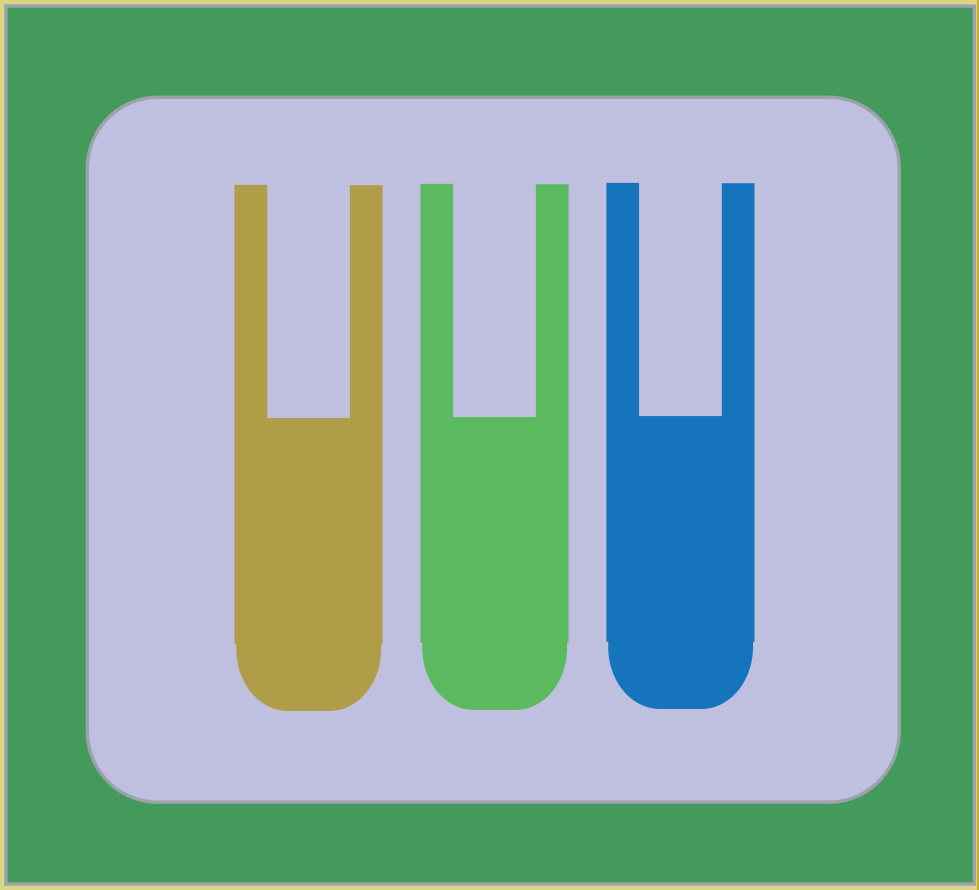
2008 • Vol. 19 no. 2 • September • Page 13 - 34 ISSN 0906-0588

EQA news

An International Journal of Quality Assurance

in CLINICAL BIOCHEMISTRY
CLINICAL IMMUNOLOGY
CLINICAL MICROBIOLOGY
CLINICAL PARASITOLOGY
CLINICAL VIROLOGY
HAEMATOLOGY, HAEMOSTASIS etc.



Issued by

EQALM

European Committee for External Quality Assurance Programmes in Laboratory Medicine

INFORMATION ABOUT EQAnews 2008

General

EQAnews provides information on quality assurance issues in Clinical Laboratory Medicine; such as Clinical Biochemistry, Clinical Immunology, Clinical Microbiology, Clinical Parasitology, Clinical Virology, Haematology, Coagulation and Haemostasis. EQA-news is issued twice a year; in May and September.

SCOPE OF EQAnews

EQAnews regards Quality Assurance (QA) as a professional activity with the aim of improving the quality of service provided by the clinical laboratory.

One important aspect of QA is External Quality Assessment (EQA, proficiency testing, inter-laboratory comparison). EQAnews sees External Quality Assessment as a rapidly developing scientific and practical area where world wide understanding and support for further development is essential.
EQAnews is established to facilitate world wide communication of scientific, organizational and practical aspects of EQA.

EQAnews is owned by the European Committee for External Quality Assurance Programs in Laboratory Medicine, EQALM.

EQALM will ensure contact with the various disciplines of Laboratory Medicine. EQAnews collaborates with the IFCC, ECLM and WASP and welcomes co-operation with other scientific organizations.

Subscription

The annual fee is 30 Euro excl. 25% VAT. Members of EQALM receive EQAnews as part of their membership fee. Readers from developing countries receive EQA-news free of charge.

Contacts regarding enrolment, invoices and payments should be made to Susanne Biron, DEKS, 54 M1, Herlev Hospital, DK-2730 Herlev, Denmark.

E-mail: susanne.biron@ deks.dk

Responsibility for issue:

EQALM board by:
Gunnar Nordin, Chair of EQALM,
Box 977, 751 09 Uppsala, Sweden.

E-mail: gunnar.nordin@equalis.se
Web-Site: www.eqalm.org

TOPICS IN THIS ISSUE

Minutes of the EQALM General Assembly 12th September 2008

1. Agenda

The meeting was opened by Gunnar Nordin, chair of the EQALM executive board. Gunnar Nordin was elected as chair and Annette Thomas as secretary for the General Assembly. Thirty eight members were present.
The Agenda was presented for discussion and accepted.

2. Working Groups Reports

The respective convenors for each Working Group gave a brief overview of activities and action points for the 7 Working Groups. It was decided that the Haematology Blood Smears and Haematology Cell counting groups would be merged and a new group established to look at the Frequency of Surveys. The chair requested that members wishing to join this group or wishing to volunteer as convenor should contact the board. A number of members indicated an interest at the meeting. It was decided that each Working group should produce a series of publications, to include aims, task plan and results.
Sverre Sandberg stated that the Board needs to define the expectation of the working group.

3. Activity Report from Executive Board for 2007

The chair reiterated the duty of the Executive Board and presented the minutes from the General Assembly meeting in 2007. The minutes were accepted.

During 2007, the Board had held 7 telephone meetings and 1 meeting in Amsterdam. Its activities included: updating the database, publishing two issues of EQA news, representing EQALM at two EEE-PT working group meetings and organising the symposium and General Assembly in Amsterdam in June 2007. Projects were being undertaken by seven Working Groups.

The total number of paid members was reported as 50. Two new members had joined during 2007 - RCPA, Australia and Eurotrol, Netherlands (Associated member). The chair welcomed the new members. A question was asked of the status of Non - European members - the chair stated that he would have to refer to the constitution. (This is available to view on the EQALM website).

4. EQALM account for 2007

The EQALM accounts for 2007 were presented. A surplus of €356 was noted. The accounts were reviewed by Xavier Albe and David Bullock. The reviewers had stated that the figure may be misleading as the DEKS statement related to the previous financial year (2006 to 2007). The accounts auditor, Xavier Albe was present at the meeting and agreed that the accounts were correct and had nothing further to add. A written statement from David Bullock stating that the accounts presented a fair financial position

of EQALM was also presented.

The chair requested that the accounts for 2007 be approved at the general assembly - this was accepted.

5. Election of EQALM Board 2008
The constitution of the existing board was discussed. The board members were identified as:
Gunnar Nordin: *Chairman.*
Gitte M. Henriksen: *Treasurer & Editor of EQA news.*
Piet Meijer: *Member.*
Minna Loikkanen: *Member.*
Annette Thomas: *Secretary.*

A notification of election of 2 Board members had been posted to all members 3 months prior to the General Assembly. Two board members, Piet Meijer and Minna Loikkanen would be completing their first term of office in 2008. No further nominations had been received during the 3 month period of notification. Piet Meijer and Minna Loikkanen were unanimously re-elected for a further term.

6. Auditors for 2008
The chair reiterated that members were welcomed to contact the Board at any time with further comments and suggestions.

7. Activity plan for 2008-2009
The chair listed the proposed plan for the forthcoming year. This included:

- Organization of the EQALM symposium in 2009 in Berlin.

The EuroMedlab meeting in Innsbruck in July was proposed as an alternative venue. The chair stated that the EQALM board had considered this option, however, previous meetings held in collaboration with large conferences had not proven to be financially viable. However, it was agreed that EQALM should have a presence at the meeting in some form.

- EQAnews - a co-ordinator was required.
- EQALM collaboration with EEE PT Working Group would continue.
- Implementation of ISO 17043 among members.
- EQALM website - it was anticipated that the website would be improved to facilitate interaction between the members and include a members area, and updates of Working group activities.
- EQALM Working groups - the board planned to revitalise the Working Group activities for 2008 - 2009.

The chair reiterated that members were welcomed to contact the Board at any time with further comments and suggestions.

8. Membership fee for 2009
The board proposed that the fee was not increased for 2009. This was unanimously accepted.

9. Budget proposal for 2009
The expenditure for web redevelopment was noted. The proposed budget was accepted.

10. AOB
No further business - the General Assembly was closed.

Silke Heller extended a warm thank you to Jonathan Middle for organising the meeting. This was echoed by all the members.

EQALM Working Group - Nomenclature

Activity during WG session 11th September, Austin Court, Birmingham
Convenor - Gunnar Norden (GN)

Aim
To produce a common description for measurement procedure, instrument, reagent and calibrator that can be utilised by all European EQA organisers.

Discussion
Unfortunately, little progress had been made by the group over the last year due in part to the ambitious aim of the project. A discussion followed on the IVD Notification numbers as possible unique codes. The European authorities have made little progress in developing the Global Medical Device Nomenclature (GMDN) database to be used for the unique identification of IVD products. It was decided that as the European Committee for Standardization (CEN) was responsible for the development of standards, the group would attempt to lobby and influence the European Commission to get CEN to undertake the task to develop a classification of measurement procedures and to development a database which could be used by both EQA organizers and authorities.

The definition of measurement procedure and measurement principle was discussed - VIM, IRMM and JCTLM definitions would be looked at.

Action Points
1. The group to draw up a position statement as to why it felt this work was necessary and the risks associated if this was not fulfilled.
2. To recruit a prominent influential scientist (possibly with IFCC links) to champion this cause. Professor Christopher Price was suggested.
3. The group to use the champion, media, publication to lobby Members of Parliament of the European Union, with the aim to influence members of the European Commission.

Goal
CEN to develop a common European Database of measurement procedures, instruments, reagents and calibrators.

EQALM Working Group - Mirror Group ISO 17043
Activity during WG session 11th September, Austin Court, Birmingham, UK

Convenor - in the absence of *Jean-Claude Libeer* the meeting was led by *Jane Gunn Munro (JGM) and Gunnar Norden (GN)*

Aim
To inform and consult members on the development and progress of ISO 17043.

Discussion
GN asked the question - Is it possible to share standards with PT in other fields?

After some discussion, it was agreed that it was possible to produce a generic standard, although a number of members felt that sector specific standards should also be established.

Areas of concern included:
1. Stability and homogenisation
- it was recognised that this was an important issue in other sectors, however concerns were expressed that it may not be easily achievable within Medical EQA. JGM stated that a number of clauses had been added to overcome difficulties within the Medical EQA sector.

2. Sub contractors and compliance to standard
- JGM emphasised that subcontractors would have to comply with ISO 17025 or 15189. It was felt that few contractors if any currently complied with these standards.

3. EN 14136
The discrepancy between the terminology and language used in 14136 and 17043 and the lack of reference to 14136 within the document was highlighted.

4. Assessors with inadequate EQA experience
Concerns were expressed over interpretation of the standard due to differences in assessors experiences. EQALM currently holds a list of members wishing to be included as assessors. The application is available on the website.

5. Qualitative investigation
It was felt that there was a lack of guidance on qualitative and interpretative investigation.

6. Regional collaboration
- JGM stated that this was covered under subcontractor.

7. Reference target values.
- JGM stated that this now only applies if the scope of the EQA organisation includes calibration laboratories.

JGM briefed the group on the official status of the document. It was now considered a draft international standard awaiting approval from members of ISO CASCO. The document was now less flexible for further changes.

Action Points

1. To undertake a survey of the accreditation status of member organisations in 1 year time. It was suggested that this be undertaken in collaboration with Eurachem and Eurolab as a sector crossing survey.
2. To consult member bodies on the language discrepancy between EN14136 and ISO17043 and the lack of reference to EN14136.

Abstracts Presentations, EQALM Symposium 2008 11th-12th September, Austin Court, Birmingham, UK:

Point-of-Care Testing: Overview and Key Challenges

Christopher P Price, Department of Clinical Biochemistry, University of Oxford, UK

The delivery of laboratory medicine has evolved, perhaps not unsurprisingly, in a similar fashion to the way in which clinical care has evolved. Thus the first testing was at the point at which the patient was seen - in early times at a meeting place, or at the bedside. S testing became more sophisticated the testing moved to the ward side room, and then to a laboratory. Now, in some parts of the world laboratories are situated many miles away from the patients and clinicians that they serve. The practice of clinical medicine has evolved in a similar way with increasing specialisation of care and an emphasis on technologically sophisticated institutions. However that approach is changing as it is recognised that this style of care does not meet patient's needs, and is unnecessarily costly. The emphasis is now on better access for patients and more care closer to home, with increasing specialisation when it is needed. How will laboratory medicine respond to this? It already recognised that centralised laboratory services do not always meet the needs of patient and carers and that the current model of delivery can lead to unnecessary errors. Perhaps point-of-care testing is the solution to this problem, improving access to patients, reducing errors reducing errors and improving health outcomes.

The goal of point-of-care testing (POCT) is to meet a clinical need. The provision of a result at the point of care enables a clinical decision to be made and action taken at the time when the clinical need first arises. There may be several points in the patient journey when POCT may be the appropriate modality of testing, with the goal being to improve health outcomes through the maximisation of benefit and minimisation of risk, at reasonable cost in the care of individual patients.

Errors can be due to a failure in a part of the process including (i) a failure to employ the right test in making the diagnosis, (ii) a failure to perform the test correctly, (iii) a failure to act on results, (iv) an error or delay in diagnosis, (v) an error in performance of procedure or test related to treatment, (vi) a delay in treatment or response to test, (vii) an error in administering treatment, (viii) inadequate monitoring or follow-up, and (ix) failure of communication at any point in the process. Quality is therefore about efficiency and effectiveness; efficiency is relation to the process from requesting, through testing to action and effectiveness ensuring that the right result is produced - and the right action taken. The Institute of Medicine in looking at the incidence of medical errors in the US health care system concluded that one of the main causes of these errors was the fragmentation of services and the poor connectivity, or disconnected nature, of the patient journey. The use of POCT can therefore help to integrate the testing element of the care plan into the process of care.

POCT may be undertaken by the patient or his/her carer. The required quality of POCT is not just a case of ensuring that the right result is produced but rather that the right patient, gets the right test, on the right sample, at the right time, producing the right result, followed by the right decision being made and the right action being taken. This fits with a classical approach to pre-analytical, analytical and post-analytical considerations with an emphasis on ensuring that the guidance is fully integrated into the care pathway.

Quality is therefore about patient, clinician and laboratory professional working together, using technology appropriately to ensure that the team works efficiently and effectively.

POCT in Haemostasis

Piet Meijer, ECAT Foundation, Leiden, The Netherlands

For coagulation testing several point-of-care test equipments are available nowadays, including e.g. the measurement of APTT, PT, INR, ACT, Fibrinogen. Also thromboelastography is frequently used in emergency and operations rooms for the monitoring of abnormalities in the coagulation and or fibrinolysis process as well as the effect of treatment.

The most frequently used POC test in haemostasis is the measurement of the INR for warfarin anti-coagulation monitoring. These POCT equipments are used both by patients for home-testing and by professionals in hospital settings.

Two approaches for external quality assessment for POCT-INR will be discussed. The first approach focus only on the between-monitor variation (imprecision) and the deviation from the consensus value. The second approach includes also accuracy.

It will be demonstrated that patients are able to perform EQA on a reliable manner.

The Dutch approach for EQA of the CoaguChek INR monitor will be discussed.

EQA of POCT within Primary Care and the High Street Pharmacist

Annette Thomas, WEQAS, Cardiff and Vale NHS Trust, UK

WEQAS is the largest provider of EQA services for the Point of Care Testing (POCT) market within the UK and provide services to Secondary Care, Primary Care, Company Occupational Health providers and pharmacies.

In the UK, we have seen a steady increase over the last year in the number of diagnostic services provided within primary care and the high street pharmacist. Our EQA programmes have been customised to meet the demands of this growing market. Over 500 packages are sent weekly to our participants, with variable and multiple sample requirements. They are customised to meet the requirement of each client, i.e. sample provided per meter/per POCT site or per operator. The EQA programmes are designed for ward staff, primary care nurses, occupational health staff and pharmacists and covers: Training, external quality assessment and problem solving.

The aim of our programme is to provide support to POCT co-ordinators, to identify non compliant sites and improve the analytical performance of users. A co-ordinator in each organisation is given a Group Administrator function and maintains the database for its own organisation. In the case of a high street pharmacy chain this would be the regional pharmacist, and within the community this role is often retained by the local laboratory. The role of performance surveillance is therefore devolved to each individual Co-ordinator at a local level and monitored nationally by the EQA organiser. The powerful database gives POCT Co-ordinators a wealth of information on method and analyser performance both within their own organisation and between organisations. The system can readily accommodate remote sites. The users can directly upload their results and access reports saving unnecessary data-entry time for the POCT Co-ordinator or EQA organiser. Distribution letters, non-compliance reports, poor performance reports and cumulative reports are generated from one system. The POCT Users Standard Report uses a simple traffic light system with clear action limits.

POCT in Microbiology

Pierre-Alain Morandi, CSCQ, Geneva, Switzerland

There are many different types of POCT devices on the market to screen for a wide panel of organisms, from viruses to bacteria or parasites. ISO requirements describe how to set up a management system for POCT, but not all national regulations have POCT specific directives. The Swiss Centre for Quality Control (CSCQ) organises EQA surveys for two point-of-care tests (Group A Streptococcus antigen and HIV1/2 antibodies detection), and for Urine Slide Devices, the three of them being mandatory according to the Swiss law. A summary of the CSCQ results collected over the last few years is presented and shows that Strep A and HIV1/2 test kits perform well, which is not always the case for the Urine Slide. This points to the need of more microbiological EQA schemes, staff training, and studies for overall improvement of POCT assessment.

The New ISO 17043 Standard - preferred Standard for EQA Providers of Medical Laboratories?

Jane Gun-Munro, QMP-LS, Toronto, Ontario, Canada

Two guidance documents, ISO/IEC Guide 43:1997: *Proficiency testing by interlaboratory comparisons* and ILAC Guide 13:2000 - *Guideline for requirements for operation of proficiency testing schemes* are available to assess competence of PT providers. In 2006, the Inter Laboratory Accreditation Cooperation (ILAC) recommended the revision of ISO/IEC Guide 43 to accommodate progress in the field of proficiency testing that had occurred since 1997 and to produce the new document as an ISO/IEC 17000 series standard. It also authorized an update to ILAC G13:2000 to meet the immediate needs of ILAC members and also provide valuable input into the new ISO standard. The overall objective was to update the management system requirements to be consistent with ISO/IEC 17025:2005, *General requirements for the competence of testing and calibration laboratories*, to review the scope of PT to explicitly include non-traditional sectors, to revise technical requirements that were ambiguous or redundant and to add new requirements where necessary.

The ISO Conformity ASsessment COmmittee (CASCO) Working Group 28 (WG28) was formed to produce ISO/IEC 17043: *Conformity Assessment - General requirements for proficiency testing*. The first meeting was in December 2006 and there have been four meetings to date. The last meeting was on September 3-5, 2008 to address reviewer's comments on the Committee Draft version of ISO/IEC: 17043. Members of this working group include representatives who provide external quality assessment (EQA) to medical laboratories. Their participation on the working group has provided the opportunity to address the fundamental differences between medical laboratories and traditional testing and calibration laboratories in the development of this new standard. This includes consideration of the following issues:

- Expanded scope of inter-laboratory comparisons beyond the examination phase of testing.
- Variable nature of medical test results which include categorical as well as numeric results.
- Homogeneity, stability and viability issues associated with biological material.
- Difficulties in determination of traceability and measurement uncertainty of assigned values in biological material.
- Method comparison.
- Educational activities.

The ISO/IEC CD 17043 document contains an Appendix A that de-

scribes traditional and non-traditional PT schemes, including those associated with EQA. The majority of the above issues have been taken into consideration in the development of the standard through broadening the definition of PT. The draft standard now describes qualitative, interpretive and reverse transmission schemes. It also accommodates activities such as circulation of case studies, questionnaires, data sets, images etc.

The draft standard also contains clauses that emphasize the following:

- Definition of PT provider responsibilities and competence.
- Responsibility of the PT provider to assure competence of subcontractors.
- Alignment of laboratories performing testing for assigned values, homogeneity and stability with ISO/IEC 17025 or ISO/IEC.
- 15189, *Medical Laboratories - Particular requirements for quality and competence.*
- Documentation, monitoring and control of appropriate accommodation and environmental conditions for operation of PT scheme.

Is ISO/IEC 17043 the preferred standard for EQA providers of medical laboratories? The answer is "Yes, absolutely!" It has been designed to provide sufficient flexibility to address the dynamic scope required for EQA of medical laboratories while at the same time providing a comprehensive assessment of competency. Of course, the success on the use and application of the standard will continue to depend on the creativity of the EQA provider to meet requirements and training of the assessor to understand and accept the evidence.

Is Accreditation of the Survey Provider Beneficial for Participants?

André Deom, CSCQ, Geneva - Switzerland

Yes or no could be the simplest answer.

But what is accreditation ? In summary it may be considered as the guarantee that the report of the survey and the certificate issued by the organiser represents the results of the laboratory and fits with the corresponding evaluation.

Accreditation of the EQA provider may be a request from a manufacturer e.g. to conduct a study. In this case there is no other option than getting the EQA samples and

services from an accredited provider.

For the laboratory using the services of an accredited organiser, it certainly offers additional value.

But accreditation may also be an additional cost to the end user. Accreditation is not the complete process in itself. It is not the end of an activity. Accreditation is an on going process. If this is not undertaken, accreditation offers little benefit to either participating laboratory, or EQA organiser as it is too expensive.

In the absence of accreditation, there may be individual areas where the organisation provides a quality service such as excellent software for the presentation of data, a well managed organisation, with pleasant, competent, staff that respond quickly to customer needs certainly, these are directly beneficial to the participants.

But isn't accreditation a means of ensuring a quality service is concentrated in all of these areas.

In conclusion, yes accreditation is certainly beneficial for participants if well understood by the survey provider.

More specific cases and recommendations will be presented.

Frequency of EQA - Results of a Questionnaire

Annette Thomas, WEQAS, Cardiff and Vale NHS Trust, UK

The EEE - PT working group, a joint activity by EA, Eurolab and Eurachem (EEE) was established to provide support on the use of proficiency testing to laboratory personnel and accreditation assessors. The group have recently drafted two position papers: "Accreditation bodies' policies on the frequency of PT participation" and the "Selection, use and interpretation of proficiency testing (PT) schemes by laboratories - 2008". In an attempt to Identify the extent to which the EEE papers reflect the requirements of EQA in Laboratory Medicine across Europe a survey was undertaken in September 2008.

Members of EQALM were asked to provide information on the frequency of EQA participation including number of samples per round, the assignment of target values and the performance criteria used for each Scheme.

Traditionally within Laboratory Medicine, each laboratory has participated in a specific EQA Scheme for every measurement technique it

uses and for every analyte for each matrix (e.g. blood, urine or serum). EA and ILAC have recently recommended that participation in an EQA Scheme should be at a minimum frequency for each subdiscipline. A subdiscipline can include more than one measurement technique, property or product as long as equivalence and comparability can be demonstrated. To ascertain the views of EQA organisers on the concept of subdisciplines, EQALM members were asked to provide their views on a series of hypothetical scenarios.

The Role of EQA in Quality Improvement of Medical Laboratories

Jonathan G Middle, UK NEQAS, Birmingham, UK

Quality improvement involves a systematic approach to continuous audit of process and outcome, with appropriate and properly recorded corrective and preventative action. It must be purposeful, i.e. not undertaken for its own sake, but focussed on the primary objective of improving patient care.

Medical Laboratories are required to undertake audit as part of their Quality System and formal accreditation standards. This may involve vertical audit, e.g. all the processes involved in handling a specimen, horizontal audit, e.g. a process for entering samples into a LIMS, or witness audit, e.g. a member of staff telephoning a result to a ward.

EQA may be regarded as a form of external vertical audit, in that it assesses the whole process of sample accession, pre-analytics, analysis, post-analytics and interpretation. An error in any part of the sequence of events can lead to poor performance. Where EQA has a continuous assessment design with relatively high frequency, pre- and post-analytical non-conformities may be readily identified and preventative and corrective action taken. Less intensive or periodic designs may not be as effective. This, of course, requires the participant to treat the EQA sample exactly as if it were a patient's sample.

With regard to the analytical process, EQA examines both comparability and accuracy (trueness). Information unobtainable by any other means may be gained about the performance of instruments and reagents. Information on recovery of pure analyte, linearity of dilution, interference and cross-reactivity, is of enormous value to laboratories and can challenge the diagnostic industry to improve the sensitivity, specificity and traceability of their assays. EQA has a major role in

the post market surveillance of instruments and reagents and is perfectly placed to monitor changes in method characteristics when raw materials or calibration algorithms are changed.

EQA can have important input into the development of diagnostic and treatment clinical guidelines, where the results of laboratory tests are used to stratify patients or direct them along different clinical pathways. Knowledge of the state-of-the-art improves understanding by health policy makers of the uncertainty in measurement that must be taken into account when deriving cut-off values.

Target Values and acceptability Criteria in EQAS

Prof. dr. med. H. Reinauer, INSTAND e.V., Düsseldorf, Germany

The EQAS shall improve the analytical performance of the laboratories, promote comparability of analytical results and, according to IVDMD, monitor the market.

The main strategy to realize these goals are the follow the traceability of all analytical methods, to define accuracy and acceptability ranges for routine analyses.

ISO standards 15193, 15194 and 15195 are helpful to attend the targets, set by the scientific-medical societies or by health authorities. Self organisations of specialists (JCTLM, IFCC Working Groups) had great influence on the quality of analytical work.

The acceptability criteria in EQAS are rather comparable in the different countries.

Nevertheless the main international discussion in this field is how to set target values and acceptability criteria enclosing the “uncertainty of measurement in routine laboratories”. Examples of medical requirements for accuracy and precision of analytes are presented, derived from the Guideline for Quality Assurance in Medical Laboratories.

Use of Reference Procedure Target Values in External Quality Assessment

Anja Kessler, Reference Institute for Bioanalytics, DGKL e.V., Bonn, Germany

The determination of reference procedure target values requires the establishment of a reference measurement system consisting of reference materials, reference measurement procedures and reference laboratories. This system provides metrological traceability to routine clinical analysis, linking the patient's laboratory measurement results to an established higher-order standard (ideally, an SI-unit such as mole or katal) through an unbroken chain of comparisons.

The implementation of the concept of traceability probably provides one of the most important strategies to achieve standardization in laboratory medicine aiming at reliable and comparable test results independent of the analytical principle of measurement, test procedure or commercial test kit and the laboratory where such clinical chemical testing is performed.

Consequently, the In-vitro Diagnostica Directive of the European Union requires that *".. the traceability of values assigned to calibrators and control materials must be assured through available reference measurement procedures and/or reference materials of higher order ..".* This is a challenge not only to the manufacturers of diagnostic test kits but also to organizers of external quality assessment schemes. The two ring trial organizations in Germany have established laboratories which provide reference measurement services for setting EQAS target values and for diagnostic kit manufacturers. These reference laboratories must demonstrate their competence by accreditation as calibration laboratories according to ISO 17025 and 15195.

Several examples form the field of metabolites and substrates (cholesterol, uric acid, creatinine) as well for low-molecular hormones (steroid and thyroid hormones) have shown that use of reference method target values is a powerful tool to demonstrate traceability of test results or occasional deficiencies of individual laboratories or test procedures offered by the manufacturers.

For many groups of substances in laboratory medicine, the measurands are not exactly known regarding their chemical or conformational structure. Before the concept of traceability to SI units can be established for these measurands, scientific work is necessary to define the measurands regarding their molecular structure and to develop reference measurement procedures

For well characterized measurands, the global agreement on the reference measurement system will improve accuracy in laboratory medicine by providing a rational basis for standardization - which will ultimately be of benefit to patient care.

Use of Peer Group Consensus Values for Performance Analysis in EQA Programmes

Steve Kitchen, UK National External Quality Assessment Scheme (NEQAS) for Blood Coagulation, Sheffield, UK

Assessment of individual results in EQA exercises is normally done by comparison against a target value or range. Currently there are no agreed reference methods for tests of haemostasis, and there is low level of standardisation and harmonisation of results obtained by different methods. Truth is frequently a matter of opinion. For this reason most EQA programmes in haemostasis use the consensus of results obtained in a series of centres and this is the case for the UK NEQAS, and WHO and World Federation of Haemophilia EQA programmes.

For screening tests there is the additional problem that results often depend on the method used, and in particular the reagent. Sometimes there is no scientific reason to anticipate agreement between different methods and a number of reasons why differences in results would be expected. For these reasons results of screening tests are grouped according to the reagent used. The result obtained in an individual centre is compared to the reagent median provide there are at least 10 users of the reagent. The overall median of all results (irrespective of reagent) is only used for performance assessment if there are less than 10 users.

The percentage deviation from the appropriate median is calculated and for most screening tests a deviation of <15% above or below is considered within the consensus, If on the other hand the deviation exceeds 15% in either direction the result is considered to be outwith consensus. The only screening test where 15% limits are not used is the APTT when performed for the purposes of heparin dosage assessment where 20% deviation limits are used. This reflects the greater imprecision and wider clinical tolerance limits in this particular setting. If a centre obtains such outwith consensus results in 3 consecutive surveys performance is reported as persistently outwith consensus. This triggers additional contact from the programme director with an offer of assistance.

The use of a percentage deviation system such as the one described above is unsuitable for a number of settings in haemostasis testing. Indeed the imprecision of assays systems varies very widely depending on the level of analyte. For example factor VIII assays in moderate haemophilia patients where the median result may be 4 IU/dl would have an inter laboratory CV of 60% whereas the same labs would have a CV of 15-20% if assaying a sample from a normal subject. For this reason a different system is employed.

Results are ranked and the median value is taken as the overall consensus median. Individual results are ranked into 5 unequal groups above and below the median, each group being designated by a letter depending on ranked distance from the median, with lower case letters (e.g. 'b') denoting a result that is below the median, and an upper case letter (e.g. 'B') denoting a result that is higher than the median:
Group A: The nearest 25% of results above and below the median (ie. 50% of results);
Group B/b: The next 10% of results above and below the median (ie. 20% of results);
Group C/c: The next 5% of results above and below the median (ie. 10% of results);
Group D/d: The next 5% of results above and below the median (ie. 10% of results);
Group E/e: The 5% of results furthest from the median, above and below it (ie. 10% of results).

In this system outwith consensus performance designation is based on grades obtained in two consecutive exercises for any particular test. Probabilities of receiving a pair of grades or worse by chance alone are:
Performance outwith consensus is defined as those pairs of grades where the probability of obtaining such a combination or worse by chance alone is less than 0.05 (i.e. 5%). Such combinations of grades are: DD, CE, EC, DE, ED, and EE. Persistent outwith consensus" performance is defined as two consecutive outwith consensus performances.

There are a number of abnormalities in haemostasis where the results of a test are highly dependent on the method selected for analysis. These include certain types of haemophilia A, Antithrombin defects, deficiencies of protein C and protein S, and Von Willebrands disease. In all these cases it is scientifically invalid to form a single group for performance analysis. In these cases method specific consensus groups are needed.

The Role of EQA in the Standardization of CDT

Anders Helander, Karolinska Institute, Stockholm, Sweden

Carbohydrate-deficient transferrin (CDT) refers to alcohol-induced changes in the glycoform pattern (i.e., carbohydrate composition) of the iron-transport glycoprotein transferrin. CDT was originally defined as the sum of the asialo-, monosialo- and disialotransferrin glycoforms but later studies revealed that disialo- and asialotransferrin, missing one complete *N*-glycan (disialotransferrin) or both *N*-glycans (asialotransferrin), are the main alcohol-related glycoforms. Compared with liver function tests (e.g., GGT), CDT is a much more alcohol-specific indicator and used as a biomarker for identification and follow-up of chronic high alcohol consumption.

Over the years, several bioanalytical methods (e.g., immunoassays, HPLC and CE) have been employed for CDT measurement. However, these "CDT" methods have sometimes covered different glycoforms and given the values in various absolute or relative amounts, which has complicated comparability of results. With some methods, there has even been an increased risk for false-positive and false-negative results. Normalisation of CDT values to the total transferrin concentration (%CDT) contributed to a significant improvement in test specificity. Another important step is the ongoing standardisation process by the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC). The standardization work aims to define the analyte, select and validate a reference method and reference materials, and make suggestions for the clinical usage of CDT.

The performance of individual laboratories and agreement of methods can be demonstrated in external quality assessment (EQA). EQA programs for CDT are available in, for example, the Netherlands, Germany and Sweden. The Swedish EQUALIS EQA scheme for CDT has been running since 1996. Every year, 10 blind samples, for which target %disialotransferrin values are set by an HPLC candidate reference method, are distributed.

Starting in 2006, the relation between the CDT values obtained by HPLC and N Latex CDT (immunoassay from Dade Behring/Siemens) gradually changed. At %disialo transferrin levels around 2% by HPLC, the corresponding N Latex CDT results were ~0.4% higher in April 2006 but roughly identical in September 2007. This change was seen over the entire measuring range. Because the HPLC method was confirmed to be stable, the observed change was due to a changed calibration of the immunoassay. In the end, the N Latex CDT method

produced ~25% lower values than the original with higher risk for false-negative results. This has finally been corrected by the manufacturer and the %CDT values obtained with the latest lot of the N Latex CDT kit are indeed ~30% higher than with the previous one.

This observation highlights the value of EQA schemes for comparison and evaluation of CDT methods. For an improved standardization of CDT measurement, a reference method and reference materials are also highly warranted.

New Areas within EQALM – Molecular Biology - the European Molecular Genetics Quality Network

Rob Elles, European Molecular Genetics Quality Network, National Genetics Reference Laboratory and Regional Molecular Genetics Service, St Mary's Hospital, Manchester, UK

The progress and completion of the human genome project has led to the recognition of more than 1000 gene targets relevant to single gene disorders. The first application of this new knowledge is usually a genetic test and the generic technologies available that use DNA as the analyte mean that progress from the research phase to clinical application is rapid.

Many genetic tests are highly predictive; the genotype is usually only established once through a single testing procedure and the results may have implications for an extended family. These features of genetic testing place a special onus on the clinical molecular genetics laboratory to establish quality assurance to help retain public confidence in this powerful technology. Furthermore an international approach is essential as most clinical molecular genetic laboratories receive and/or refer cases across national boundaries.

The approach to External Quality Assessment as an essential component of quality assurance has been developed by the EMQN and other professional networks in Europe to take account of the patient experience of genetic testing; emphasising the role of the laboratory in providing an accurate test result, interpreting the genotype, modifying genetic risks and providing appropriate information to transmit the genetic test result through counselling.

In addition to disease service specific EQA EMQN has developed a technical EQA for DNA sequencing which is applicable to most molecular genetic laboratories.

EMQN is co-ordinating its EQA scheme development with other ge-

netic disciplines (biochemical genetics and cytogenetics) through the European Commission funded platform EuroGentest which operates under the key words; genetic testing, quality assurance and harmonisation.

www.emqn.org
www.eurogentest.com

Virtual Microscopy

Barbara de la Salle[+], M. L. Brereton, J. Burthem*, L. Seal[$], P. McTaggart[+], M. West[+], K. Hyde*[+]. *Department of Haematology, Manchester Royal infirmary, Manchester, UK [+]United Kingdom National External Quality Assessment Scheme for General Haematology (UK NEQAS (H)), Watford, UK, [$]Manchester Metropolitan University, UK*

The UK National External Assessment Scheme for General Haematology (UK NEQAS (H)), in collaboration with academic, medical and scientific staff from Manchester Royal Infirmary and Manchester Metropolitan University, has developed an internet based Digital Morphology scheme for Continuing Professional Development (CPD) using large scale, high resolution, stitched virtual microscope slides. Designed as an educational tool for individuals rather than organisations, the scheme was launched in April 2008. More than 1000 individual participants in 100 UK laboratories have enrolled during the first four months of operation.

UK NEQAS (H) has operated a glass slide based scheme for Blood Films for Morphology for nearly 40 years. The glass slide based scheme assesses performance of laboratories, not individuals, and is highly valued for the range of cases and educational detail provided. In 2002, UK NEQAS (H) started to explore the use of digital technology with a series of annual exercises in which digitised images were made available to participants via the internet. The cases were mainly presented as an array single fixed images, although some stitched virtual slides were used. Participant feedback indicated a preference for the stitched slides, which could be used to navigate and zoom similar to a glass slide, although many participants reported problems in downloading and accessing these large files. However, in 2004, a total of 161 laboratories successfully took part in an exercise that required the review of 4 virtual slides prepared by stitching 40 single field images.

Those that took part in the 2004 study indicated that the most favoured uses of digital morphology were education, CPD and as a means to distribute rare material, such as bone marrow. In the field of educa-

tion and training, there is a clear advantage to the use of digital technology in that all viewers see the same cell, allowing a better consensus of opinion on cell identification to be established. Following this study, a pilot internet based CPD scheme was operated between April 2005 and September 2007 using fixed images, with participant responses returned to UK NEQAS (H) by fax. Registration was open to individuals rather than organisations and participant numbers were limited for logistical reasons.

The key driver for UK NEQAS (H) digital morphology has been participant opinion. Feedback from the pilot scheme showed that participants demand easy access to high quality images via a user-friendly IT system for the use of digital technology in EQA to be successful. Although digital technology has been used in other areas of pathology EQA for some time, achieving an acceptable quality of image in peripheral blood and bone marrow smears has proved more challenging because of the need to resolve intracellular structures such as granules, nucleoli and vacuoles. The collaborative group has developed large scale, high resolution, stitched images to provide virtual slides of a manageable size. The images are hosted by Slidepath^{TM}, with secure on-line registration, data return, analysis and reporting. Education is provided by the provision of 'Wikipedia' information links and slides with annotated morphological detail. The scheme is credited for CPD by the Institute for Biomedical Science (IBMS), allowing participants to claim one CPD credit per case. Further information on the UK NEQAS (H) CPD scheme can be obtained from:
www.ukneqash.org

Cardiovascular Ultrasound

Reinhard Volkmann, Sahlgrenska University Hospital, Gothenburg, Sweden

Background

Ultrasound investigations of cardiovascular diseases are highly user dependent. Therefore, investigators should be specialized by long ultrasound experience good pathophysiological knowledge and sufficient individual case information of clinical backgrounds. Investigators should document test out comes representatively to allow second opinions by other experts. External quality assurance programmes (EQAP) for cardiovascular ultrasound may help to improve individual diagnostic statements, initiate internal quality programmes at cardiovascular laboratories and promote national guide lines and consensus statements.

Material and Methods
Since 2003 and twice a year, EQUALIS´ expert group for clinical physiology/vascular diagnosis prepares ultrasound documentations of 5 different examinations, consisting of arterial (carotid, vertebral, lower extremity) and peripheral venous investigations, as well as peripheral ankle and toe pressure measurements. About 40-60 participants from 26 Swedish hospitals comment on each case and reply via internet. The expert group evaluate the answers and arrange yearly user meetings with vascular minisymposia and case discussions.

Since 2007, a similar EQUALIS´ expert group for echocardiography is co-operating with 110 participants from 39 different clinics. Individual results are confidential handled by the EQUALIS staff despite individual feed backs. Results: The vascular EQAP presented more or less complex cases, which is mirrored by the statistical follow-up of the test results. The echocardiographic EQAP worked with selected diagnostic subgroups. At the first user meeting, a wide inter-investigator and national spread in judgement of left ventricular function was demonstrated and discussed, which initiated efforts for standardization.

Discussion
The cardiovascular EQAP and the user meetings are today widely accepted at most Swedish cardiovascular laboratories. The members of the expert groups are representing academic and regional hospitals over the whole country and evoke thereby principal discussions of importance for future national diagnostic consensus. This is of importance for centralized interventional centres to be able to rely on diagnostic outcomes from different regions.

Editor of EQAnews is:
Gitte M. Henriksen, DEKS, 54M1, Herlev Hospital, Herlev Ringvej 75, DK-2730 Herlev, Denmark.
E-mail: gitte.m.henriksen@deks.dk

Field specific co-editors are:
Michael Noble (clinical micro-biology). Clinical Microbiology Pro-ficiency Testing, University of Bri-tish Columbia, Room 328A, Heather Pavilion C, Floor 27, Heather Stree-et, Vancouver, BC V5Z, Canada.
E-mail:mnoble@interchange.ubc.ca

Joergen Kurtzhals (clinical parasitology). Department of Clinical Microbiology 7602, Rigshospitalet, Blegdamsvej 9, DK-2100 København Ø, Denmark.
E-mail: jkcmp@rh.dk

Igor Bondarenko (clinical virology). Russian Research Institute for Metrology, 19 Moskovsky Pr., St. Petersburg, 198005 Russia.
E-mail: bigor@mail.lanck.net

Nils Joergensen (clinical biochemistry), DEKS, 54M1, Herlev Hospital, Herlev Ringvej 75, DK-2730 Herlev, Denmark.
E-mail: nils.joergensen@deks.dk

Jan Moeller (clinical biochemistry). Department of Clinical Biochemistry, Skejby Sygehus, Aarhus University Hospital, Brendstrupgaardsvej, DK-8200 Aarhus, Denmark.
E-mail: jan@kba.sks.au.dk

Vives Corrons (haematology). Haematology Lab. Dept., Escala 1 B-Planta 3, Hospital Clinic 1 Provincial, C/ Villaroel 170, ES-08036 Barcelona, Spain.
E-mail: jlvives@medicina.ub.es

Timothy AL Woods, UK NEQAS for Blood Coagulation, Rutledge Mews, 3 Southbourne Road, Sheffield,S10 2QN, United Kingdom.
E-mail:
Tim.Woods@coageqa.org.uk

AnnetteThomas (language revision). Cardiff and Vale NHS Trust, Quality Laboratory, Quadrant Centre, Cardiff Business park, Llanishen, Cardiff, CF14 5WF, United Kingdom.
E-mail:
weqasannette@btconnect.com

Manuscripts
Manuscripts should be received no later than the first working day of the *month prior* to the month of issuing EQAnews, preferably in an electronic medium.

Editorials
Communications in EQAnews which carry no identification of authorship are written by the Editor.

Correspondence to EQAnews
All correspondence to EQAnews should be send to the Editor.