ERRORS IN PHARMACEUTICAL ANALYSIS

The skill, knowledge, expertise and above all the degree of confidence involved in the ultimate result of an analyst is solely governed by the extent of accuracy and precision achieved by the analytical procedure *vis-a-vis* the possible sources of error that may be incorporated inadvertently. In fact, the quantitative pharmaceutical analysis is not merely confined to just taking a random sample, performing a single assay quickly, and finally making a loud claim that the result so obtained cannot be challenged. Truly speaking an ideal analyst must have a total in-depth knowledge of the chemistry involved along with the *pros and cons* of interferences that may be caused due to the host of compounds, elements and ions besides adequate exposure and hands-on experience of the statistical distribution of values.
The terminology 'error' invariably refers to the difference in the numerical values between a measured value and the true value. It has become universally accepted in methods of comparison that the percentage composition of a 'standard sample' provided and certified by the National Institute of Standards and Technology (NIST) or the British Pharmacopoea Chemical Reference Substance (BPCRS) or the European Pharmacopoea Chemical Reference Substance (EPCRS) must be regarded and treated as absolutely correct, pure and authentic while evaluating a new analytical method. Consequently, the differences thus obtained between the standard values and those by the new analytical methods are then treated as 'errors' in the latest procedure.

CLASSIFICATION OF ERRORS

The numerous uncertainties usually encountered in a chemical analysis give rise to a host of 'errors' that may be broadly categorised into *two* heads, namely :

(*i*) Determinate (systematic) Errors, and
 (*ii*) Indeterminate (random) Errors.

It is pertinent to mention here that it becomes rather difficult at times to place a particular 'error' into one of the above mentioned categories ; however, the classification may prove to be beneficial with regard to study of the various analytical errors that crop up in the course of routine analysis.

1. DETERMINATE (SYSTEMATIC) ERRORS

These are errors that possess a definite value together with a reasonable assignable cause; however, in principle these avoidable errors may be measured and accounted for conveniently. The most important errors belonging to this particular class are :
 (*a*) **Personal Errors :** They are exclusively caused due to 'personal equation' of an analyst and have no bearing whatsoever either on the prescribed procedure or methodology involved.

(*b*) **Instrumental Errors :** These are invariably caused due to faulty and uncalibrated instruments, such as : pH meters, single pan electric balances, uv-spectrophotometers, potentiometers etc.

(*c*) **Reagent Errors :** The errors that are solely introduced by virtue of the individual reagents, for instance : impurities inherently present in reagents ; high temperature volatalization of platinum (Pt) ; unwanted introduction of 'foreign substances' caused by the action of reagents on either porcelain or glass apparatus.

(*d*) **Constant Errors :** They are observed to be rather independent of the magnitude of the measured amount ; and turn out to be relatively less significant as the magnitude enhances.

Example : Assuming a constant equivalence—point error of 0.10 ml is introduced in a series of titrations, hence for a specific titration needing only 10.0 ml of titrant shall represent a relative error of 1% and only 0.2% for a corresponding 50 ml of titrant consumed.

(*e*) **Proportional Errors :** The absolute value of this kind of error changes with the size of the sample in such a fashion that the relative error remains constant. It is usually incorporated by a material that directly interferes in an analytical procedure.

Example : Estimation of 'chlorate'—an oxidant by iodometric determination. In this particular instance *two* things may happen, namely :

(*i*) Presence of 'Bromate'—another oxidizing agent would give rise to positively higher results, and hence, it must be duly corrected for, and

(*ii*) Absolute error might increase while dealing with large samples, whereas the relative error would remain more or less constant if the sample is perfectly homogenous,

(*f*) **Errors due to Methodology :** Both improper (incorrect) sampling and incompleteness of a reaction often lead to serious errors. A few typical examples invariably encountered in titrimetric and gravimetric analysis are cited below :

S.No.	Titrimetric Analysis	S.No.	Gravimetric Analysis
1.	Failure of reactions to proceed to completion,	1.	Significant solubility of precipitates,
2.	Involvement of either induced or side-reactions,	2.	Co-precipitation and post-precipitation,
3.	Reactions due to subtances other than the one being assayed, and	3.	Decomposition,
4.	A noticeable difference occurring between the stoichiometric equivalence point of a reaction and the observed end-point.	4.	Volatalization of weighing forms on ignition, and
		5.	Precipitation of constituents other than the desired ones.

(*g*) **Additive Errors :** It has been observed that the additive errors are independent of the quantum of the substances actually present in the assay.

*Examples :* (*i*) Errors caused due to weights, and

(*ii*) Loss in weight of a crucible in which a precipitate is incenerated.

Detection of this error is ascertained by taking samples of different weights.

2. INDETERMINATE (RANDOM) ERRORS

As the name suggests, indeterminate errors cannot be pin-pointed to any specific well-defined reasons. They are usually manifested due to the minute variations which take place inadvertently in several successive measurements performed by the same analyst, using utmost care, under almost identical experimental parameters. These errors are mostly random in nature and ultimately give rise to high as well as low results with equal probability. They can neither be corrected nor eliminated, and therefore, form the **'ultimate limitation'** on the specific measurements. It has been observed that by performing repeated measurement of the same variable, the subsequent statistical treatment of the results would have a positive impact of **'reducing their importance'** to a considerable extent.

Example : Figure-1, represents the absolute errors in nitrogen analysis by means of micro **Kjeldahl's Method***. Here, each vertical line labelled ($x'_1 - x_t$) designates the absolute deviation of the mean of the set from the true value. In Figure 3.1, A represents ($x'_1 - x_t$) the absolute error obtained by **'analyst-1'** for the assay of benzyl-iso-thioureahydrochloride, whereas B represents ($x'_2 - x_t$) the absolute error obtained by **'analyst-2'** for the assay of the same compound.
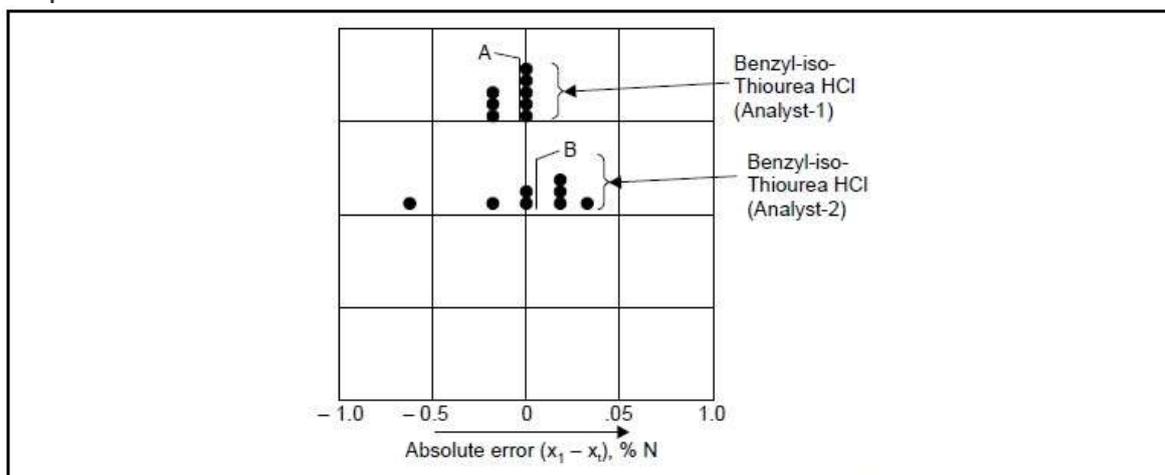
Figure-1

Thus, it is evident from Figure -1, that the broad spread of individual errors centres around the mean values ($x'_n - x$) thereby affording a direct indication of indeterminate type

uncertainties. Hence, larger indeterminate errors seem to be linked with the performance of **'analyst-2'** than with that of **'analyst-1'**.

Salient Features of Indeterminate Errors

The various salient features of indeterminate errors are enumerated below :

1)   Repeated mesurement of the same variable several times and subsequent refinement to the extent where it is simply a coincidence if the corresponding replicates eventually agree to the last digit,

2)   Both unpredictable and imperceptible factors are unavoidably incorporated in the results what generally appear to be '*random fluctuations*' in the measured quantity,

3)   Recognition of specific definite variables which are beyond anyone's control lying very close to the performance limit of an instrument, such as : temperature variations, noise as well as drift from an electronic circuit, and vibrations caused to a building by heavy vehicular-traffic,

4)   A variation that may be regarded as random by a slipshod analyst may at the same time prove to be quite evident and manageable by a careful observer, and

5)   The average of a number of fine observations having random scatter is definitely more accurate, precise and, hence, more cogent than coarse data that appear to agree perfectly.