UC 577,1; 61 ISSN 0354-3447

Jugoslov Med Biohem 24: 201–206, 2005 *Pregledni članak*[1]
Review article

EXTERNAL QUALITY ASSESSMENT PROGRAMS: PAST, PRESENT AND FUTURE

Mario Plebani

Department of Laboratory Medicine, University – Hospital of Padova, Italy

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 collected 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 perspectives 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 programs.

Key words: External quality assessment, proficiency testing, total testing process, analytical bias, imprecision, 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). External 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 Sunderman over half a century ago for haematology and clinical chemistry is still very much in use and remains a mainstay for nearly all laboratory evaluation, accreditation, and regulatory proficiency testing programs (4). In an era of total quality assessment and continuous quality improvement, the number of scientific papers appearing every year with a focus on this topic represents an evidence of the role and value of external quality assurance.

Definition and facets of EQA

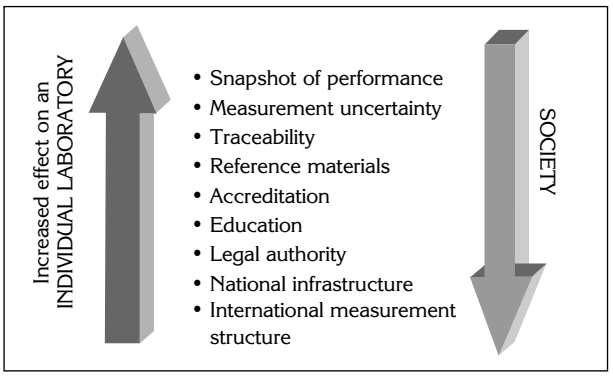
External quality assurance has been defined by Adam Uldall »an integrated professional quality assurance activity of medical laboratories«, underlying the terms »integrated« and »professional activity« as central elements of the definition itself (5). This activity comprises a broad range of applications, as shown in *Table I*, including providing participant laboratories and health authorities with estimates of measurement

Address for correspondence:

Professor Mario Plebani
Department of Laboratory Medicine,
University – Hospital of Padova, Italy

[1] Presented on Symposium for Balkan region on Education, Management and Standards in Laboratory Medicine, Belgrade, June 10–12th, 2005.

Table I The many facets of proficiency testing and external quality assurance



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-

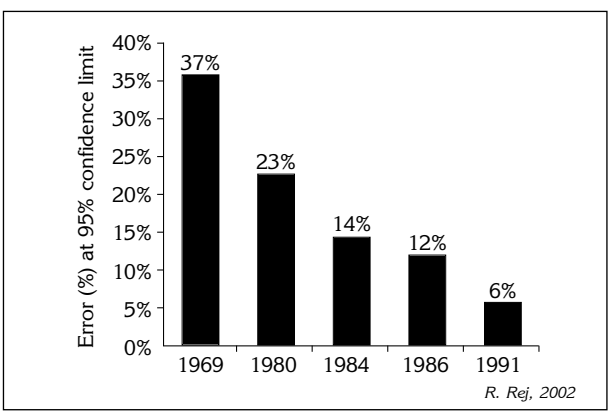


Figure 1 Interlaboratory error for cholesterol measurements: 1969–1990

Table II Distribution of laboratory performances in the cycles carried out during the years 1999–2002

Analytical performance, %				
	Cycle 1999	Cycle 2000	Cycle 2001	Cycle 2002
Troponin I (CCV=20)	n=272	n=321	n=375	n=508
Unacceptable	11.6	10.3	9.5	5.6
Acceptable	11.7	15.0	10.8	8.1
Good	27.4	24.1	20.7	24.6
Excellent	49.3	50.6	59.0	61.7
Troponin T (CCV=20)	n=22	n=58	n=109	n=60
Unacceptable	27.3	10.5	19.7	13.6
Acceptable	9.1	12.3	6.3	–
Good	9.1	29.8	18.8	20.3
Excellent	54.5	47.4	55.2	66.1
CK–MB mass (CCV=16)	n=248	n=304	n=376	n=526
Unacceptable	13.2	8.3	3.5	4.3
Acceptable	17.4	9.9	6.3	6.7
Good	26.3	25.6	20.0	23.9
Excellent	43.1	56.2	70.2	65.1
Myoglobin (CCV=10)	n=282	n=339	n=444	n=601
Unacceptable	19.5	10.7	14.2	9.0
Acceptable	12.8	8.5	9.2	10.3
Good	24.1	23.0	17.9	21.8
Excellent	43.6	57.8	58.7	58.9

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.

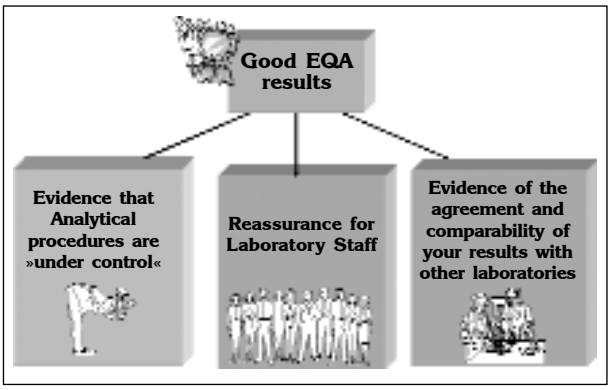


Figure 2 Outcomes of satisfactory results in EQA/PT Schemes

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

a) participant failure thus leading the laboratory to re-evaluate and modify procedures and processes, eventually improving the training and competence of the personnel,

b) 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,

c) inherent method or diagnostic system inadequacy.

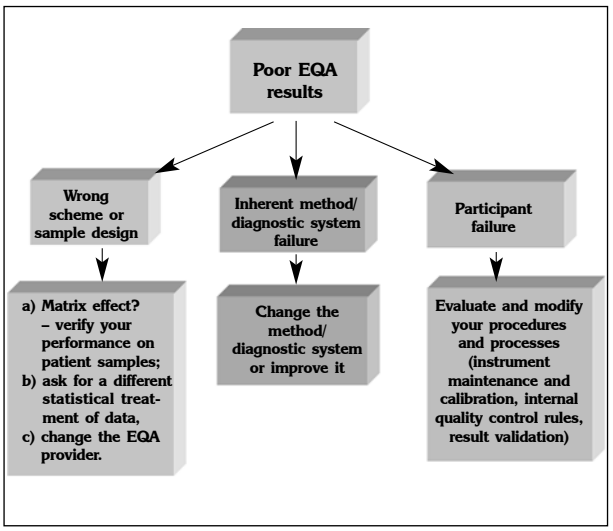


Figure 3 Possible reasons for unsatisfactory EQA/PT results

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.

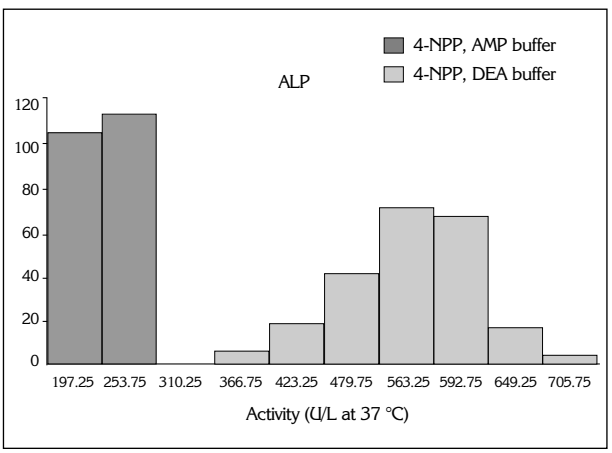


Figure 4 Clinical specimens

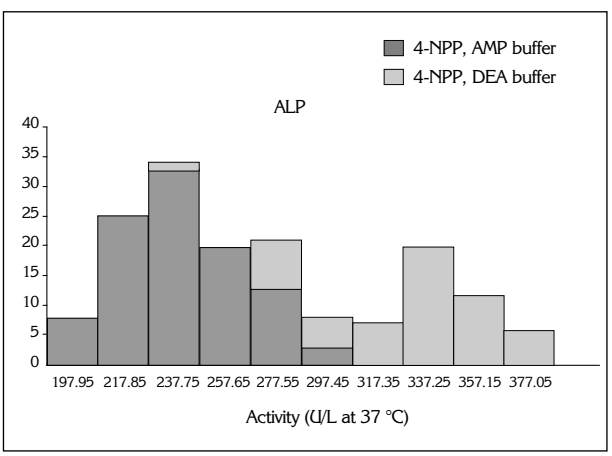


Figure 5 Commercial materials

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).

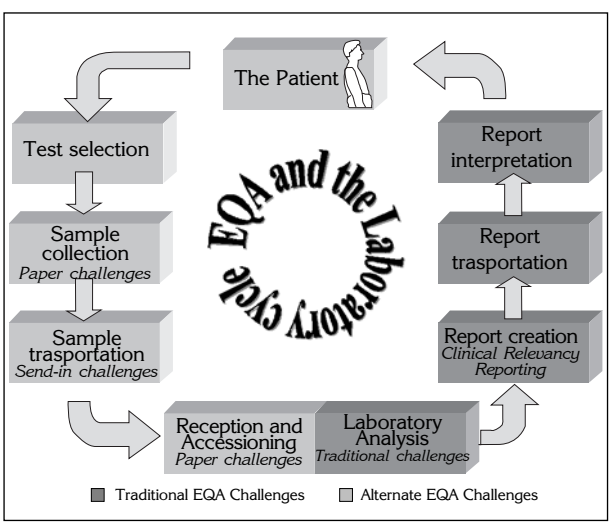


Figure 6 Total Testing Process and EQA challenges

Future perspectives

Future perspectives of EQA/PT schemes can be grouped in five emerging areas. The first regards the practicability of programs designed to asses 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.

PROGRAMI SPOLJAŠNJE KONTROLE KVALITETA: PROŠLOST, SADAŠNJOST I BUDUĆNOST

Mario Plebani

Department of Laboratory Medicine, University – Hospital of Padova, Italy

Kratak sadržaj: Programi spoljašnje kontrole kvaliteta (*eng*. External Quality Assurance, EQA) i veštine ispitivanja (*eng*. Proficiency Testing, PT), su osnovni alati za procenu kvaliteta i poboljšanja u kliničkim laboratorijama. 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 sprovođenja edukacije u laboratorijama. Buduće perspektive EQA/PT ogledaju se u mogućnostima procene pre-i post analitičkih stupnjeva, primene interneta za prijem i slanje rezultata laboratorija učesnica i programa akreditacije i sertifikacije.

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

References

1. Burke MD. Laboratory medicine in the 21st Century. Am J Clin Pathol 2000; 114 (6): 841–6.
2. Rej R. Proficiency testing and external quality assurance: crossing borders and disciplines. Accred Qual Assur 2002; 7: 335–40.
3. Belk W, Sunderman FW. A survey of the accuracy of chemical analyses clinical laboratories. By William P. Belk and F. William Sunderman, 1947. Arch Pathol Lab Med 1988; 112 (4): 320–6.
4. Rej R, Jenny RW. How good are clinical laboratories? An assessment of current performance. Clin Chem 1992; 38 (7): 1210–7.
5. Uldall A. Quality assurance in clinical chemistry. Scand J Clin Lab Invest Suppl 1987; 187: 1–95.
6. Copeland B, Doumas B, Wilding P, Rej R. Clin Chem 1992; 38: 1218–28.
7. Libeer JC, Richardson H, Bullock D, Heuck C et al. Addressing issues associated with the development and management of PT programs and with their optimum use. Accred Qual Assur 2002; 7: 320–34.
8. International Federation of Clinical Chemistry (IFCC) Fundamentals in External Quality Assessment (EQA). Guidelines on improving analytical quality by establishing and managing EQA schemes, example from basic clinical chemistry using limited resources. July 1996.
9. Lawson NS, Howanitz PJ. The College of American Pathologists, 1946–1996. Quality Assurance Service. Arch Pathol Lab Med 1997; 121 (9): 1000–8.
10. Zaninotto M, Sciacovelli L, Pagani F, Panteghini M, Plebani M. External quality assessment for biochemical markers of myocardial damage: an Italian experience. Clin Chem Lab Med 2004; 42 (12): 1434–41.
11. Sciacovelli L, Zardo L, Secchiero S, Plebani M. Quality specifications in EQA schemes: from theory to practice. Clin Chim Acta 2004, 346: 87–97.
12. Kenny D, Fraser CG, Hyltonft Petersen P, Kallner A. Consensus agreement. Scand J Clin Lab Invest 1999; 59 (7): 585.
13. Plebani M, Carraro P. Mistakes in a stat laboratory: types and frequency. Clin Chem 1997; 43 (8 Pt 1): 1348– 51.
14. Bonini P, Plebani M, Ceriotti F, Rubboli F. Errors in laboratory medicine. Clin Chem 2002; 48 (5): 691–8.
15. Secchiero S, Sciacovelli L, Giurato E, Bonvicini P, Plebani M. External Quality Assessment Scheme: tentative trial on pre-analytical phase. (Abstracts T316, T259) Clin Chem Lab Med 1999; 37; Special Supplement: S282.
16. Secchiero S, Sciacovelli L, Bonvicini P, Siviero A, Plebani M. EQA Programs for Biomedical Research Centers: (tentative) trial on the post-analytical phase. (Abstract T261) Clin Chem Lab Med 1999; 37; Special Supplement: S282.
17. Secchiero S, Sciacovelli L, Zardo L, Plebani M. Reply to W.G. Wood. Questionable results – who directs the EQAS organisers? Clin Chem Lab Med 2004; 42: 1073.
18. Sciacovelli L, Zardo L, Secchiero S, Zaninotto M, Plebani M. Interpretative comments and reference ranges in EQA Programs as a tool for improving laboratory appropriateness and effectiveness. Clin Chim Acta 2003, 333: 209–19.
19. Zardo L, Secchiero S, Sciacovelli L, Bonvicini P, Plebani M. Reference intervals: are interlaboratory differences appropriate? Clin Chem Lab Med 1999, 37, 11/12: 1131–3.
20. Sciacovelli L, Secchiero S, Zardo L, Plebani M. External Qualità Assessment Schemes. Need for recognised requirements. Clin Chim Acta 2001, 309, 2: 183–99.
21. Petersen PH. Is it possible to create a perfect external control system? Scand J Clin Lab Invest 1998; 58 (4): 265–8.

Received: April 10, 2005

Accepted: April 18, 2005