European Organisation For External Quality Assurance Providers in Laboratory Medicine

EQALM symposium 2017

19-20 October

Dublin, Ireland

ABSTRACT BOOK

Welcome to the EQALM Symposium!

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EQALM symposium 2017

October 19 – 20, Dublin, Ireland

Program

Thursday 19 October 2017

Registration		**8.00 –14.00**
Working Group Meeting (parallel sessions)		**8.30 –13.00**
	The Executive Board room	***Room 18***
8.30 – 9.55	Frequency	Virtual Microscopy
10.00 – 11.25	Haematology	---
11.30 – 12.55	Haemostasis	Microbiology
Lunch		**13.00 – 14.00**

Symposium: The role of EQA in protecting community health

14.00 – 14.10	**Opening**	**Anne Stavelin**
Microbiology	Moderator: **Michael Noble**	**14.10 – 15.30**
14.10 – 14.40	Validation of alternative microbiological methods for food, feed and environmental samples	Hilde S. Norli
14.40 – 15.00	EQA and Chlamydia; protecting the community from the spread of STIs	Rosanna Peeling
15.00 – 15.20	Pre- and peri- and post- examination of microbiology by EQA	Michael Noble
15.20 – 15.30	Questions and discussion	
Round Table	Moderator: **Finlay Mackenzie**	**15.30 – 16.00**
15.30 – 16.00	Support and education	
Break with refreshments		**16.00 – 16.30**
Adam Uldall Lecture	Moderator: **Anne Stavelin**	**16.30 – 17.30**
16.30 – 17.30	The role of EQA in the verification of in-vitro medical diagnostics	Mauro Panteghini
Social Event	Congress dinner in city center	**18.30 – 23.00**

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Friday 20 October 2017

Plenary lecture	Moderator: **Piet Meijer**	**9.00 – 9.30**
9.00 – 9.30	External Quality Assessment for developing countries: The role of WHO	Willy Urassa
Statistics in EQA	Moderator: **Piet Meijer**	**9.30 – 10.15**
9.30 – 9.55	A critical view on ISO standard 13528	Wim Coucke
9.55 – 10.15	Statistical approach for optimization of external quality assurance (EQA) studies of molecular and serological viral diagnostics	Matthias Niedrig
Break with refreshments		**10.15 – 10.45**
Members' session	Moderator: **Stephanie Albarède**	**10.45 – 11.30**
10.45 – 11.05	Definition of EQAS allowable limits for HbA1c: a candidate method	Anne Vassault
11.05 – 11.25	Quality Monitoring of pre-analytical sample labelling	Ann Leonard
Abstract presentations	Moderator: **Erika Sarkany**	**11.30 – 12.30**
11.30 – 11.45	Biochemical assays of human seminal plasma: the experience of a French EQA program	Safouane Hamdi
11.45 – 12.00	Assessment of Laboratory Performance in the Molecular Detection of Influenza A, Influenza B and RSV methods through International EQA Scheme for Multiplex Assays	Niina Kivi
12.00 – 12.15	IHC Breast Audit	Tony Badrick
Lunch		**12.30 – 13.30**
EQALM General Assembly		**13.30 – 15.30**
End of the meeting		**15.30**

ABSTRACTS

PRESENTATIONS

Validation of alternative microbiological methods for food, feed and environmental samples

Hilde Skår Norli
Chair of NordVal International, Norwegian Veterinary Institute

There are many rapid/alternative methods for detection of pathogens and indicator bacteria in food and environmental samples. In order to use these methods in the context of official controls, the methods need to be validated against reference methods according to internationally accepted protocols and assessed/certified by independent parties or authorized by the competent authority. In a third-party certification, the alternative method is compared to a reference method through extensive studies, reviewed by technical experts and finally certified by an organization like NordVal International. Hereby, it will be documented how well the method performs, the sensitivity and specificity (and hence indirectly the rate of false positives and false negatives), and how suitable the method is in detecting the bacteria strains of interest and no interfering strains (inclusivity and exclusivity). For quantitative methods, the method performance for trueness and accuracy are determined. The validations are carried out according to ISO 16140-2:2016 Microbiology of the food chain – Method validation – Part 2: Protocol for the validation of alternative (proprietary) methods against a reference method. Independent reviews also assess that the performances comply with the claims of the manufacturers.

Some methods are not granted a certificate, but still on the market. Use of certified methods is beneficial for all laboratories and their business associates; due to both the quality aspect and hence possible less risks and costs related to false or inaccurate results.

EQA and Chlamydia; protecting the community from the spread of STIs

Prof. Rosanna Peeling, Dr. Debrah Boeras
London School of Hygiene and Tropical Medicine

The World Health Organization estimates that an estimated 131 million new cases of genital chlamydial infections occur globally every year. WHO advocates the use of point-of-care (POC) tests for screening genital chlamydial infections to interrupt disease transmission and prevent the development of long term complications. However, recent studies have shown that introducing POC testing is a double-edged sword. While POC tests can increase access to testing and allow patients to be linked to evidenced-based care, its introduction can put tremendous stresses on fragile healthcare systems. Ensuring the quality of tests and testing in a decentralised testing system has presented major challenges to STI control programmes. EQA panels are available but they are too costly when they are needed for thousands of testing sites across a country. In the absence of EQA, false positive results frequently result in stigma, shame, and are often associated with gender-based violence. False negative results allow onward disease transmission and undetected/untreated infections can lead to severe complications and long term sequelae, including pelvic inflammatory disease, ectopic pregnancy, tubal infertility and chronic pelvic pain.

New POC devices for chlamydia screening with data connectivity are now available. It is possible to link EQA data to these devices and allow programme managers to have up to the hour information on test results, proficiency of the operator, instrument errors. The data can also facilitate efficient supply chain management of health commodities to avoid stock-outs. National control programmes need to develop models to estimate the most cost-effective means of introducing and managing national EQA systems for POC tests.

Pre- and peri- and post- examination of microbiology by EQA

Restelli, V and MA Noble

Medical laboratories and medical laboratory EQA are focussing more interest and attention beyond the examination phase, in part because of more comprehensive Quality Management Systems, and because of the increasing awareness of the propensity of errors in the pre-examination, post-examination and peri-examination phases that impact upon laboratory performance and importantly on patient safety. Medical laboratory EQA has a responsibility to ensure that errors are detected to protect patients, health care practitioners, and the community from harm resulting from laboratory errors.

Increasingly literature searches find manuscripts and articles reporting from many programs on the importance of EQA beyond the traditional examination phase model.

This presentation will highlight a technique that allows EQA providers to assess laboratory performance in the pre-, post, and peri- examination phases that is easy to produce, and cost effective, and objective to measure. In the spirit of “a picture is worth a thousand words” the method uses short cartoon video clips, supplemented with minimal but sufficient text. On survey we find the user satisfaction level to be high.

While the focus in this presentation is on microbiology laboratory issues, the methodology is applicable across the medical laboratory spectrum.

The role of EQA in the verification of in-vitro medical diagnostics

Mauro Panteghini
Research Centre for the Metrological Traceability in Laboratory Medicine (CIRME), University of Milan, Milan, Italy

Once an in-vitro diagnostic measuring system has been marketed and introduced into daily practice, the possible sources of degradation of its performance are numerous. It is therefore essential to put in place a continuous surveillance of the quality of performance of the commercial system and of the laboratory that perform measurements in clinical setting. This surveillance relies substantially on quality control programs, which, however, should be redesigned to meet metrological criteria. Particularly, the participation to EQA schemes that meet specific metrological criteria is mandatory for the evaluation of performance of participating laboratories in terms of standardization and clinical suitability of their measurements. The requirements for this type of EQA are as follows: in addition to the use of commutable control materials to allow transferability of participating laboratory performance to patient samples, it is necessary to assign values (and uncertainty) to them with reference measurement procedures (RMP) performed by an accredited laboratory and to define and apply clinically allowable performance specifications to verify the suitability of laboratory measurements in a clinical setting. Unfortunately, there are few permanent EQA programs covering these requirements because some practical constraints including technical (lack of certified materials, difficulties to prepare commutable samples, complicated logistics of distribution of frozen samples), psychological (lack of awareness of which quality factors make an EQA important) and economic (higher costs) aspects, which limit their introduction. It should be however emphasized how the lack of properly structured EQA schemes prevents the objective evaluation of the reliability of measuring systems and of the quality of analytical measurements provided by clinical laboratories. Only true value assignment by RMP to EQA commutable materials allows objective evaluation of the performance of laboratory measurements through a trueness-based (instead of inferior consensus-based) grading of the competency of participating clinical laboratories. Note that for quantities where no high-order RMP is available, system-dependent target values should be used to evaluate the performance of participating laboratories, but also in this case the values assigned to the EQA materials should preferentially be determined by reference institutions (possibly including the manufacturer releasing that specific analytical system), working under strictly controlled conditions in order to maintain measurement uncertainty as low as possible, and not as a group mean. The fulfillment of requirements for the applicability of EQA results in competence classification of participating laboratories in terms of traceability of their measurements involves both technical and economic efforts by EQA organizers. It is, however, clear that these aspects should be immediately solved since EQA that meet metrological criteria have unique benefits that add substantial value to the practice of laboratory medicine. The main purpose of an optimal EQA program must be to evaluate the analytical quality of laboratory measurements, including the

traceability of the calibration and of patient results and the equivalence among laboratories for the obtained results. EQA schemes are therefore in a unique position to add substantial value to the practice of Laboratory Medicine, by identifying analytes that need improved harmonization and by stimulating and sustaining standardization initiatives that are needed to support clinical practice guidelines. This will definitively help those manufacturers that produce superior products to demonstrate the superiority of those products and oblige users (and consequently industry) to abandon assays with demonstrated insufficient quality.

External Quality Assessment for developing countries: The role of WHO

Willy Urassa MD, MMED, PhD
Essential Medicine and Health Products; World Health Organization; Geneva, Switzerland

External Quality Assessment is one of the essential components in the implementation of Laboratory Quality Management System to ensure quality laboratory results. The World Health Organization Resolution 27.62, 1974 advocates strengthening of laboratory services using appropriate and cost-effective diagnostic and therapeutic procedures that are essential for the provision of quality health care. Working with partners WHO has developed several technical documents to guide establishment and running of national and regional EQA schemes for common analytes. Training at regional and national levels, provision of commercial and locally prepared Proficiency Panels in collaboration with UK NEQAS, NICD, AMREF, NRL have been implemented in the past. Recently WHO in collaboration with EQA experts published WHO manual for Organizing National External Quality Assessment Program for Health Laboratories and other testing sites. This comprehensive manual has been presented in several scientific forums, translated in Russian and there are efforts to translate into other WHO languages to ensure adequate coverage. There are very few national EQA programs. EQA services in developing countries are fragmented, uncoordinated, expensive and lack trained human resource. EQA data can play critical role in post market surveillance of IVD as countries strengthen regulatory capacities. WHO need to work with international, regional and country partners to address these challenges?

A critical view on ISO standard 13528

Wim Coucke

The ISO 13528:2015 intends to be broadly applicable, especially for new proficiency testing schemes and for both quantitative and qualitative schemes. This talk will assess to which extent these ambitions have been met for EQA schemes for clinical laboratories.

Special attention will be paid to the verification of EQA data before analysis. Although only briefly mentioned in the standard, it is important to know that statistical calculations should not be applied before the distribution of the data is verified. Some tests will be discussed that can be applied automatedly to confirm that the data are appropriate for further analysis.

A large part of the ISO standard is dedicated to the calculation of the assigned value and the standard deviation of quantitative data. The proposed algorithms will be evaluated for the purpose of calculating Z-scores and a brief overview of alternative algorithms will be given. A discussion about the minimal sample size will be given as well.

In contrast to the estimation of the assigned value and the standard deviation, the standard is very short in detailing methods to accomplish the requirement of monitoring the reasonableness of statistical procedures, the standard deviation and interlaboratory agreement over time. An example will be given to fulfill this requirement.

The section of evaluation for qualitative data is rather short and deals mainly with strategies to obtain the assigned value. Several options will be given to assist EQA organisers to derive more information from quantitative schemes.

Graphical display of data is necessary both for the EQA organiser and the participant. The proposed graphical displays will be discussed and some improvements will be proposed.

At last, homogeneity and stability testing should ensure a correct laboratory evaluation. A new light will be shed on the criteria for assessing homogeneity and stability and their assessment, both for qualitative and for quantitative data.

Statistical approach for optimization of external quality assurance (EQA) studies of molecular and serological viral diagnostics

Rumer L., C. Domingo, O. Donoso Mantke, Y. Dobrydneva, M. Greiner, M. Niedrig

Management of viral diagnostic quality is based on external quality assurance (EQA), where laboratories involved in diagnostics of a targeted virus are offered to analyze a panel of blinded samples. The utility of EQAs is compromised because of the absence of an approach to EQA design which upfront defines acceptance criteria and associated statistical analysis ensuring fair and consistent interpretation. The proficiency is determined by two factors. One is the ability to correctly test positive samples. A rigorous measure of this ability is sensitivity:
[Sensitivity = Probability of correct testing of positive sample of a particular concentration] Another is the ability to correctly test negative samples. A rigorous measure of this ability is specificity: [Specificity = Probability of correct testing of negative sample]

We offer a rigorous statistically based approach for EQA planning. Instead of a conventional performance characteristic (the score) which is calculated as the sum of the points for correctly identified samples in a blinded test panel, Youden index is used as the performance measure. Unlike the score, Youden index requires an estimate of sensitivity and specificity and incorporates the relationship of these performance parameters. Based on the assumption that the coordinator is a reputable expert of viral diagnostics, the performance of the coordinator's laboratory is defined as a proficiency standard for performance evaluation. The immediate goal of EQA is defined as to obtain a statistically reliable estimation for every laboratory whether its performance meets the proficiency standard, while the overall goal is to match every laboratory to its specific performance level. Dependence of informational capacities of test panel from the panel size and content is quantitatively analyzed and the optimal design and informational capacities of both idealized panels (whose size is not restricted by financial factors) and currently feasible panels are considered. Our approach provides the basis both for rational design of currently feasible EQA test panels and for an increased panel size.

In conclusion, our approach provides the basis for the upfront planning of EQAs ensuring that the data will allow objective statistical evaluation and comparison of participant performances. It enables both the rational design of currently feasible test panels and to provide reasons for rational panel size increase.

Definition of EQAS allowable limits for HbA1c: a candidate method

A. Vassault[1], S. Albarede[2], P. Joly[3], Jp Siest[4], M. Fonfrede[1], Jc Eynard[3], J. De Graeve[2], B. Poggi[3]

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2- CTCB, 33 route de Bayonne, 31300 TOULOUSE – http://www.ctcb.com,

3- PROBIOQUAL, 7 Rue Antoine Lumière, 69008 LYON – http://www.probioqual.com,

4- BIOLOGIE PROSPECTIVE, 3 Route de l'aviation, BP 60070, 54602 VILLERS LES NANCY – http://www.biologie-prospective.org; Members of FEDERATION of EQAS ORGANISERS (FAEEQ)

Introduction, scope and purpose

EQAS are implemented to evaluate the reliability of the results provided by medical laboratories and, if necessary, helping to improve the practices. Assessment of results provided by the participants' laboratories to EQAS programs, depends on the value defined to be allowable for their intended use. Criteria to evaluate the performances of HBA1c measurements are not harmonised in France, ranging from 6 to 8% according to the organiser. Total error based on biological variation is +/- 3%. The objective of this study is to evaluate the impact of the determination of allowable limits (AL) on the classification of the participants.

Materials and methods

Data from 4 FRENCH EQAS organisations including the results provided during 2015 by a thousand laboratories were collected and analysed according to the level of concentration, the nature of QC samples and the method used. The number of acceptable results was determined for different AL values ranging from 2 to 20%. Quality control (QC) samples were lyophilized haemolysed human blood from different commercial origin (AALTO, BIOLABO, EUROTROL, POLYMED, RANDOX). They have been assigned by reference method. A fresh human blood sample was also provided. Results are also evaluated according to the methods used (HPLC, immunological, enzymatic...).

Results and discussion

The number of acceptable results does not depend on the concentration level but greatly on the control materials used. For AL at 6%, results obtained with fresh human blood demonstrate higher performance: 97% of the results are acceptable instead of 92% when using lyophilised haemolysed blood.

HPLC methods demonstrate the lower acceptable limits: with AL +/-6%, acceptable results could be obtained by only 80% of the overall results and 95% for the HPLC methods.

Conclusion

The consequence of the definition of allowable limits was evaluated for different methods, different QC matrices and different concentration levels. No influence of the concentration level was observed.

The impact of QC materials behaviour used as compared to fresh human blood is shown to be one of the major factors of variation.

Furthermore, the quality of the results observed depends on the analytical method used by the participants.

The method used for this study could be used as a model for harmonization of the allowable limits taking into account the state of the art.

Quality Monitoring of pre-analytical sample labelling

Ann Leonard[1], Dympna Murphy[2], Heather Baker[2], Fionnuala O Dwyer[2], Sarah Hickey[2], Margaret Finnegan[2], Niamh Strahan[2], Tony Moulton[2], Ursula Fox[2] and Gerard Boran[1]

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Key words

PID, Specimen, Six Sigma

Background

There is substantial evidence to support the view that the pre-analytical phase although not under the direct control of laboratory maybe the most error prone of all the phases. The aim of this project, was to implement and monitor a six-sigma metric score to assess the quality of specimen and request-form labeling and ultimately patient identification.

Materials and Methods

A working group was established to develop a process which supported the documented identified sample labelling quality issues and develop/assign an appropriate coding structure. All patient samples in the study were registered on the Laboratory Information System (LIS Clinisys® Ver.5.32). Central to the process was the implementation of a barcode system to facilitate data code capture and QM codes being recorded against individual patient requests. Six sigma scores were calculated from total number of errors recorded versus the total number of requests. This was supported through data extraction linked to Microsoft Excel 2010®.

Results

A total of approximately 623,875 samples were received in the Laboratory Department between January and June 2017. Over 40,000 sample labelling issues were identified through the use of QM codes. The highest number of labelling errors identified were QM16 no location specified (24724) and QM15 no clinician specified (13395) followed by QM1 Unlabelled sample (305). This resulted in an overall sigma score for the quality of sample labelling on samples (including request form completion) received in the department as 3.02.

Conclusion

The unequivocal identification of the patient is a crucial step in delivery of timely and accurate laboratory results. The sigma score for sample labelling quality performs poorly compared to other industries i.e. Airline safety 6.0, Baggage handlers 4.0. The final clinical impact of sample labelling issues is difficult to determine as the laboratory detection and management of such issues may mitigate the impact.

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Biochemical assays of human seminal plasma: the experience of a French EQA program

S. Albarede, E. Sanchez, D. Garimbay, SM Hamdi

Male factor is involved in near half of infertile couples worldwide. Semen analysis, which assesses number, motility and morphology of spermatozoa, is the centre-piece of male infertility diagnosis. Poor-quality semen may result from an abnormal testicular production but also from a pathological genital tract (i.e with congenital abnormalities and/or acquired defects of accessory gland secretions). In the 2010 laboratory manual, WHO recommended several biochemistry assays to assess the main accessory glands: epididymis, seminal vesicles and prostate. According to international recommendations, medical laboratories are expected to participate to EQA schemes. However, there was neither scheme available for biochemical markers of seminal plasma nor desirable total error. Thus, CTCB coined in 2014 the first national EQA program for French laboratories and reports here the results of the three first years. For each survey, biological material was a pool of 100 individual seminal plasmas that were mixed, centrifuged and aliquoted in vials of 1 mL and then shipped to participants at -20°C. Only one level was tested (within the normal ranges). Results were analyzed according to the NF ISO 13528 guideline and algorithm. From 5 to 7 laboratories participated to the three surveys and performed an average panel of 4 biochemical assays: 2 for prostate (zinc and citric acid), 1 for seminal vesicles (fructose) and 1 for epididymis (alpha-1,4-glucosidase) which are those recommended by the WHO guideline. They used either in-house or commercial assays. For the last survey, inter-laboratory CV for zinc, citric acid, fructose and alpha-glucosidase were respectively: 5.9%, 2.4%, 5.1% and 12.5%. This first report about a national EQA for seminal biomarkers reveals a lock: few laboratories are involved in this this specialized exploration. To reach the goal of standardization and to fit to clinical purposes, more laboratories are expected to participate to such survey.

Assessment of Laboratory Performance in the Molecular Detection of Influenza A, Influenza B and RSV methods through International EQA Scheme for Multiplex Assays

Niina Kivi[(1)], Jaana Paakkanen[(1)], Matti Waris[(2)]
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(2) University of Turku, Turku, Finland

The use of multiplex nucleic acid assays in diagnostics has become more common and the number of multi-analyte detection methods has increased. Thus the need for external quality assessment (EQA) for this type of diagnostic assays has become relevant. Multiplex nucleic acid tests are useful in especially respiratory infections where several viruses or bacteria can cause similar symptoms and screening of these pathogens in one assay fasten the turnaround time significantly. Diagnostic tests detecting multiple analytes in one nucleic acid amplification reaction may have decreased sensitivity and/or challenges in specificity, and for this EQA is relevant to ensure proper performance of diagnostic methods.

EQA providers have offered antigen detection schemes suitable for many types of methods. In many occasions the pathogen levels in positive specimens are more suitable for traditional antigen detection methods, thus not ideal for very sensitive nucleic acid amplification methods. In these schemes nucleic acid methods get correct results quite easily, but it does not give a realistic view on assay performance - especially on critical sensitivity and specificity. To emphasize the importance of clinically relevant specimens, separate schemes designed for nucleic acid testing are necessary.

Several laboratories using nucleic acid testing methods have participated in the traditional antigen detection EQA schemes for influenza A+B and RS virus organized by Labquality. To serve customers using nucleic acid testing methods better, Labquality started in 2017 to offer multiplex EQA scheme Influenza A+B and RS virus NAT, where specimen levels have been designed specifically for molecular amplification methods. 53 participants from seven different countries participated in the first round. The round consisted of 5 artificial specimens (1 negative, 2 RSV positive and 2 influenza A virus positive specimens). Specimens were pre-screened using RT-qPCR methods. Results were surprising: one RSV positive specimen (Ct-value 29.2) was challenging, only 51.4% of the participants reported the specimen correctly as positive. Specimen contained an old group A type of strain (Randall). Success rate of the other RSV positive specimen (Ct-value 26.2) was also low, only 82.9%. Most of the false negative results of these specimens were obtained with the most commonly used method, having RSV detection rate of 57.5 % (23/40). Results for influenza A virus specimens and for the negative specimen were excellent with only few occasional errors. The results from this first round strengthen the importance of external quality assessment programs for influenza and RS virus multiplex nucleic acid methods to ensure the quality of testing and diagnostics.

IHC Breast Audit

Martyn Peck, Tony Badrick

Implemented in 2005, the RCPAQAP Immunohistochemistry (IHC) Breast Markers Audit survey was primarily established to assist participants in evaluating and improving the quality of their oestrogen, progesterone and HER2 receptor reporting within their laboratory. 100 cases/laboratory are required for assessment in the survey analysis.

The online survey is formatted so that laboratory participants may enter test receptor results (i.e. positive or negative) for a requested 100 cases of invasive breast carcinoma, irrespective of type or grade, however stage 4 disease is excluded. If pertinent, values for HER2 (IHC only) status are also requested of participants. HER2 positivity is defined as 3+ (strong) membrane staining, HER2 equivocal staining is defined as 2+ (moderate) membrane staining, and HER2 negativity is defined as 0 or 1+ (negative - weak) membrane staining.

If pertinent, values for HER2 single probe in-situ hybridization (e.g. CISH) are requested. These mean cell counts are defined as non-amplified diploid (1 to <2.5), non-amplified polysomy (2.5 to <4.0), equivocal (4.0 to <6.0), low amplification (6.0 to 10.0), and high amplification (>10). If pertinent, laboratories may submit mean cell count values for HER2 dual probe in-situ hybridization (SISH) are non-amplified (<2.0) and amplified (≥2.0).

RCPAQAP provides confidential feedback to participants from the statistical analysis of the cases for which their breast marker results were submitted. Each breast marker analyte has pre-determined parameters which specify whether a result is deemed within the relevant expected range or whether a review is recommended or definitively required.

RCPAQAP has reported a sustained overall improvement in laboratory performance in its IHC Breast Markers Audit survey in recent years, with % concordance increasing from 30% (2013) to 85% (2016).

ABSTRACTS

POSTERS

1. High rates of variation in HLA-DQ2/DQ8 diagnostic testing: Results from an RCPAQAP Pilot Program

T. Badrick, M. Horan, A. J. Daveson, J.A. Tye-Din, L. Wienholt

Coeliac disease (CD) is a highly prevalent, chronic, gluten-dependent, autoimmune enteropathy. While the diagnostic hallmark of the disease is positive serology followed by confirmatory small bowel biopsy, serotyping of the human leukocyte antigens (HLA) DQ2 and DQ8 genes has been shown have a high negative predictive value in patients who do not carry either allele, thus limiting the need for life long screening in some patient groups.

The characterisation of HLA-DQ2/DQ8 antigens has now become one of the most requested genetic tests in Australia. However, as more laboratories perform this test, issues with the accuracy of results across methods and variations in interpretation have risen. In response to clinician feedback whom identified major discrepancies in patient samples when they were analysed at multiple laboratories, the Royal College of Pathologists of Australasia Quality Assurance Programs (RCPAQAP) undertook a pilot module was to assess laboratory performance in the detection of HLA-DQ2/DQ8 antigens and associated HLA-DQA1 and HLA-DQB1 gene variants using routine methods. Ten laboratories participated with each receiving five patient-derived genomic DNA samples.

Results of this study showed poor concordance in reporting the detection of HLA-DQ2/DQ8 antigens. Reports from laboratories were difficult to interpret and showed varied clinical interpretation. These preliminary findings raise serious concerns about CD HLA testing errors and the potential adverse impact that this is likely to have on patient care.

2. Identifying the possible errors in medical laboratories using the outliers from the external quality control

Alexandra Cîrstea, Georgiana Pascale, Georgeta Sorescu, Constanța Popa, Tatiana Vassu-Dimov

The **purpose** of this paper is to present the possible errors occurred during external quality control (EQC) schemes in Biochemistry, Immunology and Haematology, by analyzing the results of the Romanian participating laboratories and by identifying the outliers.

The International Standard EN ISO 17043:2010 mentions that the proficiency testing provider (PT provider) should evaluate all the reported results, therefore CALILAB monitors the outliers in order to achieve an adequate performance assessment.

Materials and methods

We used the results of 200 participating laboratories to analyse the quantitative data obtained from EQC schemes in 2016 and the beginning of 2017 (March, April, May) then to centralise the outliers.

Results

From the total amount of 318 outliers identified in 2016, 138 outliers were found in Biochemistry, 132 in Immunology and 48 in Haematology.

During 2016 and the beginning of 2017, the number of outliers somehow remained constant for each domain; for Biochemistry the number of outliers was between 20 and 48 per proficiency testing round, for Immunology we established a range between 11 and 45 and for Haematology the number was between 5 and 19 outliers. We have also analysed the outliers per analytes and the ones with the most relevant number of outliers were: C4 Complement (29 cases), C-reactive Protein (26 cases), Ionic Calcium (18 cases) and Redcell Distribution Width (16 cases).

The study helped us identify the errors that usually lead to outliers: incorrect reconstitution of the material, innapropriate application of the IQC procedure, errors when introducing results in the online forms, reporting the EQA results in the online forms without verifying, incorrect use of calculation formulas for certain analytes, choosing the wrong group of comparison for their results. The most frequent error was the one when introducing the results in the online forms.

Conclusion

Our study showed that the main error causes in EQC are the lack of attention, communication and the need to improve professional education of participating laboratories. The reason why the standard requires the PT provider to support professional development of specialists is precisely to decrease the number of outliers.

3. Six Sigma methodology application in the evaluation of the glucose results (2014-2016) obtained by the participant laboratories of Programa Nacional de Avaliação Externa da Qualidade (PNAEQ)

João Reguengos[1,2], Ana Faria[1], Armandina Miranda[1], Helena Correia[1], Ana Cardoso[1], Susana Silva[1], José Requeijo[2]

(1) Instituto Nacional de Saúde Dr. Ricardo Jorge – Departamento de Epidemiologia – Unidade de Avaliação Externa da Qualidade

(2) Departamento de Engenharia Mecânica e Gestão Industrial. Faculdade de Ciências e Tecnologias, Universidade Nova de Lisboa, Lisboa, Portugal

Objective

Glucose quantification plays a key role in the Diabetes diagnosis and treatment monitoring. The main objective of this study was to evaluate the Sigma level of the participant laboratories of the Clinical Chemistry program of PNAEQ (2014-2016) regarding the Glucose quantification, through two different approaches: by applying a linear regression model which enables performance evaluation of each laboratory individually over time; and by evaluating the general performance of all laboratories on each sample.

Methods

In the evaluation by laboratory, a linear regression model was applied to the quantitative glucose results of 79 laboratories, which have presented at least 8 results over the considered period. The laboratories results were compared with the consensus value of the respective sample, calculated trough Algorithm A, and the Sigma level was obtained considering the desirable specification of the

total allowable error based on biological variation.

In the evaluation per sample, the mean bias of each of the 33 samples was determined and its Normal distribution accessed with the Kolmogorov-Smirnov test. The Box-Cox and Johnson transformations were applied when necessary. The Sigma level was determined considering the bias minimum quality specification based on biological variability.

Results and discussion

The mean Sigma level obtained in the approach per laboratory was 1.70 Sigma, ranging from 0.56 Sigma till 3.40 Sigma, with 34.2% of the laboratories presenting a Sigma level above 2 Sigma. The mean Sigma level obtained in the approach by sample was 1.63 Sigma, varying between 0.74 Sigma and 2.15 Sigma with 15.2% of the samples presenting a Sigma level greater than 2 Sigma.

Even though the two approaches are not comparable, the mean Sigma level was similar in both evaluations. The fact that the mean Sigma level is less than 2 Sigma and that only 34.2% of the laboratories presented a Sigma level above 2 Sigma, highlights the need to implement improvement actions. Therefore, it is necessary to identify the results variability causes in order to develop the right measures to eliminate or reduce the occurrence of errors and improve the harmonization of the laboratories results.

4. Sweat chloride measurement in Croatia: an improvement guided by EQA program

Jasna Lenicek Krleza, Merica Aralica

Sweat test is a gold standard in diagnosis of cystic fibrosis, the most frequent inherited disease in Caucasians. Although internationally proposed evidence based guidelines for the sweat test measurement exist, its everyday performance in medical laboratories is not harmonized. In 2015, the Croatian Centre for Quality Assurance in Laboratory Medicine (CROQALM) introduced a sweat test scheme as a pilot program for all registered medical laboratories (ML) which perform sweat chloride measurement by mercurimetric titration (N=8). The quality controls distributed in all external quality assessment (EQA) exercises were prepared according to 'in house' protocol for the internal quality controls. Reported results (mean ± SD, mmol/L) for chloride concentration in three exercises in 2015 were: 53.0±15.0; 25.5±7.4 and 45.4±16.1 with coefficients of variation (CV) 28.9%, 29% and 35%, respectively. In the first EQA exercise in 2016 uniform sweat chloride measurement protocol was introduced by CROQALM and adopted by all participating ML for all measurements in the future. Using proposed protocol, reported chloride concentrations in 2016 were 29.7±4.6; 21.5±3.2 and 65.2±4.8 with continuously decreasing CV from 15.5% to 14.7% and finally 7.4%.

Evident a progress in the analytical performance of sweat chloride measurement in Croatian ML came as a result of adoption of uniform protocol proposed by national EQA.

5. The first Malaria Molecular EQA scheme launched by UK NEQAS(P) [United Kingdom National External Quality Assessment Service Parasitology]

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Aim

To address the growing use of molecular assays in diagnosis and ensure data generated are reliable and comparable, UKNEQAS(P) developed a new EQA scheme, Malaria Molecular.

Methods

UKNEQAS (P) ran a pre-pilot followed by a pilot survey prior to the scheme going live.

For the pre-pilot, two distributions each containing eight lyophilised blood specimens were dispatched to 35 participants in 24 countries. Specimens contained parasite densities from 1 – 20 parasites/μL. The pilot also comprised two distributions of eight lyophilised blood specimens which were sent to 25 participants in 20 countries. Specimens contained parasite densities from 1 – 40 parasites/μL.

The full scheme went live in January 2016. Four distributions, each containing 4 samples, are sent annually. Parasite densities range from 0.018 - 10 parasites/μL.

Samples include single infections of *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium malariae* and *Plasmodium ovale* and negatives. Participants report on the presence or absence of malarial nucleic acid using qualitative or quantitative methods.

Outcomes / Results

The lower the parasite density, the more false negative results were reported. False negative results were reported by both real time and nested PCR.

Conclusion

UKNEQAS(P) has established a successful Malaria Molecular EQA scheme. Results were in agreement with intended results for most participants. Errors were detected which will enable laboratories to investigate and improve performance ultimately leading to improved patient outcomes.

6. Integrated external quality assessment schemes – right way to meet requirements of ISO 15189

Dalius Vitkus

Background

ISO 15189 Standard “Medical laboratories – Requirements for quality and competence” has been widely accepted throughout the world by medical laboratories for developing quality management systems and accreditation bodies assessing their competence. It states that “interlaboratory comparison programmes chosen by the laboratory shall, as far as possible, provide clinically relevant

challenges that mimic patient samples and have the effect of checking the entire examination process, including pre-examination and post-examination procedures". ISO 15189 also requires from laboratory to develop criteria for acceptance or rejection of samples and add necessary comments to the report if the sample quality might compromise test results.

Materials and methods

Labquality has developed integrated EQA service – completely new approach to external quality assessment with the target participants both laboratories and point-of-care sites. Traditional specimens are sent to participants with pre-analytical or post-analytical cases related to the scheme to be evaluated or specimens might include disturbing agents (haemolysis, lipemia, etc.)

Results

New programs have been launched in May 2017. First integrated EQA schemes included written pre-analytical cases related to the scope of scheme: basic analytes of hormone and immunochemistry, acid-base status and electrolytes, and general bacteriology. Number of respondents varied between 63% and 71% from those presenting traditional EQA results or findings. Expected actions in presented cases were given from slightly more than 50% to 66% of participating laboratories. Differences between participant's professions on actions to be taken have been identified in case of acid-base status and electrolytes scheme. 59% of laboratories confirmed they have dedicated procedures for interference testing and described the way they act if interference is expected in hormone and immunochemistry testing.

Conclusions

High number of respondents proved that laboratories are interested both in pre-analytical case analysis and integrated EQA in total. First results show that there is a room for improvement in almost half of laboratories in the different pre-examination processes as well as reporting of results according to ISO 15189 requirements.

7. How can the EQA provider encourage the participation in Pre-Analytical schemes

Ana Cardoso, Helena Correia, Ana Paula Faria

Introduction

Providing a quality sample and ensuring good laboratory practices should be the aim of pre-analytical phase.

It is important to have in place a proper system for error detection and to be able to detect errors that have a significant negative effect on sample quality and patient health. The participation rate on the national program on pre-analytical phase is very low, which means that EQA provider should have a more active intervention.

Aim and Objective

To contradict this weak participation, were launched two types of schemes in which laboratories participation depends mainly of the EQA provider. One is the “mystery client” which simulates a real scenario to verify if the information provided to the patient depends on the collaborator. The other is a presential audit, which identify some of the real errors occurred during blood drawing. The aim is to demonstrate that most of the pre-analytical errors are detectable and they can be corrected or eliminated when pre-analytical phase is controlled.

Methods

PNAEQ has 196 participants in clinical EQA’s in 2017. Only 10% are registered on pre-analytical program. Three of them are from developing Portuguese spelling countries.

In 2015 PNAEQ has created a national Working Group on Extra-Analytical Phases. Since then, all participants are invited to participate on this annual meeting.

Mystery client: two anonymous calls were made to laboratories on 2 different days, in the morning and in the afternoon period. Calls were based on an interview guide simulating a patient with questions. The required analyzes were for Haematology, Clinical Chemistry and Microbiology areas.

Presential audit: In the annual WG meeting was proposed that PNAEQ would perform an audit in two randomly selected laboratories (Lab A and Lab B). There were observed 5 blood drawings by 3 different technicians, in a total of 15 observations. Items observed focused on three main themes: sample identification, sample quality and safety practices, spread over 10 items. This audit form was previously provided to all participants as a tool to be used by laboratories and in order to compare and validate results obtained by laboratory auto evaluation.

A report was sent to each laboratory and it was asked what actions were implemented to improve good practices.

Results

Mystery client: In 2017 were received 19/20 results (95% participation rate). There was no coherence in the information provided by collaborators in 40% of the questions.

Presential audit: For laboratory A, PNAEQ audit evidenced non-compliance with good practices in 3 items (blood draw system used, order of draw and identification of samples in the presence of the patient), comparing with laboratory auto evaluation. For laboratory B, PNAEQ audit confirmed good practices comparing with laboratory auto evaluation.

Conclusion

These tools were created to facilitate detection, monitoring, evaluation and correction or elimination of pre-analytical errors when regularly used by laboratories. This is possible while participants can use these real situations to compare their practices with other laboratories and within the corporation comparing collaborators practices. The approach of these types of surveys is especially educational.

8. Approach to a patient with abnormal Activated Partial Thromboplastin Time (APTT) – results from survey of EQAS participants in India

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The discovery of an abnormal activated partial thromboplastin time, discovered incidentally in a hospital setting is a significant event that leads to many follow-up activities that may ultimately result in a transfusion of the patient, especially in a pre-procedure setting. There are many considerations in haemostasis testing and important pre-analytic variables including non-standard collection procedures or contamination of samples must be considered prior to arriving at a pathological diagnosis. The latter is especially true in the in-patient scenario where the possibility of heparin contamination is high. Further, the lack of clear information on the anticoagulation status of the patient and the mode of collection (direct venepuncture or collection from a pre-existing line) adds to the problem.

We have conducted a survey among the participants of the haemostasis module of the ISHBT-CMCEQAS where different scenarios linked to a patient and the investigations were presented to participants who responded according to their current practice protocols.

Results

Of the 701 participants surveyed, 116 (15%) responded and their results have been evaluated. The majority (40%) of the respondents were laboratory haematologists followed by specialist doctors (33%) located mostly in teaching hospitals. The most common indication for an APTT among samples received in the labs was for screening for a haemorrhagic disorder (42.4%), followed by monitoring of heparin therapy (33.7%). A majority of laboratories (85%) used only one APTT reagent in with 12% using a different one for screening for lupus anticoagulant. Almost two-thirds of the respondents used automated methods for performing APTT.

In the given clinical scenario, most of the laboratories (90%) considered a pre-analytic variable when a prolonged APTT was encountered. A significant proportion also suggested that they would interact with the concerned clinician or requested a fresh sample. A third of the respondents' labs do not perform APTT mixing studies. When it was performed, 17% of labs used single "normal patient" sample for this purpose. Only 21.7% of these labs perform an APTT based factor assay. The most common reason for this was the lack of test volume or clinical demand.

This information is useful for the PT program to plan future educational programs among the participants. The need for normal pooled plasma and standard testing protocols is highlighted. There is also scope for increasing awareness among clinicians about the use of haemostasis testing and pre-analytic variables.

9. External Quality Assessment for Bacterial Identification: A 4-Year Multicentre Implementation Study

G. Morabito, C. Di Rosa, C. Lacava

Aim of the Study

The accurate identification of bacterial species isolated from different biological sources (blood, urine, sputum, swab and wound) is of pivotal importance in the diagnosis and management of bacterial infections and, consequently, in preventing increased morbidity and healthcare costs. Regular participation to External Quality Assessment (EQA) schemes plays an essential role in ensuring accurate bacterial identification through monitoring aimed at improving labs' performance. The aim of this study was to analyze the results collected for Bacterial Identification EQA in a systematic manner and based on a yearly schedule (test events) and to identify potential benefits of participation to an EQA scheme as well as the common issues encountered by the participants.

Methods

The EQA scheme for Bacterial Identification was designed and implemented by Oneworld Accuracy, renowned EQA Provider, to test laboratories' proficiency. This study's focus was on 8 EQA test events that were conducted between 2014 – 2017 across Italian laboratories. In each EQA test event, five samples consisting of inoculated loops or KWIK-STIK™ Ampoule/Swab of various matrixes including blood, urine, sputum, swab, wound were provided to labs. Samples were challenged using both manual and automated methods from Becton Dickinson, Biomerieux, Liofilchem and Siemens. Data collected over the 4 years of EQA test events have been analyzed and segregated based on the evaluation's outcome (graded as Acceptable or Unacceptable). Samples have then been grouped according to source material and compared amongst each other. The established criterion was the identification of bacteria at the species' level. Labs that identified the bacterial species were thus employed to establish the overall performance.

Results

A total of 110 laboratories, with participation to all 8 EQA test events, were included in this study. Although participation rate varied based on sample matrixes, the average participation rate was 84% across the study arc. Overall, laboratories demonstrated good proficiency proving their ability to identify bacteria at the species' level in urine, sputum, swab and wound with high accuracy. Lower accuracy was shown when identifying bacteria from blood matrixes and in cases when anaerobic cultures were required.

Other issues encountered by laboratories, preventing them from meeting the study's criterion, included sample contamination, misidentification, wrong culture media employed, missed correlation between source material and clinical history.

Conclusions

Our data show that systematic participation to EQA schemes can be instrumental to improve labs' performance and detection of common issues so that corrective actions can be promptly identified and taken in a timely manner to restore high quality services.

CONTENT

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