R. Caprita, et all. Journal of Agroalimentary Processes and Technologies, Volume XII, No. 1 (2006), 107-112
Full Paper - Food Control Section

ANALYTICAL VALIDATION OF CLINICAL LABORATORY RESULTS

Rodica Capriță[1], Georgeta Ursulescu[2], A. Capriță[3], M. Ursulescu[3]
[1]Banat's University of Agricultural Sciences and Veterinary Medicine Timisoara Faculty of Animal Sciences and Biotechnologies, Romania
[2]City Hospital, Otelu Rosu, Romania
[3]Banat's University of Agricultural Sciences and Veterinary Medicine Timisoara, Faculty of Food Processing Technology, 119 Calea Aradului, 300645, Romania

Abstract

An important step in quality management is the analytical validation. In order to continuously perform correct measurements, analytical utilized measuring and test equipment were monitored and calibrated on a regular basis during three months. Standard reference materials and test sera were used as calibrators. Quality control processes disclosed errors in the analytical results, which are reduced by periodical calibrations.
***Keywords**: analytical validation, calibration, standard.*

Introduction

One purpose of internal quality control is to estimate errors in an analytical run and to prevent release of data if the errors are unacceptably high. A second purpose is to monitor the performance of the assay over a period of time and detect trends (Libeer, 1997).

The validation of clinical laboratory results is complex and includes the follow-up of check and acceptance procedures all steps involved in the production of these results. Validation of laboratory results includes: method validation, instrument validation, pre-analytical validation procedures, analytical validation procedures, and post-analytical validation procedures. Most laboratory tests are performed with industrially prepared kits and reagents. Methods quality has been improved substantially during the last 20 years. Libeer (1997) could demonstrate that inter-laboratory coefficients of variation during the 1980s for most routine clinical chemistry were halved between 1980 and 1990. This improvement is explained by better reagent kits and by automation in this field. Performance characteristics of a given reagent

kit are only valid if this kit is used as recommended by the manufacturer.

Instrument validation not only includes the measurement equipment, but also small utensils (pipettes, dispensors, dilutors, incubators, washing devices). Instrument validation method also includes control of speed of centrifuges, calibration of balances and small spectrophotometers.

All testing from pre-analytic phase to the reporting involves with error and uncertainty sources. In quantitative analyses, the reliability of the measurement quality is expressed as random error (i. e. precision) and systematic error (i. e. trueness, or bias). Several errors in clinical laboratories are made during the pre-analytic phase. After serum/plasma separation, the sample view must be verified: hemolysed, lipemic, and icteric samples must be identified. In some cases interferences can be corrected (Passey, 1982).

An important step in quality management is the analytical validation (NCCLCS, 1991). Traceability to accuracy of a method will depend on traceability of the calibrators used. Therefore, it is important that manufacturers recommend appropriate calibrators for each reagent kit. This also means that laboratories should use a reagent kit as such, otherwise all industry traceability efforts are worthless.

Depending on the type of analysis and the type of equipment, the number of control samples and the frequency of controls will be different. Relevant calibration items are: preset values and tolerated deviations, frequency of calibration, what calibration standards are used, relation to national or international standards, environmental conditions during calibration, measures to minimize shifts in adjustment.

Experimental

In order to continuously perform correct measurements, utilized measuring and test equipment were monitored and calibrated on a regular basis during three months (Vassault, 1986).

The experiment was performed in the clinical chemistry laboratory from the City Hospital in Oţelu Roşu. Biochemical blood indices were analyzed by automatic biochemical analyzer EOS-BRAVO (Hospitex diagnostics, Firenze, Italy), using Hospitex diagnostic reagents.

We used for calibration control materials (standards and test sera) produced by the same manufacturer. The test serum (HDN) is a lyophilised control serum based on human serum, with concentrations /activities in the normal range. HDN is for use in the quality chemistry methods for the quantitative determination of substrates, electrolytes, lipids, enzymes and proteins. The control is used to monitor accuracy or precision both for manual and automated analytical procedures.

Results and Discussions

Calibration means determining the value of the deviation(s) of an instrument from an applicable standard. We calculated for each batch of analyses the main statistical parameter (White, 1986): the standard deviation (SD) and the coefficient of variation. (CV). CV is the standard deviation of the mean. Ideally CV should be less than 5%.

Table 1. The concentration factors for Ca and Mg

Kit	Sample	Ca			Mg		
		Fv	Fn	Fn-Fv	Fv	Fn	Fn-Fv
1	1		940			1587	
	2	940	886	54	1587	1418	169
	3	886	893	-7	1418	1504	-86
	4	893	836	57	1504	2062	-558
	5				2062	1205	857
	6				1205	1316	-111
2	1	836	897	-61	1316	2222	-906
	2	897	934	-37	2222	1527	695
	3	934	1087	-153	1527	1835	-308
	4	1087	941	146	1835	2083	-248
	5	941	898	43	2083	1471	612
	6	898	1000	-102	1471	1504	-33
3	1	1000	973	27	1504	1667	-163
	2	973	1274	-301	1667	1653	14
	3	1274	914	360	1653	1739	-86
4	1	914	1007	-93	1739	1626	113
	2	1007	1005	2	1626	1923	-297
	3	1005	1087	-82	1923	1176	747
	4				1176	2778	-1602
5	1	1087	827	260	2778	1527	1251
	2	827	910	-83			
	3	910	943	-33			
$\bar{X}$ ±SD			960.63± 103.82			1691± 379.57	
CV%			10.80			22.44	

The experimental data (table 1) reveal a dynamic of the concentration factors between two calibrations (Figures 1 and 2). Common causes of systematic error are: improperly prepared reagents, deterioration of reagents or calibrators, inappropriate storage of reagents, etc. Random errors may also occur due to power fluctuations, air bubbles in the reagent, imprecisely pipetting, etc. Systematic errors are predictable and cause shifts or trends on control charts. The trends of both charts do not indicate a systematic error.

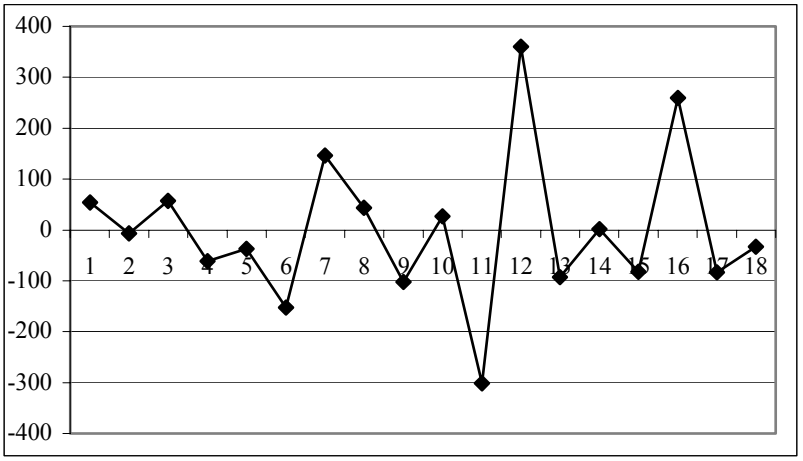

Fig. 1. The dynamic of the concentration factors for Ca

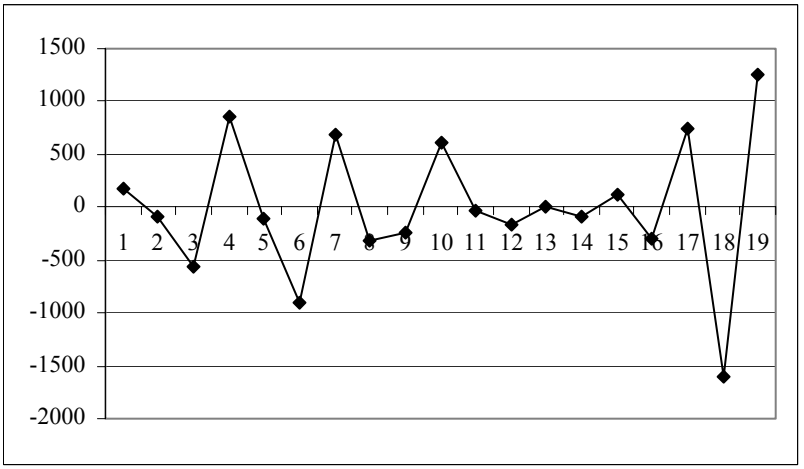

Fig. 2. The dynamic of the concentration factors for Mg

The coefficients of variation, 22.44% for Mg and 10.8% for Ca, confirm a greater difference between the old (Fv) and the new (Fn) restandardized values (Figure 3).

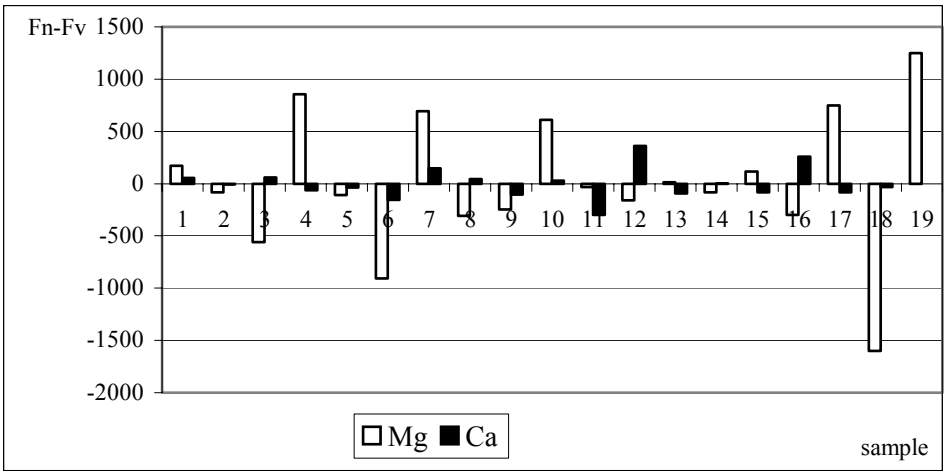

Fig. 3. The dynamic of the factor differences for Ca and Mg

Validation of clinical laboratory results is mandatory. We observed an ascendant trend of the concentration factors during the monitoring period (Figures 4 and 5). Quality control processes can disclose or reject errors at best, but the revelation of errors may be the first step in a trouble shooting process which may lead to correction of the error, and thereby, to improvement in the analytical quality.

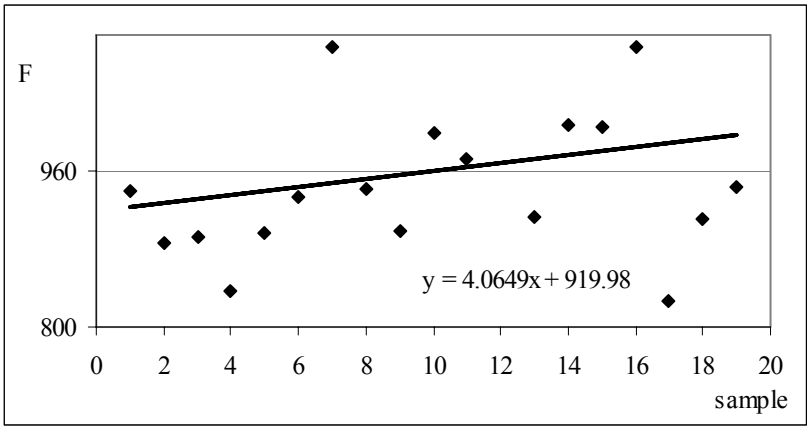

Fig. 4. The concentration factors for Ca

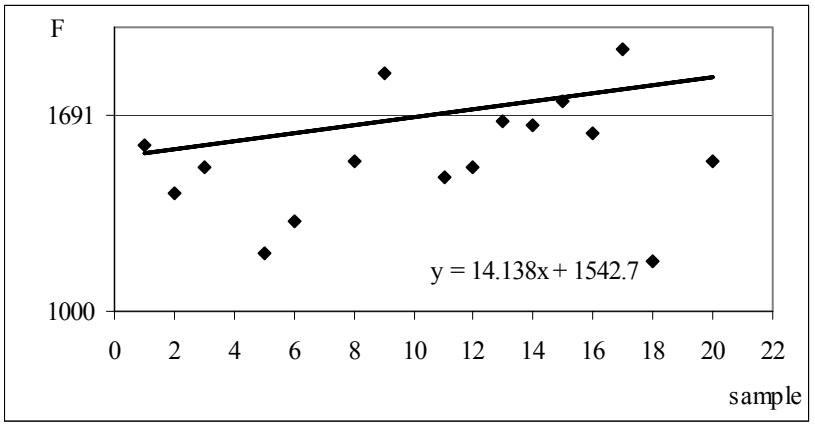

Fig. 5. The concentration factors for Mg

Conclusions

Validation of clinical laboratory results is mandatory for improving the analytical quality. The experimental data reveal a dynamic of the concentration factors between two calibrations. The difference between the old (Fv) and the new values (Fn) are greater in the case of Mg. The concentration factors for Ca and Mg have an ascendant trend.

References

Libeer, J. C. (1997) Validation of clinical laboratory results, *Drug information Journal, 31*, 243-250.

National Committee for Clinical Laboratory Standards (1991) Internal Quality Control Testing: Principles and Definitions, *NCCLS Document C24-A*, 11 (4).

Passey, R. B. (1982) Mabuf KC. Foundations for validation of quantitative analytical methods in the clinical laboratory, *Arch Pathol Lab Med., 116*, 732–738.

Vassault, A, et al. (1986) Protocol de validation des techniques, *Ann Biol Clin., 44*, 686–745.

White, G. H., Fraser, C. G. (1984) The evaluation kit for clinical chemistry: a practical guide for the evaluation of methods, instruments and reagent kits, *J. Autom. Chem., 6* (3), 122-141.