THE METROLOGICAL CORRECTNESS OF AN IN VITRO RESEARCHES AS A CRITERION OF A MEDICAL LABORATORY DIAGNOSTICS OBJECTIVITY

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Summary: This review demonstrates the formation of metrological principles in laboratory medicine, allowing to change the health care paradigm from "helping the patient" to preventing diseases. The special metrological criteria that ensuring the fulfillment of laboratory research at the analytical level as necessary for solving clinical problems are considered: biological variation, measurement uncertainty, traceability to standards.

Keywords: biological variation, traceability, analytical variation, bias, standard materials, measurement uncertainty

I will allow presenting saying of great Louis Pasteur epigraph of performance: "I adjure you, care of these sacred buildings that distinctly name laboratories. Require, that the number of them multiply and to equip them. These temples of future riches and welfare. There humanity grows up, collects force and becomes better." The role of the field of knowledge was so sagaciously certain, that only through a century got the name "Laboratory medicine". Let us turn to the origins of the formation of our "workshop", because "He has no future, who does not remember his past". Our specialty has rich history. Justly for acquisition of the name of our activity the Latin verb "LABORO" is used, that means - I WORK! And for short period of time we "produced" such new knowledge that resulted in changing of sense of medical treatment as a kind publicly to useful activity. So, historically, we are accustomed to wisdom, stating that "Medicine is the highest of the arts". However, in the early 20th century, William Osler put forward a different argument, simply characterizing the "Medicine – as a science of uncertainty and art of probability." At the same time, remembering the testament of D. I. Mendeleev, that "Science starts where starts the measurement". Well, the science of measurement is Metrology. Humanity naturally came to understand the importance of metrology in any field of activity. Metrology is the philosophy of science and its technical realization in the institutions of civilization. We leaf through the pages of history and see that the formation of metrology was the natural result of a series of technical revolutions: the Great Industrial Revolution (industrialization) - XVII-XIX centuries, which led to industrial production. Then the technological revolution of the second half of XIX and early XX centuries, when economic development was predominantly based on scientific achievements, not just successful inventions. All these achievements have led to the development of information technology. Now in the beginning of the XXI century we are experiencing the pressure of the so-called sixth information revolution, which led to a global information space. But back to another definition of Metrology, as the science of "measurements" and therefore "the standards". With what accuracy we must measure. The great Einstein that said, "Exact science, do what you can, as necessary, and applied what you need, as you can". How do these issues to move on the laboratory medicine? What is "the quality of laboratory diagnostics" there is confidence that correct and timely administered the test to the needy in this patient, performed at a sufficient level of analytical and accompanied by the necessary information for its interpretation. I.e. have to measure accurately, but not more accurately than you need! Today, a well-founded position has formed: focus on clinical feasibility. With what accuracy is it necessary to carry out laboratory research? As an example, we will analyze the measurement of one of the most important homeostasis parameters: blood osmolality, which determines the movement of fluid in the water sectors of the body.

So, an idea has formed about the diagnostic value of the deviation of the content of the analyte under investigation patient for the range of "normal values" which is determined by the extent of their so-called biological variation. An interesting variation on the evaluation of information content of fluctuations of the concentration of analytes is called the "index of individuality" as the relationship of the coefficients individual and interindividual variations of these analytes: II = CVI / CVG where II is the index of individuality, CVI is the coefficient individual biological variation and CVG is the coefficient of interindividual biological variation. If the value of this index less than 0.6 analyte, it is difficult to count on the diagnostic informativeness of the test,

rather, it can be used to monitor the disease. When the value of the index more than 1.4 test has distinct diagnostic information content.

These characteristics of biological variation have thus become, and the measure of objective basis, the maximum allowable analytical non-reproducibility. It is accepted that the coefficient of variation of research methods should be less than half of individual biological variation. And the so-called "correctness" of the study, expressed by the permissible shift of the measured value from the true value, is also calculated from the variation of the individual and the interindividual.

In last years, the concept of "6 sigma" has been increasingly used in laboratory medicine, according to which the so-called "sigma" is used to calculate the accuracy of studies. The maximum error permissible from the clinic's point of view (TEmax), as well as the analytical variation (CVa) and the displacement of the measured measurements (B): Sigma = (TEmax-B) / CVa.

However, the most important and difficult condition for applying the results of laboratory research is their "COMPARISON", which is provided by metrological traceability to the metrological reference value.

In this connection, we focus attention on the fact that physical measurements are required measurement, and chemical measurement, it is necessary, in addition, the presence of a complex validated the analytical process and, accordingly, analytical systems. In other words, the comparability of results of chemical measurements require additional transmission chain measured value characterizing the chemical composition of the objects of study.

The key link, in fact, the "Golden Key" for solving the problems of assuring the quality of measurements is the use of STANDARD SAMPLES when monitoring the activities of complex analytical systems that ensure TRACKING to international reference materials or reference methods. This function is usually performed by the manufacturer of test systems for IVD. At the level of practical laboratories should be performed in the procedure "Validation" techniques, i.e. experimental verification in a laboratory the main characteristics of techniques: accuracy, reproducibility, linearity. The whole set of technologies for obtaining objective information about the composition of the organism at the cellular and molecular level, which allows radically to change the paradigm of the health function of medical science. This primarily concerns the development of the so-called. "Personified medicine" as a direction based on the use of complex diagnostic approaches that take into account individual, genetically determined and phenotypically conditioned features of the human body.

So using modern laboratory and instrumental technology have led to a perception about the medicine of the XXI century: "Medicine 5 "b" s: preventive (maintenance), predictive (predictive), precision, personalized (individual) and participatory, i.e. the patient is a participant in the process.

Thus laboratory medicine as a scientific discipline and a medical specialty is translational and forms the basis for evidence-based medicine.

Reference:

[1] **Fraser, C.G.** Biological variation in clinical chemistry: from principles to practice / C.G. Fraser. – Washington: AACC Press, 2001. – 151 p.

[2] **Garber, C.C.** Quality System for Clinical Laboratory in the 21st Century / C.C. Garber, H.W. Kaufman // Clinical Diagnostic Technology / Eds. Ward-Cook K.M., Lehman C.A., Schoeff L.E., Williams R.H. − Washington: AACC Press, 2006. – Vol. 3, Postanalytical Phase. – 201 p.

[3] **Harry, M.** Six Sigma: The Breakthrough Management Strategy Revolutionizing the World's Top Corporations / M. Harry, R. Schroeder. − New York: Currency, 2009. − 301 p.

[4] **Kallner, A**. Accreditation of medical laboratories. Some reflections from the Nordic Horizon / A. Kallner // Clin. Chim. Acta. – 2001. – Vol. 309. – P. 163-165.

[5] **McQueen, M.** Overview of evidence-based medicine: Challenges for evidence-based laboratory medicine / M. McQueen // Clin. Chim. Lab. Med. − 2005. − Vol. 47, № 8. − P. 1536-1546.

[6] **Ricos, C.** Quality indicators and specifications for the extra-analytical phases in clinical laboratory management / C. Ricos, M. Garsia-Victoria, B. Fuente // Clin. Chem. Lab. Med. − 2004. − Vol. 42, № 6. − P. 578-582.

[7] Verificaition of instruments using statistical procedures / L.A. Khorovskay [et al.] // Clinical Chemistry. – 2008. – Vol. 54, № 56. – P. A49.

[8] **Westgard, J.O.** Six Sigma Quality Design and Control / J.O. Westgard. – Madison, WI: Westgard QC. Inc., 2006. – 348 p.

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