The faulty step is repeated every time the determination is performed. Whether a sample is analyzed 5 times or 50 times, the results may agree with each other but differ widely from the true answer.

- Systemic error is under the control of the analyst.
- How are determinate errors identified and corrected...?
- One is to analyze the sample by a completely different analytical procedure that is known to involve no systematic errors. Such methods are often called “standard methods”; they have been evaluated extensively by many laboratories & shown to be precise and accurate.

- If the results from two analytical methods agree, it is reasonable to assume that both analytical procedures are free of determinate errors.

- The 2nd method is to run several analyses of a reference material of known, accepted concentration of analyte. The difference between the known concentration and that measured by analysis should reveal the error.

- If the results of analysis of a known reference std. are consistently high or low, then a determinate error is involved in the method.

- Determinate error can arise from uncalibrated balances, improperly calibrated volumetric flasks or pipettes, malfunctioning instruments, impure chemicals, incorrect analytical procedures or techniques and analyst error.

- Analyst error : They may be the result of inexperience, insufficient training.
- An analyst may use the instrument incorrectly,
- Perhaps by placing the sample in the instrument incorrectly each time.
- Setting the instrument to the wrong conditions for analysis.
- Misreading a meniscus in a volumetric flask as high(or low)

- Operational and Personal errors :
- These are due to factors for which the individual analyst is responsible and are not connected with the method or procedure they form part of the personal equation of an observer.

- Examples are:
- Mechanical loss of materials in various steps of analysis.
- Underwashing or over washing of precipitates.
- Ignition of ppts at incorrect temperatures.

- Some analyst are unable to judge color changes sharply in visual titrations, which may result in slight overstepping of the end point.

- Some other analyst – related errors are :
- Carelessness
- Transcription errors, i.e. copying the wrong information into a lab notebook or onto a label.

Proper training, experience, and attention to detail on the part of the analyst can correct these types of errors.

- Reagents and instrumentation :
- Contaminated or decomposed reagents can cause determinate errors.
- Prepared reagents may also be improperly labeled.

- Impurities in the reagents may interfere with the determination of the analyte, especially at the ppm level or below.

- Numerous errors involving instrumentation are possible, including
- Faulty construction of balances,
- Incorrect instrument alignment,
- Incorrect wavelength settings,
- Use of uncalibrated or improperly calibrated weights.

- These problems can be eliminated by a systematic procedure to check the instrument settings and operation before use. Such procedures are called std. operating (SOPs) in the many labs.

- There should be a written SOP for each instrument and each analytical method used in the laboratory.

- In instrumental analysis, electrical line voltage fluctuations are a particular problem. This is especially true for automated instruments running unattended overnight.

- Instruments are often calibrated during the day, when electrical power is in high demand.
- At night , when power demand is lower, completely changing the relationship between conc. Of analyte and measured signal.

- Analytical Method :The most serious errors are those in the method itself.

Examples of method include

- Incorrect sampling
- Incomplete reaction for chemical methods,
- Unexpected interferences from the sample itself or reagents used.
- Loss of analyte during sample preparation by volatilization or precipitation.

- In titrimetric analysis errors may occur :
- Failure of reactions to proceed to completion.
- Occurrence of induced and side reactions.

- In gravimetric analysis:
- Decomposition
- co- precipitation and post – precipitation.
- Precipitation of constituents other than the desired ones.

- Contamination:

Contamination of sample by external sources can be a serious source of error and may be extremely variable.

Aluminum levels in the dust in the normal laboratory are so high that dust prohibits the determination of low ppb levels of aluminum in samples.

Indeterminate errors :

- Indeterminate errors can not be pin- pointed to any specific well defined reasons.

- They are random in nature & take place in several successive measurements performed by the same analyst under the same conditions and identical experimental parameters.

- Sources of random error include the limitations of reading balances, electrical noise in instruments and vibrations caused to the building by heavy vehicular-trafficking , which are beyond anyone's control.
- For eg. A balance that is capable of measuring only to 0.001 g can not distinguish between two samples with masses of 1.0151 & 1.0149 g.
- In one case the measured mass is low, in the other case it is high.

ACCURACY :

- An accurate result is the one which matches very nearly with true value of a measured amount.
- Accuracy is inversely proportional to the error i.e. the greater the accuracy, smaller is the error.

PRECISION:

- Agreement among a cluster of experimental results however it does not imply anything with respect to their relation to the true value.

- Precision designates reproducibility of a measurement, whereas accuracy the correctness of a measurement.

Minimizing systematic errors:

- Calibration of instruments, apparatus and applying necessary corrections:
- Instruments commonly used in lab, such as spectrophotometer, electrical balance etc must be calibrated before use.
- Pipettes, burettes, volumetric flasks, thermometers must be calibrated.

The response of most of the instruments changes with time because of wear corrosion or mishandling, etc.

The determinate personal errors may be eliminated by care, practice and self discipline

Analysis of standard samples:

The errors of method can be checked by carrying out the analysis of standard sample prepared in such a way that its composition is exactly the same as that of material to be analyzed.

For this purpose, standard materials containing carefully analyzed constituents are available from National Bureau of Standards.

Independent method of analysis

It is carried out to maintain accuracy of the result
e. g. Iron (III) is first determined gravimetrically by precipitation method as iron (III) hydroxide and then determined titrimetrically by reduction to the iron (II) state.

Performing a parallel control determination :

- Performing a separate estimation under almost identical experimental parameters with a quantity of a standard substance that consists of exactly the same weight of the components as is present in the unknown sample.

- Can be calculated by following expression:

Wt. of component in std. substance = result obtained for std. substance

x result obtained for unknown sample

Where , x = wt. of the component present in the unknown sample.

BLANK DETERMINATION:

To determine the effect of impurities present in the reagents & vessels used and where it is necessary to locate the exact end point.

It may be accomplished by performing a separate parallel estimation, without using the sample.

Cross – checking results by different methods of analysis:

- In certain specific cases the accuracy of a result may be cross linked by performing another analysis of the same substance by another method.

- Eg. HCl –Solution : It may be assayed either by titration with a std. sol. Of NaOH, or by precipitation and weighing as AgCl.