EXTERNAL QUALITY ASSESSMENT PROGRAMS:
PAST, PRESENT AND FUTURE

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Summary: External Quality Assurance (EQA) and Proficiency Testing (PT) programs are fundamental
tools for quality evaluation and improvement in clinical laboratories. A growing body of evidence has been col-
clected to demonstrate the usefulness of these programs for reducing inter-laboratory variation, analytical
errors and for improving the »state-of-the-art«. The validity of EQA/PT programs is strongly affected by the
quality of control materials, the design of the program, namely the ability to estimate analytical bias and
imprecision, and the commitment of providers to assist in the education participant laboratories. Future per-
spectives of EQA/PT are the possibility to evaluate pre- and post-analytical steps, the utilisation of Internet for
receiving and communicating results to participant laboratories and the accreditation/certification of the pro-
grams.

Key words: External quality assessment, proficiency testing, total testing process, analytical bias, impre-
cision, clinical laboratories

Introduction

Although it has a »foundation« and roots dating back centuries, laboratory medicine is a relative young
discipline that became established at the dawn of the twentieth century, with contributions from medicine
and paediatrics, as well as biochemistry and microbiology (1). Only through biomedical research after the
Second World War modern clinical laboratories were established. External quality assurance (EQA) and
proficiency testing (PT) have been integral to modern medical laboratories almost from the outset (2). Exter-
nal quality assurance of medical laboratories is now entering its sixth decade and it remains a fundamental
tool for the evaluation and continuous quality improvement of laboratory services.

Unlike many developments in medicine and biological sciences, EQA did not evolve from the work of many sequential studies, but rather emerged, nearly fully formed, from the seminal work of Belk and
Sunderman in 1947 (3). The model used by Belk and

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uncertainty, education and provision of an effective indicator for an objective assessment of laboratory quality as a part of accreditation, certification and regulatory compliance assessment programs. Some of the most important facets and aspects of EQA are outlined in the same table arranged from pertinence to an individual participant (top) to pertinence to society as a whole (bottom). Although EQA has a multifaceted role, its appropriateness, applicability, and cost-effectiveness have been debated (6). However, because EQA monitors actual analytical performance, it might be regarded as the single most relevant indicator of laboratory quality, or better an efficient system to monitor the analytic result, that is an important part of the so-called total testing process (TTP). While terms »External quality assurance-EQA« and »Proficiency testing-PT« sometimes are used interchangeably, they underline different aspects. In particular EQA, that is more widely used in European countries, stresses the voluntary participation of individual laboratories, encourages educational and improvement aspects, as well as its use as a self-assessment tool. PT are mandatory, compulsory programs used as a point-sampling of laboratory output to judge the quality of laboratory testing. However, there is the need for an integration of EQA and PT elements, both presenting strengths and weaknesses (7). In fact, regulatory PT schemes encourage more participation and treat all laboratories equally. However, because of sanctions, laboratories do not treat PT samples the same as routine samples, and the programs may reduce the use of more challenging samples. EQA schemes have a stronger educational component, reduce the punitive atmosphere, use samples materials that mimic as far as possible patient material, but this may increase the costs. Because there are more similarities than differences in the meaning of these two terms, a synonymous spirit will be used in this paper that will focus on the role of EQA/PT in allowing clinical laboratories to assess and improve their services.

Are EQA/PT schemes surrogate markers of quality in clinical laboratories?

The value of EQA/PT schemes in highlighting areas of analytical inadequacy and for stimulating improvements in between-laboratory variation has been demonstrated in many countries. EQA/PT survey in countries without EQA/PT programs or effective Internal Quality Control have shown that up to 50% of laboratory results for basic clinical chemistry tests are so far from the target value as to be of no clinical value (8). The laboratory performance in CAP survey after the introduction of the first EQA/PT scheme, demonstrate that the coefficient of variation (CV%) of glucose measurement decreased from 16.3 in 1949, to 8.0% in 1983 and to 4.2% in 1996. In the same period, the CV% of BUN decreases from 63.5% to 13.3% and, finally, 4.4% (9).

Figure 1 shows the interlaboratory error for cholesterol measurements from 1969 to 1990 and it is easy to observe the continuous and significant decrease of the error rate (2). Table II reports the main findings observed during the 4-year experience of the EQA scheme for biochemical markers of myocardial damage in Italy (10). The number of unacceptable performances decreased from 11.6% to 5.6% for troponin I, from 19.5% to 9.0% for myoglobin, and from 13.2% to 4.3% for creatine kinase myocardial isoenzyme (CK-MB).

In quantitative laboratory testing, a number of techniques are used to establish the correct value of a given test, including gravimetric addition, reference value analysis, and consensus values from participants. In most schemes designed for medical laboratories the last procedure is often used, and for at least some tests this technique has been demonstrated to provide a basis of comparison that is comparable to reference value analysis (6). Therefore, not only the reproducibility, but also the bias of the method adopted by the individual laboratory can be assessed and improved. The preponderance of evidence suggests that participation in EQA/PT pro-
grams does indeed result in improved performance. The improvements in performance, in turn, are likely due to improvement in the laboratory analysis itself, to greater familiarity with the external survey scheme, and to improvements by manufacturers of the reagents and instrument systems. Therefore, the impressive improvement in analytical quality that has been documented by many EQA/PT programs is an evidence of their value in assessing the «state-of-the-art» and in stimulating clinical laboratories to reduce mistakes and improve the reliability of laboratory results over time.

Are the results from EQA/PT programs an affective information for medical laboratories?

Satisfactory results in EQA/PT schemes are an important evidence that analytical procedures are under control, that technicians work in an appropriate way, and that effective internal quality control rules are in place (Figure 2). This information reassures clinical laboratory staff, represents an evidence of inter-laboratory agreement and comparability, and it is an effective indicator of outcome to produce during surveys and external quality assessment programs. A much more intriguing question is if and eventually how this information can be delivered to the users and patients.

On the other hand, poor EQA/PT results may derive from different sources, and in particular:

- participant failure thus leading the laboratory to re-evaluate and modify procedures and processes, eventually improving the training and competence of the personnel,
- wrong scheme or sample design. For example, a wrong result in EQA/PT specimens cannot be reproduced in patients deriving from a scarce commutability of the adopted materials that present matrix effects or other problems,
- inherent method or diagnostic system inadequacy.

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![Figure 2](#)
If errors derive from this source, this may represent a stimulus to seriously consider the need to change or modify the method/diagnostic system itself. For example, EQA/PT schemes have documented the progressive shift in analytical techniques used for CK-MB measurement that led to the disappearance of chromatographic and electrophoretic methods and the conversion to the adoption of immunoassays for its measurement. This represents, again, a very useful information for all medical laboratories (Figure 3).

What are the fundamental elements that assure validity to EQA/PT programs?

Table III shows the most critical characteristics of EQA/PT schemes. The quality of control materials is a pre-requisite for assuring validity and effectiveness to any EQA/PT program. The commutability of materials and the minimization of matrix effects are absolutely essential to guarantee the quality of results and, in turn, any further action. The problem, in fact, is the processing of control materials that may alter not only the composition of the material, but also molecular structures.

Figures 4 and 5 show the different results obtained in the same participant laboratories by sending a control material obtained from human sera (Figure 4) and a commercial, poorly commutable material (Figure 5) in measuring alkaline phosphatase with different buffers (AMP and DEA). The overlap between the two methods, using the commercial material, is an artefact, while the other specimen really mimics what happens in patient sera (11).

Other important characteristics are the ability to estimate analytical bias and imprecision, also adopting target values traceable to reference methods or certified reference materials. It is increasingly important to progressively abandon the use of «peer-group» targets that can mask true analytical problems and do not allow to improve harmonization and inter-laboratory comparability of results.

Table III Validity of an External Quality Assessment scheme

- Quality of control materials.
- Design:
  - Ability to estimate analytical bias and imprecision (separately);
  - Target values traceable to reference methods or certified reference materials;
  - Acceptability criteria (analytical quality specifications) based on well-defined criteria.
- Commitment of the Provider to assist in the education of all potential participants and to activate interactive communications.
Regarding acceptability criteria, after the consensus Conference organized in 1988 by IFCC jointly with the WHO, the hierarchy models of quality specifications represents a proper basis for defining these criteria (12). Finally, the commitment of the provider to assist in the education of all potential participants and to activate interactive communications, represent an added-value to the program.

May satisfactory results in EQA/PT schemes guarantee total quality of laboratory services?

Available data on laboratory error rates and stratification demonstrate that analytical quality significantly improved in the last decades. Currently pre- and post-analytical phases are more vulnerable to errors than the analytical one (13,14). Usually, EQA/PT schemes evaluate only a part of the total testing process (Figure 6), and therefore they cannot be the unique tool for assessing and improving the ultimate quality of laboratory services. However, it is possible to design and implement EQA/PT schemes that allow the evaluation of pre-analytical and post-analytical phases (15,16). For instance, the collection and transport of samples, the laboratory specimen reception and accessioning process, and the procedures for traceability can be evaluated by document examination or by using simulated specimens. Regarding the post-analytical steps, in some EQA/PT schemes, medical laboratories are requested to produce the results by using the report form commonly adopted for patients (17). Report generation, therefore, should include in addition to the analytical data, result review and acceptance, verification of all calculations, appropriateness of reference intervals and eventually decision limits and, finally, clinical utility of any interpretation (18).

Future perspectives

Future perspectives of EQA/PT schemes can be grouped in five emerging areas. The first regards the practicability of programs designed to assess not only analytical steps but also pre- and post-analytical phases too. This is extremely useful because we have demonstrated that while inter-laboratory comparability of analytical results is improved, large differences exists in reference intervals so that the same analytical result can be interpreted as normal or increased/decreased when related to the reference interval adopted by individual laboratories (19).

The second perspective is the utilisation of Internet: The main advantage of Internet is that results can be communicated in real time, reducing the actual delay, with consequent cost reduction, possible inexpensive delivery of graphics and analyses of data and reduction of transcription errors.

The third perspective is accreditation/certification of the programs. There are at least three major advances from accreditation: a) for the program, accreditation improves reliability, b) for participants, it improves communication, and c) for providers, it improves staff commitment and credibility (20).

Moreover, accreditation/certification programs accelerate the harmonisation of EQ/PT schemes at an international levels and stimulate the creation of networks of EQA/PT providers.

Conclusions

A large body of evidence has been accumulated to demonstrate that EQA/PT programs are effective tools for assessing and improving the quality of medical laboratories. The validity of these programs depends on the quality of control materials and of the design. The perfect EQA/PT scheme does not exists, but a few projects are pending, surmounting most of «old» problems (21). In order to co-operate in the search for total quality, pre- and post-analytical aspects should be evaluated by specific programs, thus allowing clinical laboratories to assess and improve, in addition to analytical steps, other important aspects of their activity. Finally, it should clarify that as any control system, an EQA/PT program cannot improve the analytical quality by itself. It can, at best, tell that something is wrong, so only changes in the laboratories may improve the quality. For a true quality improvement, medical laboratories has to carefully evaluate the data of EQA/PT schemes and to use this information for improving their procedures and processes.
References


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PROGRAMI SPOLJAŠNJE KONTROLE KVALITETA: PROTOSL, SADAŠNOST I BUDUČNOST

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Kratko sadržaj: Programi spoljaštne kontrole kvaliteta (eng. External Quality Assurance, EQA) i veštine ispitivanja (eng. Proficiency Testing, PT), su osnovni alati za procenu kvaliteta i poboljšanja u kliničkim laboratorijima. Sakupljeni su brojni dokazi koji ukazuju na korisnost ovih programa za umanjenje interlaboratorijske varijacije, analitičkih grešaka, kao i za poboljšanje izvodljivosti. Validnost EQA/PT programa je izrazito zavisna od kvaliteta kontrolnih materijala, dizajna programa, odnosno sposobnosti procenjivanja analitičkog odstupanja i nepreciznosti i sposobnosti sprovedenja edukacije u laboratorijima. Buduće perspektive EQA/PT ogledaju se u mogućnostima pre-i post analitičkih stupnjeva, primene interneta za prijem i slanje rezultata laboratorija, učesnica i programa akreditacije i sertifikacije.

Ključne reči: programi spoljaštne kontrole, ispitivanje veština, ukupni proces ispitivanja, analitičko odstupanje, nepreciznost, kliničke laboratorije