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1. A PERSONAL VIEW ON QUALITY ASSURANCE

Jens E.T. Andersen

1.1. Scientific results

The European Commission's EURAMET and IMEP programmes,^{1–2} together with IRMM,³ have elucidated the challenges related to reaching compliance between results for the same sample obtained in different laboratories (industrial and/or academic). Inter-laboratory comparisons showed that costumers had a high risk of receiving significantly different results from independent professional laboratories, which should not happen given the advanced technologies available in contemporary analytical chemistry laboratories. It was further demonstrated that results differed significantly not only when samples were analysed by different instruments and procedures but also when analysed by identical methodologies. It seemed that this was a genuine scientific issue that needed attention from scientists able to evaluate accepted statistical procedures. As a first approach the celebrated EURACHEM/CITAC guide⁴ to quantify uncertainty in analytical measurements and the VIM guide⁵ allowed scientists to check the traceability of measurements by establishing uncertainty budgets for their methods. The introduction of the concept 'uncertainty' is now a key factor in experimental work. Secondly, the concept of certified reference materials was introduced and is now an integral aspect of analytical chemistry and a growing in-

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dustry where certificated values for many analytes in various mixtures (matrices) are available. The latter approach has provided much greater confidence in many analytical methods. The philosophy of measurement is that the true amount of an analyte in a sample is not known but everyone makes a reliable estimate of the amount and the uncertainty of measurement is also estimated correctly. The result obtained as the mean value from results submitted by several laboratories is then announced as the consensus value. Right or wrong, the result represents the combined effort of all laboratories and all results have the same eligibility since they belong to the same distribution. With this philosophy of 'consensus science' in mind it becomes possible to arrive at compliance or agreement between analytical results; an idea which also has significance beyond the analytical community itself. Consensus science should be discussed as a future framework for scientific methodology.

1.2. Operational calibrations

Construction of calibration lines or regression lines is a key operation in analytical chemistry; it is widely believed that the operational calibration takes care of day-to-day variations of the apparatus sensitivity, which allows one to eliminate the influence of the apparatus on the result. Although some variations of the apparatus are eliminated by the operational calibration, it is still not possible to explain large uncertainties observed for results obtained on different days as compared with the uncertainty predicted by the parent uncertainty budget. There are several explanations as to these discrepancies, one of which is related to systematic errors. It is a well-known fact that no apparatus displays a linear response. The response is always non-linear, and analytical chemists frequently identify the linear range of calibrations by means of an intuitive feeling. Since the full extension of the regression line must be evaluated on the basis of uncertainty, the extension of the calibration line could be estimated by considering the difference, in terms of uncertainty of fitting parameters, between using a straight line and, for example, a second order polynomial. However, differences and decisions can only be made when the data set has a certain magnitude. It is recommended that the central limit theorem is strictly followed during method validations, which means that at least one hundred repetitions are required in order to provide a reliable estimate of standard deviation. In fact two hundred repetitions are required to obtain a standard deviation that is correct with 95 % probability. Another reason for systematic deviations is related to ordinary-linear regression (ODL) as opposed to orthogonal-linear regression (OLR).⁶ The former is nearly always used in analytical chemistry because it is an option available in most software packages and spread sheets. It is anticipated that systematic differences introduced by using ODL instead of OLR is not a serious problem in comparison with other systematic errors that follow routine work in the laboratory. The ODL

proposed by Currie and Danzer⁶ predicts a centroid value at which concentration the confidence band has a minimum that has not been verified experimentally; a peculiarity of the model. Weighted-linear regression (WLR) relies on the assumption that variance is uniform and independent of concentration, which has never been verified experimentally. Therefore WLR cannot be recommended; not only for this reason but also because the outcome of WLR is weighted uncertainty that is impossible to report to costumers unless the data are re-calculated using an un-weighting scheme. This makes WLR laborious, inconvenient and an unsuitable alternative as it does not provide results different from those of OLR.⁷ These examples indicate that some of the systematic errors associated with the straight line are of relatively minor importance to accuracy in analytical chemistry, and they cannot explain the large variations in results found by inter-laboratory exercises.

1.3. Uncertainty and outliers

Uncertainty of measurement has replaced the concept of error of measurement because errors are not supposed to influence the result; rather they should be discarded. In addition, the term “random errors” creates an incorrect impression and the term “uncertainty” is therefore recommended. Despite the importance of the concept of uncertainty it is considered an inconvenience to many scientists because there are many ways to approach it and it can greatly increase the amount of work involved in evaluating the results.

For the sake of simplification only two schools of estimating uncertainty are considered: The IUPAC method and the method introduced by EURACHEM/CITAC. The majority of professional laboratories follow the directives of the IUPAC methodology⁶ that is represented in ISO standards, ISO 5725, ISO 17025 and others. These guidelines and standards have many positive aspects and include several examples but some of the concepts and procedures are outdated, such as error of measurement and true value, and the issue of sampling is not considered. Further, ISO recommends outlier rejection and the guidelines introduce procedures for outlier testing which may be a cause for concern. Rejection of outliers requires that two laboratories comparing independent measurements on the same sample must reject any observed outliers in such a manner that neither the mean value nor the standard deviations are influenced by the rejection. Otherwise they will inevitably arrive at significantly different results. This situation is very likely, particularly when a low number of repetitive measurements are made. The main reason to retain outliers rather than rejecting them is that outliers inherently possess important information about the actual performance of the method with respect to accuracy. In brief, it can be stated that rejection of outliers promotes disagreement and it is recommended never to reject outliers. Errors should be reported and discarded from a data set but outliers must

be left unaltered. Rejection of outliers depends on uncertainty of measurement; a concept that is treated by both the ISO guides and by the EURACHEM/CITAC guide.⁴ An uncertainty budget and expanded uncertainty are the main concepts introduced by the EURACHEM/CITAC guide⁴ with the intention of ensuring traceability and reliability and creating an overview of all uncertainty contributions. The combined uncertainty obtained by the uncertainty budget is multiplied by a factor of two, referring to student's *t*-value at a very high number of repetitions, to yield the expanded uncertainty. The expanded uncertainty corresponds to the 95 % confidence range and it covers 95 % of all measurements, which is an advantage when reporting results to customers. In an extension of the efforts by EURACHEM and CITAC, it is suggested that statistical control is obtained when the uncertainty of calibrations corresponds to the uncertainty of repetitions, and hence is a worthwhile addition to the protocol.

1.4. Statistics revisited

A potential problem with the application of statistical methods in Analytical Science is related to the concept of short-term precision *versus* long-term precision. Many scientists assume that one type of precision prevails but this is nowhere near the truth. Contemporary digital-data acquisition can be performed at very high rates; under normal laboratory conditions sampling rates of millions of samples per second are possible. Sampling data at very high rates allows the collection of large amounts of data within a short period of time, which in terms of the central-limit theorem of statistics, fulfills all the requirements to produce a valid and reliable value of precision; a precision that may be expressed in terms of a measurement uncertainty. This type of precision we denote as the short-term precision whereas the long-term precision is of a completely different nature, with a much higher uncertainty than that of short-term precision. The long-term precision is determined on the basis of multiple independent series of measurements where a shut-down and turn-on sequence is performed between each series. Such an operation challenges the apparatus in a manner much different from that of short-term precision. Although operational calibrations are performed on a daily basis there is no guarantee that the apparatus produces the same concentration of the unknown every day. The concentration of the unknown is, to some extent, un-correlated with the characteristic parameters of the calibration curve, *e.g.*, with the slope of a calibration line. That is within certain limits of long-term precision. Statistics works equally well for both short-term precision and long-term precision but statistics cannot account for accuracy; the true concentration is an unknown quantity that can only be estimated by multiple independent measurements. The true value is a matter of consensus and not statistics. Manipulation of data in science is not allowed but removal of outliers from a data set is an option that is sustained by ISO. This can be a serious problem in Analytical Che-

mistry. Certificates of certified reference materials show those outliers of “poor laboratories” that were removed in order to arrive at the final consensus value. The question is: How can the manufacturer of the reference material make sure that the laboratory using the product removes the same number of outliers when it tries to reproduce the results? Some manufacturers of CRMs supply information about the data set both before and after the removal of outliers and they also clearly state the number of results used for calculation of the certified value, making it easy to compare laboratory result to the certified value. Reporting data sets before and after the selection of outliers should be general practice in science or, alternatively, a comment should be made in the text if no outliers have been removed from the data set. Both outlier rejection and confusion between short-term precision and long-term precision may help to explain the large deviations observed in inter-laboratory tests.

1.5. Conclusions

The search for compliance, both with respect to consensus values and with respect to uncertainty of measurement, is not yet complete. There are several peculiarities in Analytical Science that can lead scientists in the wrong direction when they search for accuracy of measurements. Eventually, customers and colleagues are interested in accuracy in preference to precision. Generally, a customer cares less about the performance of the apparatus but focuses on the validity of the result. It has been proven by inter-laboratory tests that independent laboratories produce different results and different uncertainties. It is a challenge to Analytical Chemistry, as well as to related fields of science, to promote scientific methodology in order to reach compliance. Two sets of apparatus of the same type measuring the same measurand can produce significantly different results and the discrepancy increases when more repetitions are performed simply because the confidence band narrows as a function of the inverse-square root of the number of repetitions. This is a scientific paradox that originates from small differences between sets of apparatus that lead to a difference in accuracy. This paradox needs be resolved before we can explain all of the deviations of inter-laboratory tests. Such actions benefit Analytical Chemistry and it is much more rewarding to scientists to discuss genuine topics related to mechanisms of nature rather than focusing on differences that may readily be explained by uncertainty of measurement. Consensus science might be the way ahead.⁸⁻⁹

2. INFORMATION FROM THE EUCHEMS DIVISION OF ANALYTICAL CHEMISTRY (DAC)

Wolfgang Buchberger

The DAC Annual Meeting 2012 was held in Prague on 26 August, 2012. It coincided with the 4th EuCheMS Chemistry Congress in Prague. Many thanks are

due to Jiri Barek, who hosted the Annual Meeting and was also a member of the local organizing committee of the EuCheMS conference.

Within this Meeting, the „DAC Tribute“ was awarded to Prof. Yuri Zolotov (Moscow State University) for his long, committed involvement in DAC and his professional contributions to various DAC working groups and Euroanalysis conferences.

DAC activities, together with strategic planning, are coordinated by the DAC Steering Committee. In 2012 it consisted of Paul Worsfold (Chair of DAC, UK), Jens Andersen (Secretary of DAC, Denmark), Wolfgang Buchberger (Austria), Slavica Razic (Serbia), Jiri Barek (Czech Republic) and Majiej Jarocz (Poland). The Annual Meeting delegates endorsed the proposal that Wolfgang Buchberger takes over as Secretary in 2013. DAC is indebted to Jens for his efficient work as Secretary during the last five years. The vacant position on the Steering Committee will be taken by Christian Rolando (France) who will be co-organiser of the Euroanalysis 2015 conference in Bordeaux. Further details of DAC activities can be found at <http://www.euchems.eu/divisions/analytical-chemistry.html>.

In 2012 the Steering Committee had meetings in Warsaw, 27 April (together with a meeting of the Euroanalysis Presidium), and in Prague (25 August). Another meeting of the Chair and the Secretaries took place in Copenhagen (5 July). Among other things, the DAC strategy for the years 2012–2014 has been drafted which has been accepted by the delegates at the Annual Meeting.

For 2013, DAC has the following Study Groups: Education in Analytical Chemistry (R.Salzer), Quality Assurance and Accreditation (J. Andersen, H. Emons as liaison person to CITAC), History (D.T.Burns), Bioanalytics (G. Horvai), Chemometrics (R.Tauler). It was decided to close the Study Group European Analytical Chemistry on the Web, which had been headed by B. Karlberg. Efforts have been made to establish a new task force on Archaeometry and Cultural Heritage in Analytical Chemistry.

Several events have been organized in cooperation with DAC-EuCheMS during the year 2012; Isranalytica, 24–25 January (Tel-Aviv, Israel), 12th Eurasia Conference on Chemical Sciences, 16–20 April (Corfu, Greece), Analysdagarna, 11–13 June (Uppsala, Sweden), 1st International Congress on Analytical Chemistry, 18–21 September (Targoviste, Romania), and the European Chemistry and Chemical Engineering Education Network EC2E2N.

One of the main activities of DAC in 2013 will be the promotion and support of the Euroanalysis conference 2013, 25–29 August, Warsaw. The Chairpersons Maciej Jarosz and Ewa Bulska are working hard to provide a perfect environment for a high-quality analytical conference. Further details can be found at www.euroanalysis2013.pl. We invite all analytical chemists to participate in this event, to present their scientific work, and to strengthen the network in Analytical

Sciences. Euroanalysis 2013 will also be the event at which the Annual Meeting 2013 of DAC will be held.

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