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THE QUALITY CONCEPT: YESTERDAY VS TODAY

Quality is the result of a chain-reaction: you cannot obtain a good quality system if that derives from another low quality system.

The concept of quality has changed in the last few years: from a negative vision, i.e. absence of defects to a positive vision, i.e. presence of particularly desirable characteristics. Today, the concept of quality is successfully applied to many fields (industry, services, agriculture, environment, health, safety, cultural heritage). Food safety, for instance, in the past referred to the absence of harmful contaminants or adulterants, rarely to food itself. Now-a-days, generally, some specific qualities (such as antioxidant capacity, antiallergic- and immunoactivity, vitamin content) are required in food.

The quality of a system is strictly related to the quality of the measurements needed to characterise it. Chemical metrology was introduced in the Sixties when many government agencies applied metrological concepts to the analysis of natural products; then the first reference materials, national and international rules and agreements among different countries were established, with mutual recognition of the respective Total Quality Systems. TQSs were developed in the Eighties with the first accreditation schemes. By this new approach, society wanted to find a remedy to the too many errors registered in tests and certified data while saving costs. The first statistical studies on these topics indicated 20-30% wrong results in Europe, especially in the field of medical analysis. For instance, about 200,000 deaths a year and 7 billion euros are the European cost of medical lab errors. If we think that this death rate is estimated to be about 5% of total deaths, and that the money which could be saved is about 30% of the available resources, the importance of quality measurement is quite apparent.

Generally, industrialized countries spend about 6% of their gross domestic product on measurements and related operations. Many of these resources are wasted because they either represent repeated analysis or produce unreliable data. It was estimated that, each year, about 25 million measurements performed in the USA produced unreliable results and had to be repeated at an additional cost of 5 billion euros. Similarly, in Germany an additional unnec-

essary cost of about 12 billion euros was estimated. In UK, approximately 30,000 laboratories with 220,000 analysts perform one billion tests, which correspond to 30 measurements every second. Out of these, about 20%, corresponding to about 3000 billion euros, do not meet the aim of the analysis.

Some of the critical points that affect the quality of a test result are: sampling, transport of sample, pre-treatment of sample, test method and instrumentation, reagents, environmental factors, skill of the analyst, handling of data.

At least three types of error can be detected: skill-based errors (consisting of unconscious glitches in automatic activity), rule-based errors (consisting of the deviation from well known rules), knowledge-based errors (consisting of faulty knowledge, which translates into conscious wrong actions). While the rule-based errors derive from misapplied expertise, the knowledge-based errors are much more complex and can involve different schemes. The tendency to use the first information coming to mind is the main reason for knowledge-based errors.

A very topical instance of frequent poor-quality measurements is provided by the urban environment monitoring stations which are designed to permit local authorities to define traffic limitation measures aimed at safeguarding citizen's health. These stations often suffer from inadequate or absent calibration, wrong positioning - especially concerning their height from the ground - and poor maintenance. Thus, the reliability of these stations is questionable and requires a different approach. Many more significant wrong measurements, however, can produce heavy damages and risks (just think about the emergency services).

Quality in the market

To speak of quality in a market capable of consuming any type of goods and characterised by a low degree of competition, means to speak mainly of compliance to rules and guide-lines. Today, quality has become a point of reference to organise and manage the strategic control of every activity. Both in private and public business, quality means an actual synergic management of skills, projects, subjects, and correlations capable of concurring in the definition of the customer's satisfaction, which is strictly correlated to the quality of a product. The focal points are:

- system regulations (ISO 9001, ISO 14001, Regulation EMAS II, OHSAS 18001)
- certification of products and CE brand
- bodies in charge of certification and crediting functions
- characteristics required by either a manager or a system inspector
- mandatory and voluntary requirements connected to a certification
- advantages of the quality certification of either a product or an environment, both indoors and outdoors.

As already mentioned, a particular focal point of quality measurements is certainly related to upkeep strategies. These foresee the optimization of the mix of programs and corrections; this balance is needed due to two coexisting statements:

- no event in nature has zero probability to occur;
- the prevention effort of bringing down to zero the probable malfunction is financially unsustainable.

The ideal situation would be that all the interventions of upkeep

L'economia della misura scientifica

Quando un Paese si trova nella necessità di riqualificare il proprio bilancio è evidente che tutti i settori risultano influenzati da considerazioni, motivazioni, input di carattere economico.

Anche la misura scientifica non può sottrarsi a queste regole. Se perciò una misura sbagliata rappresenta di per sé una risorsa sprecata, a maggior ragione questo vale nelle condizioni a cui si faceva riferimento. Le misure forniscono dati preziosi quando affidabili, altrimenti sono solo produzione di numeri di nessun significato e per di più responsabili di sperpero di risorse tanto più preziose quando la situazione finanziaria complessiva non è floridissima.

Vorremmo cercare di avviare su ***La Chimica e l'Industria*** una sorta di campagna in questa direzione, in difesa cioè della qualità della misura, promovendo la pubblicazione di articoli di sensibilizzazione.

Ho scritto il primo per dare l'esempio.

Conto e spero nell'aiuto di molti altri colleghi da sempre come me sensibili a queste problematiche. L'obbiettivo del Direttore del giornale, Ferruccio Trifirò, e mio è quello di pubblicare un numero speciale dedicato a questi temi. In mancanza di tale traguardo anche singoli articoli riceveranno la massima attenzione e considerazione. *L.C.*

belong to the class of sanctioned dysfunctions. So - as done by some authors - an index of decision assuming ability could be defined in order to measure the performance of a system. This index would be represented by the ratio between the number of interventions of sanctioned corrections and the total number of corrective interventions. This could help in rehabilitating the corrective upkeep and in focusing on it.

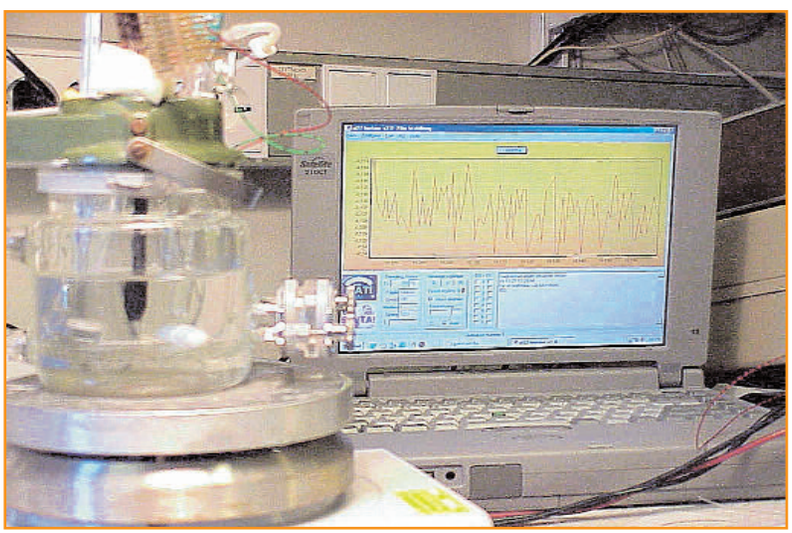
Proficiency testing (PT) is a tool capable of regulating analytical quality while providing many benefits to participant labs. PT is an integral component of total quality control, a tool for self improvement, a mechanism for continuous education, and a tool of compliance to regulatory requirements. PT should not be used as the only indicator of acceptable laboratory performance; unacceptable results should trigger further investigations and the relevant corrective actions.

Quality in labs

Lab analysis, if applied to environment, plays an essential role in the characterisation of the effects of anthropogenic activities. Therefore, the application of a system guaranteeing both the quality of the performed activities and the reliability of the obtained results is essential. In order to reach this goal, between the laboratory and the other interested subjects, the presence of a third party which is responsible for quality recognition is required.

Good lab practice requires an identification list of all the instruments present in the lab itself. This ensures that the manager has control over the calibration of all the instruments. If several instruments of the same type are present, each one must be identified with the corresponding calibration frequency and its responsible operator. Calibration must follow international procedures. The information on calibration must be recorded in a central logbook that should report at least the following data:

- description of the instrument;
- its identification;
- calibration standards;
- calibration results;
- calibration acceptability limits;
- results;
- date and operator performing each test.



At present, two regulations apply to labs of environmental analysis: the ISO 9001 promulgated by the International Organisation for Standardisation in 1999 and the UNICEL EN ISO/IEC 17025 promulgated by ISO. The two regulations are respectively “Requested characteristics for the systems of quality management” and “General Qualifications for the testing and calibration laboratories competences”. The former concerns institutions that want to show their ability: i) to regularly yield products which meet customers’ and rules’ demands; and ii) to increase the satisfaction level of their response to both types of demand. These demands concern the offer of tests with reference to applied methods and laboratory practice. ISO 9001 considers the organisation and management of the lab without paying any attention to the technical and scientific skills. The other regulation concerns the crediting of the test labs independently on their particular kind of analysis; it is generated by two previous regulations in the European (EN 45001) and International (ISO/IES Guide 25) context, and it goes more in detail than them: actually, it lists the qualities required by the quality management competence as well as some items regarding the technical skill, like the evaluation of the experimental uncertainty, choice and validation of testing methods, and the ensured quality of results. Thus, this second regulation becomes interesting for both the management and technique. The two regulations do not concern the compliance of the staff, premises, and instruments. The labs to be credited must be headed by a Director who is in charge of safeguarding the quality of the work: i.e. of the calibration and the correct use of instruments, the correct storage of samples, the registration and cataloguing of the results. In the case of labs which perform tests in fields other than environment, different locations for each kind of matrix must be ensured, in order to prevent any contamination. Therefore, the two regulations refer to two different procedures: one of crediting for the management conformity, the other for the experimental measuring activity, which, generally, is limited to some specific tests.

Through mutual recognition acts, both the acquired titles can be valid internationally. Many environmental analysis labs have chosen the immediate implementation of the ISO 9001 regulation. As a matter of fact, they deem it essential to improve quality both inside and outside the lab, without facing high costs and with an international

recognition thanks to the above mentioned mutual recognition acts; very few labs have chosen the implementation of the ISO/IEC 17025 regulation, most of them due to the relevant high costs.

Quality of methods

A test method can be considered validated when:

- it is adequate to the destination of its results;
- it yields test results which are useful in given situations;
- it meets the demands of the test problem taken into account;
- it ensures the preset quality level.

The main validation indexes are:

- specificity/selectivity;
- recovery level;
- sensitivity;
- detection and quantification limit;
- accuracy;
- experimental time;
- robustness;
- uncertainty;
- comparability;
- representativity.

All these indexes do not always need to be evaluated; the choice depends on the kind of method so that the optimized use of the available resources is met.

Anyway, some details about all the above mentioned indexes are as follows:

- specificity/selectivity is the first factor to be evaluated as it is the only one capable of suggesting whether or not to go on;
- specificity refers to a method which produces a single answer, while selectivity produces more responses; the method applied for their evaluation foresees the preparation of samples containing all the analytes, without the one of interest.

Recovery is defined as the ratio between the amount of analyte experimentally determined in samples of well known concentration by means of reference solutions of the pure analyte, and the expected results. Sensitivity is the variation response of an instrument when varying the stimulus.

Calibration curve is basic for the analysis; it is preferred when represented by a straight line, the equation of which (y=mx+q) is calculated by the linear regression; the most used algorithm is generally that of the least squares, and the validity of the linear model is checked by the linear correlation coefficient.

Accuracy is the most important index as it corresponds to either the ability of a method to yield experimental values near the “true” values or the full agreement between the experimental analytical datum and the reference value when a certified sample is analysed.

Precision is the agreement level of independent results obtained with a procedure performed in well defined conditions. On varying some experimental conditions, the precision assumes the meaning of repeatability and reproducibility. The confidence interval of the mean is intended as the one possibly attributed to the best evaluation of the measured property. Detection limit is the analyte concentration in a tested sample that can be distinguished from blank with a certain risk (about 5%). It is often defined as three times the uncertainty of the blank; in any case, LOD must be between xi/2 and xi, xi being the blank value. The quantification limit is defined as the lowest concentration quantitatively determined with acceptable precision and accuracy, and it is generally assumed as 3 times the LOD value. It is reasonable that the quantification limit results at least 1/5 - 1/10 of the legally set out maximum value to be respected for the considered analyte. The interval of work is represented by the concentration interval for which it was verified that the indexes characteristic of the method assume reasonable values; generally it is included within the linearity one.

Robustness will be largely dealt with in following paragraphs.

Representativity is the variety of the effects occurring during the normal use. Comparability is the ability of an experimental result on a known or unknown sample to be related to national or international standards through a whole comparison chain. To evaluate the comparability the following reference procedures can be followed: to adopt traceable standards, to use a primary method or to compare the experimental results with those of a primary method, to use a pure substance as Certified Reference Material.

One of the most important properties of a test procedure is the ability of its data to be compared with those obtained by other procedures. The best way to achieve this is to associate to the result an uncertainty index, as related to the uncertainties in the referibility chain of each lab. The identification of the uncertainty sources gives

multiple indications, the most meaningful concerning the sampling, the storage of the samples, the effects of the instrumentation, the purity of the reagents, the experimental conditions, the matrix effects, the stability of the sample, the effects of the calculation, the correction for the blank, the operator's effects, and chance.

Robustness testing became part of validation testing (initially performed at the end of validation, currently during optimization) due to transfer problems which were observed during interlaboratory studies. It is varyingly defined; for instance United States Pharmacopeia defines it as it follows: the robustness of an analytical method is the degree of reproducibility of test results obtained by the analysis of the same sample under a variety of normal test conditions such as different laboratories, different analysts, different instruments, different reagents, etc. So we can summarize that robustness of an analytical procedure is a measure of its capacity to remain unaffected by small but definite variations in method parameters. In a robustness test different aspects can be distinguished:

- selection of factors and their levels;
- selection of an experimental design;
- selection of responses;
- definition of the experimental protocol and of the execution of experiments;
- estimation of factor effects;
- graphical and/or statistical analysis of effects;
- drawing conclusions and, if necessary, adopting care procedures.

The future

In a few months the first Italian companies should be certified ISO 22000, a new world standard guaranteeing a correct management of the company system for food safety.

This standard - just presented in Italy by UNI, the Italian institution for normative rules - sets out a group of procedures designed to identify dangers arising from the contamination and alteration of food as well as to determine preventative measures in order that subsequent risks can be minimized. ISO 22000 also requires measures such as the constitution of a working group on the subject of food safety as well as on the monitoring of preventive procedures. The standard also sets out an information-gathering system at all stages of the food production process, so that a manufacturer of canned products must also be responsible for the raw material. In effect, this standard should produce a chain of beneficial effects. Actually, if the indicated procedures are followed, also the previous and next steps are guaranteed by the involved companies, which are consequently stimulated to respect these procedures. ISO rules are only voluntary measures, not being obligatory even if many customers, particularly government departments and companies increasingly require certification showing that they have been met. For the operators of the food industry, the adoption of ISO 22000 can represent a chance to rationalise processes aimed at ensuring consumer safety and eliminating risk products.

Another advantage expected from ISO 22000 is an increase in companies' ability to respect the law's requirements, such as those concerning the traceability of particular products (e.g. meat) and the food safety standards demanded by the market: in countries such as France, Germany and Great Britain the large-scale chain stores require their suppliers, including Italian exporters, to respect these standards, each varying according to the countries, while in Italy these stores are only requested to comply with detailed regulations. Being a certification regarding the producer and not the product, unlike the PDO or PGI marks, end consumers will not find the indication of ISO 22000 certification on the packaging of the product.

References

[1] H.M. Hill, R.H. Brown, *Anal. Chem.*, 1968, **376R**, 40.
[2] B. Kratochvil, J.K.Taylor, *Anal. Chem.*, 53, **924A**, 1981.
[3] W.E. Harris, Sampling, Manipulative, Observational, and Evaluative Errors, Int. Lab., Jan./Feb. 1978, 53.
[4] A. Cambieri, *Janus*, 2004, **14**, 10.
[5] T.P. Hofer *et al.*, *Effective Clinical Practice*, 2000, **3**, 261.
[6] J. Zhang *et al.*, *J. Biochem. Inform.*, 2004, **37**, 193.
[7] J. Kalra, *Clin. Biochem.*, 2004, **37**, 1043.
[8] D. Antiseri, *Medicina dei Ruoli*, 1976, **2**, 307.
[9] G. Federspil, C. Scandellari, L'errore clinico: una introduzione, in Atti del 94° Convegno della Società Italiana di Medicina Interna, Roma 14-17 ottobre 1993, Pozzi, Roma, 1994.
[10] J. Kalra, *Clin. Biochem.*, 2004, **37**, 1052.
[11] B. Dejaegher, Y.V. Heyden, Robustness tests, LC-GC Europe 418, 2006.
[12] J.W. Cooper, *Anal. Chem.*, 1978, **801A**, 50.
[13] W. Horwitz, *Anal. Chem.*, 1982, **67A**, 54.