Chapter 2
Quality of Analytical Results: Classifiying Errors and Estimating Measurement Uncertainty

Piotr Konieczka

2.1 Introduction

The most important parameter of each analytical result is its reliability. An analytical result is not a constant value; each result has two properties, error and uncertainty. The sources of both these parameters have to be known and their values determined (estimated).

All analytical results are obtained by applying an appropriate measuring procedure. The need for reliable results requires application of reliable analytical procedures, from sampling to final determination.

Conclusions obtained on the basis of analytical results should reflect the real ("true") content (concentration) of analyte in the analyzed object (sample). For this, two basic conditions must be fulfilled:

- The collected sample composition should reflect the composition of the analyzed object (requirement of sample representativeness).
- A measurement result should reflect the true content of analyte in the analyzed sample (requirement of measurement reliability).

The main trend in the development of analytical chemistry is the determination of lower and lower concentrations of analyte in samples of an increasingly complex matrix (trace analysis). In the case of trace analysis, several problems arise from the following [1]:

- Decreasing analyte concentration
- Increasing complexity of the sample matrix composition
- Introduction of new notions associated with the application of metrology principles in analytics

P. Konieczka (✉)
Department of Analytical Chemistry, Gdańsk University of Technology, Gdańsk, Poland
e-mail: piotr.konieczka@pg.gda.pl

I. Baranowska (ed.), *Handbook of Trace Analysis*,
DOI 10.1007/978-3-319-19614-5_2

– Necessity of traceability documentation and uncertainty estimation as necessary parameters of an analytical result
– Globalization and the associated need to compare results from different laboratories

Analytical data are a specific type of information. This information is not usually obtained through analysis of the whole object, but is based on the analysis of appropriate samples. Measurement results must be reliable, which means that they must accurately (both truly and precisely) reflect the real content (amount) of analyte in a sample that is representative of the material object under study. This task is extremely difficult and complicated, which poses a great challenge for analysts and requires attention to be paid to the problem of quality assurance (QA) and quality control (QC) of the obtained results [2].

The term "reliable data" is closely related to data quality. It is the quality of a measurement, and its control and assurance make it possible to determine and prove the reliability of a measurement.

Different aspects of quality have specific meanings in an analysis. According VIM (*International Vocabulary of Metrology*) [3], quality is defined as the degree of realization of specific requirements (those included in a standard of the quality control system and its "own" accepted requirements).

Analytical quality is an agreement of the obtained results of the chemical analysis with the accepted assumptions [3]. The quality of information can be divided into several components:

– Quality of results
– Quality of the process
– Quality of the instruments
– Quality of work and organization

The result of a measurement is the product of the analyst's work. The quality of this product depends on the quality of the tools used (i.e., the analytical procedure and the laboratory work). The quality of the obtained measurement result depends on the measurement error and the estimated uncertainty values.

2.2 Measurement Errors

Error is defined as the difference between the expected (true) value and the value obtained as a result of the determination. Thus, error can be calculated as a measured quantity value minus a reference value [3]. Measurement error is the consequence of the accuracy (as trueness and precision) of the analytical procedure applied for obtaining the measured quantity:

Accuracy: closeness of agreement between a measured quantity value (as a single result) and reference quantity value [3].

Trueness: closeness of agreement between the average of an infinite number of replicate measured quantity values and a reference quantity value [3].

Both of these parameters are closely connected with the estimation of errors. Depending on the type of error, their influence on measurements varies.

The value of a single measurement result may differ (and actually always differs) from the expected (real) value. The difference is a result of the occurrence of different errors. There are three basic types of errors:

- Gross errors
- Systematic errors (biases)
- Random errors

With regard to the manner of presenting a determination result, one can distinguish between absolute and relative errors:

- *Absolute error* (d_x): described by the dependence:

$$d_{x_i} = x_i - \mu_x \tag{2.1}$$

where:

x_i value of a measurement result
μ_x expected (true) value

- *Relative error* (e_x): described by the equation:

$$e_{x_i} = \frac{d_{x_i}}{\mu_x} \tag{2.2}$$

With regard to the source of errors, one can distinguish:

- Methodological errors
- Instrumental errors
- Human errors

The total error of a single measurement result can be divided into three components, as described by the following equation [2]:

$$d_{x_i} = x_i - \mu_x = \Delta x_{\text{sys}} + \Delta x_i + \delta x_i \tag{2.3}$$

where:

d_{x_i} total error of a measurement result
Δx_{sys} bias
Δx_i random error
δx_i gross error

For a measurement series (at least three parallel analyte determinations in the same sample), there is a high probability of detecting a result(s) with a gross error. Gross error is the result of the single influence of a cause acting temporarily and causing the measurement result to differ significantly from the mean value (outlier result deviated). It appears only in some measurements and it is a random variable. This error is the easiest to detect and, therefore, the easiest to eliminate.

There are many known ways of detecting results with gross errors. Each is applied in certain specific conditions [2]. After eliminating results with gross errors, the trueness of the obtained final determination (most often the mean value of the measurement series) is influenced by biases and/or random errors.

An analytical result (arithmetical mean of a series of parallel measurements) can only have a bias and random error according to the following dependence [2]:

$$d_{x_m} = x_m - \mu_x = \Delta x_{\text{sys}} + \Delta x_m \tag{2.4}$$

where:

d_{x_m} total error of a determination result (arithmetical mean of the series of measurements)
x_m mean value of the series of measurement results
Δx_m random error

Random error is an error resulting from typical fluctuations in the experimental field. The value decreases in the case of multiple designation of the same analyte in samples of the same material. It is not possible to calculate this error for a single result, nor to predict its value. In spite of their low value, these errors are the basis for calculating precision and are a component of the uncertainty of analytical results [2].

Systematic error is an error that, during multiple measurements performed under the same conditions, remains constant. Its value cannot be calculated without knowing the actual value or a value contractually accepted as real. Systematic errors, which should be small, determine the trueness of measurement. This type of error can be a parameter of a single measurement or of an analytical process, in which case it is known as "bias" [2].

The determination of bias is one way to determine the trueness of an analytical method. If the determined bias refers to an analytical method, then with a large number of measurements, the random error is negligibly small with relation to the bias (when $n \to \infty$, then $s \to 0$) (where s is standard deviation).

In this case, the following dependence is true [2]:

$$d_{x_{\text{met}}} = E(x_{\text{met}}) - \mu_x = \Delta x_{\text{sys}} \tag{2.5}$$

where:

$d_{x_{\text{met}}}$ total error of a determination result for the applied analytical method
$E(x_{\text{met}})$ expected value for a given analytical method

The occurrence of bias makes a given series of measurement (analytical method) results differ from the expected value by a constant value; hence, results are either overstated or understated. There are two types of bias:

- *Constant bias* (a_{sys}): value does not depend on analyte concentration levels
- *Variable bias* ($b_{sys}\mu_x$): value depends (most often linearly) on analyte concentration levels

Total bias can be described by the dependence:

$$\Delta x_{sys} = a_{sys} + b_{sys}\mu_x \tag{2.6}$$

Assuming that the value of a random error is negligibly small compared with the bias value, one can present the following dependence:

$$x_m = \mu_x + \Delta x_{sys} = \mu_x + a_{sys} + b_{sys} \;\; \mu_x = a_{sys} + \left(1 + b_{sys}\right)\mu_x \tag{2.7}$$

Schematically, the impact of individual types of errors on the final result of the measurement is shown in Fig. 2.1.

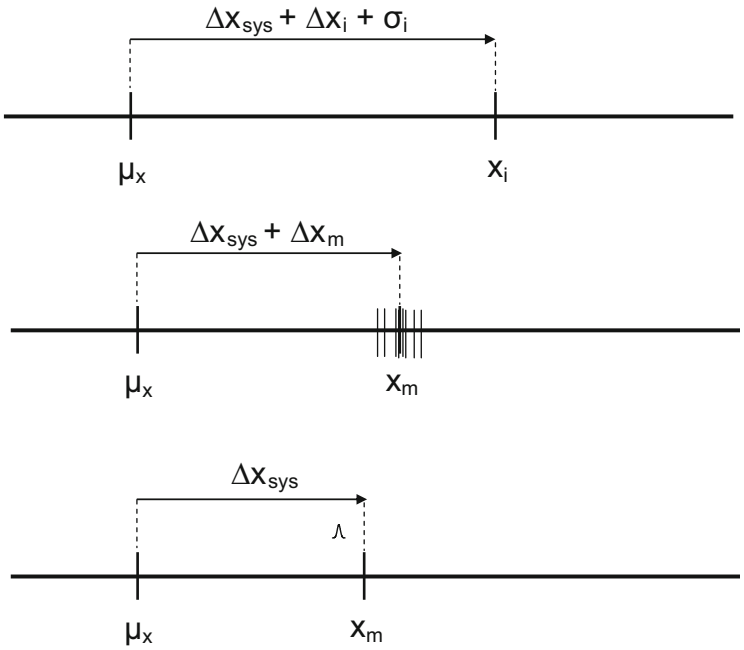

Fig. 2.1 The influence of the various types of errors on the final result of the measurement; Δx_{sys} bias, Δx_i random error for a single measurement, σ_i gross error, μ_x expected (true) value, x_i measurement result, x_m mean value of the series of measurement results, and Δx_m random error for a series of measurements

After rejecting results with a gross error and determining biases (regarding their values and correcting the determination result), the results still contain a random error. The value of the random error influences the precision of the obtained results.

Precision is defined as closeness of agreement between indications or measured quantity values obtained by replicate measurements on the same or similar objects under specified conditions [3]. It is associated with random errors and is a measure of dispersion or scattering around the mean value, usually expressed by a standard deviation. Depending on the conditions under which the received a series of measurements is obtained, measurement precision can be used to define the following:

- *Repeatability*: measurement precision under a set of repeatable conditions of measurement [3]; precision of results obtained under the same measurement conditions (a given laboratory, analyst, measuring instrument, reagents, etc.).
- *Intermediate precision*: precision of results obtained in a given laboratory over a long-term process of measuring. Intermediate precision is a more general notion (due to the possibility of changes in the greater number of determination parameters) than repeatability [3].
- *Reproducibility*: precision of results obtained by different analysts in different laboratories using a given measurement method [3].

2.3 Uncertainty

Uncertainty is a fundamental property of each measurement. It always occurs at each stage of the analytical procedure. It is necessary to distinguish between:

- *Uncertainty of measurement*: non-negative parameter characterizing the dispersion of the quantity values being attributed to a measurand, based on the information used [3]
- *Definitional uncertainty*: component of measurement uncertainty resulting from the finite amount of detail in the definition of a measurand [3]

The basic sources of uncertainty in the course of examination of samples using appropriate analytical procedures are listed in Table 2.1 [4].

Determining the uncertainty of a measurement increases its reliability, and in turn allows comparison of results obtained in interlaboratory studies and helps in deciding the significance of any difference between the obtained result and the reference value. The uncertainty of measurement is a component of uncertainty in all single steps of analytical procedures [5–9]. Therefore, the source of values and uncertainties for individual stages of individual analytical procedure should be specified [10–12].

There are various possible approaches for uncertainty estimation [10–13]:

- *Bottom-up*: based on the identification, quantification, and combination of all individual sources of measurement uncertainty

Table 2.1 Possible sources of uncertainty in the conduct of analysis [4]

Sources of uncertainty	
Personal factors	Instrument factors
Inaccurate or imprecise definition of the measurand	Insufficient resolution of the applied measurement instrument
Lack of representativeness at the step of collecting a sample from an examined material object	Uncertainties associated with the applied standards and/or reference materials
Inappropriate methodology of determinations	Uncertainties of parameters determined in separate measurements and used in calculating the final result, such as physicochemical constants
Personal deviations in reading the analog signals	
Not recognizing the influence of all the external factors on the result of an analytical measurement	Approximations and assumptions associated with using a given instrument, applied during measurement
Uncertainty associated with the calibration of an applied measurement instrument	Fluctuations of the measurement instrument gauge over the course of repeated measurements, with seemingly identical external conditions

- *Fitness-for-purpose*: based on the definition of a single parameter called the fitness function, which takes the form of an algebraic expression and describes the relation between uncertainty and analyte content
- *Top-down*: based on data obtained from interlaboratory studies (precision)
- *Validation-based*: based on interlaboratory or within-laboratory validation processes (precision, trueness, calibration, limit of detection, robustness)
- *Robustness-based*: based on robustness tests from interlaboratory tests

The final result of the analysis consists, therefore, of [13]:

- Determination of the measured value and its unit
  - The result with the expanded uncertainty value ($y \pm U$, along with units for y and U) (where y is result and U is expanded uncertainty)
  - Value of the factor k, for which the expanded uncertainty has been calculated (where k is the coverage factor)

An estimate of uncertainty is one of the necessary parameters of analytical measurement result. Uncertainty is a fundamental property of each measurement. It always occurs at each stage of each measurement procedure. This is not, therefore, a property that gives rise to additional difficulties during the measuring process.

There is a difference between measurement error and uncertainty. Measurement error is the difference between the determined and expected values, and uncertainty is a range into which the expected value may fall within a certain probability. Therefore, the uncertainty cannot be used to correct a measurement result.

2.4 Summary

The main problem during quality assurance and quality control of analytical results arises from insufficient information about the tools used during this process, and about how they are used. First and foremost should be described the statistical tools used, which lie at the heart of metrology.

Results of analytical measurements are a kind of a product of the chemical analyst's work. Both manufactured products (object of analysis) and analytical results must be of an appropriate quality. In addition, the quality of analytical measurements appears to have its own accumulative requirement: the quality of every product is a result of comparison of the obtained value (analytical result) with the reference value (expected, standard, norm, required). In order for the obtained result to be comparable (authoritative, reliable) to the reference value, its (high) quality must be documented and maintained. The quality of analytical results must be assured in the first place before drawing conclusions about the quality of the examined products.

It should be noted that the basic and necessary parameters that characterize an analytical result are traceability and measurement uncertainty. An analytical result without documented traceability and estimated uncertainty is a source of misinformation. These two parameters are the basic requirements of reliable analytical results.

The values of errors and uncertainty strongly depend on the level of analyte content (concentration). High values of these parameters, unacceptable in the case of an analyte content at the percentage level, can be satisfying in the case of trace analysis.

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