

27th Symposium
Croatian Society of Medical Biochemistry and Laboratory Medicine

**National external quality assessment:
from sample to evaluation**

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CROQALM today

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The first records on external quality assessment in Croatia date to the 1950s. Since 1973, it has been conducted continuously under the auspices of the Croatian Society of Medical Biochemistry and Laboratory Medicine (CSMBLM).

In 2012, with the new CSMBLM's statute, the Croatian Centre for Quality Assessment in Laboratory Medicine (CROQALM) was established which provides external quality assessment in laboratory medicine for Croatian medical laboratories three times per year. According to the decision of the Croatian Chamber of Medical Biochemists (CCMB) from 2013, participation to the national EQA program is mandatory for all medical laboratories in Croatia, with all tests they perform and are offered in CROQALM schemes. Results from CROQALM are a major part in CCMB professional supervision of Croatian medical laboratories. In the same year, CROQALM defined new activities in terms of improvement and compliance with international requirements for the implementation of external quality control which are adapted to national regulations.

After two years of work in detecting weak point-and areas for improvement, the rules of registration, financial strategy, definition of analytes and modules in CROQALM scheme as well as a strategic plan for further activities were established. For this purpose, in addition to responsibility for individual modules, CROQALM members are organized into working groups to improve the quality and prepare commutable quality control samples, as well as results processing (allowable limits of performance and assessment), participant's education and at last, information update through the website. The most important and current activities are presented in the Symposium lectures.

Today (2016), Croatia has 194 registered medical laboratories. CROQALM team gathers fourteen members on voluntary basis, and has a quality assessment program for 150 different analytes grouped into 10 modules. Preanalytical and postanalytical phase modules are included. External quality assessment of medical laboratories is performed using a web interface with software support for the evaluation of quality in laboratory medicine - inlab2*QALM. All information about CROQALM can be found on the new website (<http://croqalm.hdmblm.hr/index.php/hr/>).

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Ideal sample characteristics for external quality assessment

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Evaluation capability of any external quality assessment (EQA) scheme for clinical laboratories is highly dependent on the characteristics of the sample distributed to participants. The ideal sample should mimic the actual patient sample and the results obtained should be considered as patient's results released from laboratory. However, EQA samples need additional characteristics in order to be distributed to numerous laboratories whose performance needs to be evaluated. They need to be stable enough through storage, transportation and distribution, homogenous across all aliquots produced, inexpensive enough to be easily affordable to participants, include clinically relevant concentration ranges and be available in sufficient volume. It is hard to achieve all of these goals in one sample and commutability with clinical samples is often discordant with some of the mentioned characteristics (e.g. clinical relevant

concentration range, sample volume, stability). On the other hand, commutability is one of the most important sample characteristic that defines the scheme design, target value choice and further interpretation of laboratories' results.

Commutability of a control sample can be defined as the equivalence of the mathematical relationship between the results of different measurement procedures for control sample and representative samples from healthy and diseased individuals. Due to processing steps applied to control samples in order to achieve many needed sample characteristics for EQA, commutability is often compromised in a way that a sample does not behave as a patient's sample for a particular method/instrument group. Validating commutability of control samples is of utmost importance for any EQA provider so that appropriate target values can be chosen for evaluation of laboratories' performance. Commutable samples enable assessment of traceability of the result to a reference system and where commutability cannot be proven, evaluation of results is restricted to peer group evaluation gathering method/instrument groups that are likely to have the same matrix-related bias for the given EQA sample.

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Control material for external quality assessment in haematology

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As in other laboratory diagnostic fields, the main goal of external quality assessment (EQA) in haematology is to achieve the lowest possible inter-laboratory variation for haematological parameters, since those parameters are mainly used for

monitoring purposes and the differences between two patient results should not be jeopardized by analytical variation between different cell counting principles.

Commercial control materials made for EQA purposes are, mostly, analyser specific. Specificity derives from striving to achieve long-term stability of the control material. Manufactures use different approaches to resolve stability issues. Usually, controls are made of preserved and stabilised fresh human blood and/or by addition of surrogate materials (avian, porcine, bovine *etc.* cells) in leucocytes and platelets deprived blood. Control materials prepared in such way result with morphologically altered red blood cells causing problems in cell counting when obtained by different analysers. Consequently, the comparability of results could be threatened.

In terms of commutability, the best control material for inter-laboratory comparison in haematology is the fresh blood sample. Despite its indisputable advantages, this sample type has numerous disadvantages, which EQA providers must overcome if fresh blood sample is to be served as a control material in their haematology scheme.

The main reason why fresh human blood is not used for EQA in haematology is its short stability and limited blood volume which can be obtained from a donor. To overcome stability problems every EQA provider uses different receipt. The most convenient solution is minimal preservation of blood cells in order to preserve the morphological characteristics of the cells. However, maximum stability still could not be longer than a few days.

CROQALM successfully provided three exercises in haematology scheme using human fresh blood as a control sample. Since haematology scheme has nearly 180 participants, blood dose from single donor is enough to ensure that every laboratory obtains sufficient volume for analysis. Stability issues are prevailed by postal delivery within 48 hours.

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Acceptance criteria and evaluation in external quality assessment (EQA)

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Acceptance criteria in EQA scheme are quality standards required by scheme organizers in order to evaluate individual laboratory performance and monitor standardisation and harmonisation of measurement procedures used in clinical laboratories. Strategies and hierarchy of models applied in setting analytical quality specifications were initially described during the WHO, IFCC and IUPAC conference organised in 1999 and are commonly known as the 'Stockholm hierarchy'. The hierarchy was further revised and simplified during the first Strategic Conference of the European Federation of Clinical Chemistry and Laboratory Medicine held in Milano in 2014, with emphasis that a model higher in hierarchy should be chosen for setting up quality standards for analytical performance of the test. The first model requires limits to be set based on direct and indirect clinical outcome studies. This is the preferred model, although currently, very few papers have been published that address impact of analytical performance based on clinical classifications and decisions. Second model, based on measured components of biological variation is used by various EQA schemes and usually includes various levels of requirements (minimal, desirable and optimal) set for each analyte depending on the purpose of measurement (monitoring or diagnosis) and current analytical performance in the scheme. The last one, state-of-the-art model, sets limits that are technically achievable by a certain percentage of laboratories within the scheme and these limits may be considered encouraging and inspirational where improvement in analytical performance to meet clinical requirements is needed.

Regardless of limits used for evaluation of individual laboratory's performance, the basis for their choice must be clear to participants. Furthermore,

they must be chosen so that any particularity of data distribution, number of participants and peer group heterogeneity is taken into consideration and they have to be both achievable and stimulating for participants.

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Variability of immunochemistry methods and its clinical impact

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Laboratory users expect that obtained laboratory results are accurate, comparable and interpretable in a reliable and consistent manner. That is why the quality of issued results is in every laboratory's focus. The value of external quality assessment (EQA) is to indicate areas of analytical problems and to stimulate improvements in between-laboratory variation.

Beside usual problems related to EQA (sample preparation, matrix effects, clerical functions, selection of statistical methods for evaluation, and peer group definition), there is another problem related to immunochemistry methods. It is well known that results obtained by immunochemistry methods could not be simply compared, but still there is a strong need for their standardization, especially for analytes which are used as diagnostic tools and have the same reference ranges or cut-off levels obtained by different immunochemical methods.

We have evaluated all results of immunochemistry modules submitted in CROQALM since 2013. It is interesting that even on national level laboratories use up to ten different immunochemical methods for determination of single analyte. Large number of these analytes is used for diagnosis and their concentrations are crucial for making decisions about patient treatment. There is also a problem in judging quality of those methods when there are less than seven laboratories which use one particu-

lar immunochemical method, because number of results is not sufficient for statistical evaluation.

However, EQA will not detect all problems in the laboratory, especially those related to the pre- and post-examination procedures. Furthermore, a single unacceptable result does not necessarily mean that there is a problem in laboratory or problem of specific method. However, besides meeting stated quality requirements, we have to be aware how our results or used methods may generate an error in clinical judgement and decision-making.

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Medical biochemistry laboratories assessment by Croatian Chamber of Medical Biochemistry - the external quality assessment role

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Croatia's medical biochemistry laboratories are obliged to participate in the National external quality assessment (EQA) scheme as specified by Croatian Chamber of Medical Biochemists (CCMB). All tests performed in the laboratory have to be checked by external quality assessment or by inter-laboratory comparisons. Between many different organizers, the priority has to be given to the National EQA organizer (CROQALM). Laboratories have to participate in each offered round. It is expected that EQA samples are handled in the same way and by the same laboratory staff as routine samples without paying any additional attention to the instrument than anticipated that day. According to the Ethical codex, it is not allowed to collaborate or comment results with other participants before reporting its own results. The laboratory head has the responsibility to discourage such behaviour. The EQA certificate interpretation depends on whether the sample type was commutable or not. Results for commutable samples are used to assess accuracy against a reference

measurement procedure or a designated comparison method. The peer group evaluation is used for the non-commutable samples. This type of evaluation allows assessment of measurement procedures between all laboratories using the same technology and it can confirm conformance to the manufacturer's specifications. According to the contract, CROQALM is obligated to inform CCMB in detail (about participants, their achievement for each test, original quality control sample's certificates). In case of incorrect results, the CCMB requires the root causes to be explored and documented. The main benefit of EQA is to force laboratories to reveal the root causes of each incorrect result, tracking back available data from all phases: pre-analytic (storage condition, proper reconstitution, proper labelling), analytic (retrospective analysis of calibration and/or internal quality control data, instrument maintenance data), post-analytic (possible transcription errors or wrong interpretation).

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Sponsored lecture

See the complete picture of external quality control with RIQAS

Nikolina Belamaric

Randox Laboratories Ltd
RIQAS - Randox Laboratories Ltd, United Kingdom

With more than 35,000 participants in 123 countries and a choice of 32 flexible programmes, RIQAS is the largest international external quality assessment (EQA) scheme available. When combined with more than 30 years within the in vitro diagnostics (IVD) market, their knowledge and expertise in this area is extensive. The aim of this presentation is to highlight the importance of EQA and its role within the laboratory. In addition, the guidelines that customers should consider when selecting the EQA provider will be presented.

RIQAS have developed based on ISO 15189:2012 and own experiences within the market. Furthermore, case studies from RIQAS customers will be

used to illustrate the relevance of the guidelines discussed, allowing seeing the complete picture.

This is an excellent opportunity to meet with RIQAS presenter and share our experiences with other col-

leagues and opportunities to ask questions regarding RIQAS, their available programmes and how they can help us to complete our view of EQA.

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