

**NATIONAL EXTERNAL QUALITY
ASSESSMENT SCHEME
IN
CLINICAL CYTOGENETICS**

ANNUAL REPORT

2007

UK NEQAS for Clinical Cytogenetics

Room 2802, Women's Centre, John Radcliffe Hospital, Headington, Oxford OX3 9DU. UK.
(Tel: +44 1865 857644; Fax: +44 1865 857632 and email: ros.hastings@orh.nhs.uk)

Personnel

Scheme Organiser (S.O):
Deputy Scheme Organiser:
Quality Manager

Dr Ros Hastings (Oxford)
Mr Eddy Maher (Edinburgh)
Mrs Bettina Quellhorst-Pawley (Oxford)

Assessors

Constitutional Scheme

Dr Heleen Shchuring (Utrecht, Netherlands)
Dr Ron Hochstenbach (Utrecht, Netherlands)
Mrs Kath Smith (Sheffield)
Dr Lorraine Gaunt (Manchester)
Mr Graham Fewes (Birmingham)

Mr Richard Ellis (KGC, Harrow)
Mr Eddy Maher (Edinburgh)
Mrs Carolyn Campbell (Oxford)
Dr Carol English (Newcastle)

Haemato-Oncology Scheme

Mrs Helen Dickinson (Leeds)
Mrs Sarah Ryley (KGC, Harrow)
Mr Eddy Maher (Edinburgh)
Ms Nicola Foot (Barts, London)
Dr Manual Teixeira (Oporto, Portugal)

Mr Mike Griffiths (Birmingham)
Mrs Polly Talley (Sheffield)
Mr Dom McMullan (Birmingham)
Mr Paul Roberts (Leeds)
Mr Nick Bown (Newcastle)

Molecular Rapid Aneuploidy (MRA) Joint EQA with Molecular Genetics (MG)

Dr Kathy Mann (Guys, London)
Dr Ros Hastings (S.O)
Simon Ramsden (ex S.O)

Mrs Cathy McConnell (Glasgow)
Dr Sandi Deans (S.O)

Lymphoma and LPD Pilot

Dr Fiona Ross (Salisbury)
Mrs Sandra Birdsall (Cardiff)

Dr Sheila O'Connor (HMDS, Leeds)
Mr Mike Griffiths (Birmingham)

Steering Group

Dr Tony Parkin (Chair, Nottingham)
Mr Eddy Maher (Deputy S.O, Edinburgh)
Mr Mike Griffiths (Birmingham)
Mrs Carolyn Campbell (Oxford)
Dr Lorraine Gaunt (Manchester)
Dr Steven Richards (Leeds)
Mr Roger Mountford (NQAAP, Liverpool) /
Dr Fiona MacDonald (Birmingham) /

Dr Ros Hastings (S.O, Oxford)
Mr Paul Roberts (Secretary, Leeds)
Mrs Helen Dickinson (Leeds)
Mrs Sarah Ryley (London)
Dr Sheila O'Connor (Co-opted, Leeds)
Prof Andrew Green (Dublin)
Mrs Val Davison (NQAAP, Birmingham)
Dr Sandi Deans (MG S.O., Newcastle)

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1. Introduction to the Scheme

The National External Quality Assessment Scheme (NEQAS) for Clinical Cytogenetics is a member of the UK NEQAS Consortium. The Scheme had an accreditation inspection under the new CPA guidelines (ILAC 43) in November 2006. There were seven non-critical non-compliances. These have been addressed and the Scheme received official notification of its accreditation status from CPA (UK) Ltd in July 2007. The next accreditation inspection is planned for November 2008.

The annual management review was completed in March 2008 and will be reviewed by the Steering Committee in July before a summary report is sent to the CPA office. Quality objectives for 2008 have been set and are available on request.

For further information about the Clinical Cytogenetics Scheme please contact the Scheme Organiser or visit the Scheme web site at www.cneqas.org.uk or via the UK NEQAS web site, www.ukneqas.org.uk

2. External Quality Assessment (EQA) distributions in 2007

The EQA assessments consider **technical, analytical and interpretive performance**

- Technical proficiency tested via submitted slides
- Analytical proficiency tested via validated slides and online EQA
- Interpretive proficiency tested via case scenarios and retrospective external audit of reports on work undertaken in diagnostic laboratories.

2.1 Constitutional Scheme

In 2007 there were the following EQA distributions

- Amniotic fluid (case scenario)
- CVS (retrospective reports)
- Blood (online)
- Urgent blood (slide distribution)
- Molecular Rapid Aneuploidy (MRA) (DNA distribution)

2.2 Haematological Scheme

In 2007 there were the following EQA distributions

- CML (case scenario)
- MDS (retrospective reports)
- ALL (online)
- Solid Tumour (slide distribution)

2.3 Pilot EQA Schemes

- Lymphoma & LPD

The online Lymphoma & LPD EQA pilot involved the analysis of FISH images from two cases. 30 laboratories participated in this pilot.

3. Scheme participation

In 2007 93 laboratories participated in the scheme; 36 UK cytogenetic laboratories, 4 UK haematology or histopathology laboratories and 53 non-UK cytogenetic laboratories. A total of 400 EQA distributions were sent out by the scheme office and more than 850 cases were assessed. UK cytogenetic laboratories participated in an average of 6 EQAs while non-UK laboratories participated in an average of 3 EQAs.

4. Scheme submissions

- Reports must be thoroughly anonymised with respect to laboratory and patient identification. This includes consultant, GP and hospital names. Some laboratories failed to anonymise their laboratory identification this year, on the reports or referral cards.
- For non-UK labs:- Interpretation of a cytogenetic result is an essential part of the diagnostic result. In this EQA scheme, laboratories must submit an interpretation with the report. If the interpretation is routinely done by a clinician or Clinical Geneticist in your department, please (a) involve them when completing the case online and (b) submit a copy of the clinician's or Clinical Geneticist's letter with the retrospective reports.
- UK NEQAS for Clinical Cytogenetics does not determine the Professional Guidelines. The ACC Professional Standards Committee (UK), CPA UK Ltd and other European or International bodies (e.g. ECA, ISO standards, ISCN, leukaemia trial studies) produce the guidelines and standards. UK NEQAS marks the laboratory submissions against its interpretation of these guidelines/standards. Use the appeals process if you have issues in the way the guidelines/standards have been interpreted by UK NEQAS. UK NEQAS for Clinical Cytogenetics has referred issues arising out of the EQA rounds to the Professional Standards Committee and the ISCN Committee in the past and will continue to approach the professional organisations if additional guidance/clarification is required.

4.1 ISCN 2005

- There were fewer ISCN errors this year presumably because laboratories were now familiar with ISCN 2005. A summary of the most common errors is given in Appendix A for information.
- Minor non-significant ISCN errors will no longer be mentioned in the individual laboratory reports (ILRs). These are ISCN errors that are not misleading in any way, for instance a hyphen (-) instead of a tilde (~), bracket missing, comma missing, - instead of →.
N.B. However, if the omission of a plus or minus sign would result in a totally different karyotype this will incur a penalty.

4.2 Management System (QA Manager)

- In collaboration with Cytogenetic European Quality Assessment (CEQA) and EuroGentest, UK NEQAS for Clinical Cytogenetics developed a web based management system that was launched for the Autumn EQA round. The system allows:-
 - Online registration
 - Electronic submission and transmission of results
 - Access to individual reports and summary letters online
 - Access to participation/performance certificates.
- The QA Manager is a sophisticated IT system. While β -testing eliminated the majority of programme errors, some 'teething problems' were identified after the system launch in September 2007. The majority of the problems experienced fell into the following five categories:-
 - Unable to access EQA due to incorrect password entered
 - Access to the online blood analysis
 - Uploading documents
 - Downloading documents
 - Sliding doors

The majority of the problems within these categories were unique or isolated to a handful of laboratories. Many were due to an incomplete specification supplied by Microsoft for its various Office Word products. However, it was nevertheless frustrating and stressful for those laboratories that experienced these problems when the system was implemented. The EQA Scheme thanks participants for the patience and understanding shown during this time.

- An IT questionnaire was sent in December to all laboratories that participated in the Autumn EQA round. Feedback was received from 16/103 laboratories and the findings of this review were sent to participants on the 17th March 2008. This feedback was helpful as it identified four previously unknown problems. Suggestions from laboratories have been taken into account in a further phase of development of the QA Manager system.
- All programme errors identified in 2007 have now been rectified. Changes the functionality of the QA Manager will continue to be implemented throughout 2008. While it is hoped no more errors will be encountered in 2008, feedback from laboratories will be welcome if a laboratory does experience problems.

5. Performance scoring

In accordance with the performance criteria, the baseline for all laboratories to reach is the satisfactory standard (CPA (EQA) Standards E5 and F5). The laboratories' performance scores (after completion of the appeals process) for the constitutional and haemato-oncology EQA schemes are given in Appendix B. Poor performance due to non-submissions have not been included in these data. All cytogenetic reports written after September 2006 were assessed by the Scheme according to ISCN 2005.

5.1 Consistency across the Scheme

The Scheme tries to be consistent between EQA schemes and across both constitutional and haemato-oncology areas but inevitably some inconsistencies occur. The complexity of haemato-oncology karyotypes and presence of small side-lines is taken into account when marking the Haemato-Oncology Scheme (see slight differences in the marking in the constitutional and haemato-oncology cytogenetics performance criteria)

5.2 Appeals

The performance criteria (v3.1) were used to assess all the EQA rounds and pilots this year. There were 27 appeals to the Scheme, of which 16 were upheld, 5 were partially upheld and 6 were not upheld.

5.3 Poor performance

A zero mark in the analytical or interpretative score will automatically result in poor performance (see Performance Criteria). Poor performance can also occur if the laboratory accumulates four or more penalty points. The Steering Committee has confirmed that from Autumn 2007 additional EQA rounds will no longer be sent to non-UK laboratories following a poor performance.

There were no instances of poor performance in the Solid Tumours, MDS and MRA EQA rounds this year. However, 26 laboratories received a poor performance in one or more of the following EQAs: Blood (8), Amniotic Fluid (7), CVS (1), Urgent Blood (1), ALL (3) and CML (1). Fourteen non-UK laboratories received a poor performance categorisation in 2007. In addition, four non-UK laboratories failed to participate in the EQAs for which they had registered for and were therefore automatically given a poor performance (see Performance Criteria).

5.4 Persistent poor performance

Three non-UK laboratories received a persistent poor performance designation this year having had a previous history of poor performance and were referred to the Steering Committee.

6. Scheme personnel

- **Scheme Organiser:** Dr Ros Hastings was appointed in June 2003.
- **Deputy Scheme Organiser:** Mr Eddy Maher was appointed in November 2003.

- **Quality Manager:** Bettina Quellhorst-Pawley was appointed in October 2005. Bettina is also the CEQA (European Cytogenetics EQA) QM/administrator.
- **Steering Committee:** Dr Lorraine Gaunt was invited to join the Steering Committee and replaced Dr Edna Maltby in March 2007.
- **Steering Committee Executive:** Consists of the Chair, Scheme Organiser, Deputy Scheme Organiser, Secretary and a senior cytogeneticist specialising in haematology (Mike Griffiths) from the Steering Committee.

6.1 Assessors –

The Scheme is recruiting assessors for 2008/9 at the moment, particularly from laboratories not represented by the current panel and with a satisfactory EQA performance last year. UK assessors normally have part 1 of the FRCPath and non-UK assessors are normally recognised experts with 10 years experience in the specialist area. Potential assessors should send a brief curriculum vitae to the scheme office (ros.hastings@orh.nhs.uk) in the first instance. All assessor appointments will be ratified by the Steering Committee.

7. Changes to the Scheme for 2008

7.1 Constitutional Scheme –

Molecular Rapid Aneuploidy (MRA) will continue to run as a full EQA in the Spring in collaboration with UK NEQAS for Molecular Genetics. There will be a distribution of 3 cases.

7.2 Haemato-Oncology Scheme –

The Lymphoma and LPD scheme will run as a full EQA in 2008.

7.3 Microarray

This exploratory pilot will involve a questionnaire and one constitutional case to analyse. As different platforms are used, there will be two sets of data supplied initially, one for BACs and one for oligonucleotides.

7.4 Laboratory codes

Please use your unique laboratory code in all communications with the Scheme (including emails).

7.5 Future Developments to Management System (QA Manager)

Some features of the website will be available for the first time later in 2008.

For laboratories this will include purchase of EQA schemes, performance certificates and tracking. A secure participants' area will be available on the static website for annual reports, participants' manuals and user guides.

For assessors this is likely to include a 'print all' facility for laboratory submissions which will zip file all the documents to your computer.

7.6 EQA structure and format

- Details of all EQAs are available online this year (download document under diary). Most EQAs will involve submission of documentation or analysis online. Only the slide distribution EQA will require laboratories to submit slides via the post.
- All EQA summary letters will include the range of actual scores, so laboratories can see how their performance compares with other laboratories. The standard that should be obtained continues to be 'satisfactory'.
- UK Laboratories receiving additional EQA rounds following a poor performance will be charged an additional fee of £100 to cover the increased administration costs. Non-UK laboratories will be notified by letter of any poor performance.
- Laboratories have 15 working days to appeal against any penalties/comments in their individual laboratory reports.

- The performance criteria have been reviewed and ratified by NQAAP.
- Three new non-UK Assessors will be involved in the ALL and Microarray EQAs this year, bringing the number of non-UK Assessors to six.

8. Scheme finances

The financial position of the Scheme is a standing item on the agenda at the annual participants' meeting. The fees remain unchanged for 2008, with the exception of Lymphoma and LPD which becomes a full EQA scheme and hence the full fee becomes payable. Laboratories who provide assessors for the Scheme receive a credit of £100 per assessor on the invoice for 2008.

9. CPD recognition for activities within the Scheme

Scheme-based activities performed by the Organiser and Assessors are accredited for CPD by the Royal College of Pathologists within its CPD Scheme. The participants' meeting has also been registered as a CPD activity (6 CPD credits).

10. Scheme presentations

The Scheme Organiser or Quality Manager for UK NEQAS for Clinical Cytogenetics have given presentations on quality issues at the following meetings:-

- Eurogentest meeting (WP1.9) with accreditation bodies and EQA providers, Geneva, February 2007 (BQP)
- ACC Spring meeting, London, April 2007 (RJH)
- Italian Cytogenetic Laboratories, Rome, May 2007 (RJH)
- Eurogentest Steering Meeting, Rome, May 2007 (RJH)
- ESHG Conference, Nice, June 2007 (RJH)
- Participants' Meeting, Birmingham, June 2007 (BQP & RJH)
- ECA Conference, Istanbul, July 2007 (BQP & RJH)
- Czech Human Genetics Society, Prague, September 2007 (RJH)
- Italian EQA participants meeting, Rome, September 2007 (RJH)
- Eurogentest (Unit 1) Board Meeting, Leuven, September 2007 (RJH)
- 5th National EQA providers Forum Meeting, Brussels, October 2007 (RJH)
- Portuguese Society of Human Genetics, Porto, November 2007 (RJH)
- Eurogentest General Assembly and Steering Meeting, Leuven, November 2007 (RJH)

The ACC Spring meeting and Participants' Meeting expenses were met from UK NEQAS income. Expenses for the other meetings were met from other income sources.

11. Annual Participants' Meeting

The next participants' meeting will be held on **Monday 16th June 2008** in the Lecture Theatre, **Institute of Child Health, London**. In response to feedback from participating laboratories, this will continue to be a whole day meeting and will involve talks from invited speakers, an interactive session, as well as a discussion on the format of the Microarray EQA and related issues. Participants attending the workshops should be grade 8a and above (UK labs) or responsible for reporting in their department (non-UK labs). There will be a registration charge of £50 towards the cost of the venue and speakers' travel expenses. Laboratories will be notified when the registration forms and the programme are available.

Appendix A

The follow comments have been taken from the EQA summary letters.

Comments from the Blood EQA

- Minor ISCN error. Both cases had a de novo abnormality. Several laboratories had not recognised that the nomenclature for de novo is now 'dn' (ISCN 2005).

Comments from the CML EQA

- The use of 'c' in the karyotype ISCN prior to confirmation of the constitutional nature of the rearrangement is not appropriate; however, it is important to alert the clinician to this possibility within the text of the report.

Comments from the ALL EQA

- A few laboratories did not give cell numbers in the ISCN (see UK haemato-oncology guidelines, 2007 and ISCN 2005). Some inconsistency in reporting patterns was noted, for instance cell numbers were given for case ALL12007 with the two sidelines but not for the hyperdiploid case (ALL22007) where no sideline was present.
- Some laboratories gave a summary FISH statement but nowhere in the report was any information given on how many cells were examined for the FISH probes. This information is of particular importance when excluding the presence of a rearrangement.

Comments from the MDS EQA

Scoring a complex karyotype

Although the prognosis of a complex karyotype is poor, the interpretation of "complexity" to aid clinical interpretation of the IPSS scoring system is generally not being done. The IPSS scoring system refers to complexity as three or more abnormalities, but does not clearly define a chromosome abnormality. Is a translocation one or two abnormalities given there are two breakpoints? How should dicentric chromosomes or unbalanced translocations be scored? Is -Y included in the abnormality scoring? How should subclones be evaluated?

The assessors and Steering Committee suggested that the following criteria may be helpful to define a chromosome abnormality when using the IPSS scoring system:-

- Scoring is based on unrelated abnormalities.
- If there is more than one clone present, evaluate the most complex subclone.
- Consider translocations, dicentrics and unbalanced translocations as one abnormality each.
- Include a '-Y' in the scoring only if other chromosome abnormalities are present.
- A second copy of a 'der' or 'mar' chromosome is considered to be part of the original abnormality
- Consider '+1,der(1;7)' as one abnormality.
- Normal tetraploid cells are not included in the scoring.
- Abnormal tetraploid cells can be scored independently of the tetraploid nature.

Appendix B
CONSTITUTIONAL SCHEME
PERFORMANCE SCORES

POSTNATAL BLOODS

Satisfactory	47
Poor	8
Non submission	1
Total	56

AMNIOTIC FLUID (AF)

Satisfactory	43
Poor	7
Non submission	2
Total	52

CHORIONIC VILLUS (CVS)

Satisfactory	36
Poor	1
Incomplete submission	1
Total	38

URGENT BLOOD

Satisfactory (>16/20)	32
Poor ($\leq 16/20$)	1
Total	33

MRA

Satisfactory	34
Poor	0
Total	34

HAEMATO-ONCOLOGY SCHEME
PERFORMANCE SCORES

CML

Satisfactory	45
Poor	1
Non submission	1
Total	47

MDS

Satisfactory	42
Poor	0
Non submission	1
Total	43

ALL

Satisfactory	41
Poor	3
Non submission	1
Total	45

SOLID TUMOUR

Satisfactory	18
Poor	0
Non submission	2
Total	20

****Please note that the scores for three laboratories have not been included in these tables. These laboratories only participated in part 2 of the ALL EQA making their total score different.**