UK NEQAS

Blood Coagulation

2020/21

UK National External Quality Assessment Scheme for Blood Coagulation

PARTICIPATION MANUAL & GENERAL INFORMATION

LABORATORY PROGRAMME

UK NEQAS for Blood Coagulation
3rd Floor, Pegasus House, 463A Glossop Road, Sheffield S10 2QD, UK

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UK NEQAS for Blood Coagulation Web site: www.ukneqasbc.org

BACKGROUND

UK NEQAS for Blood Coagulation was originally founded in 1967, with recognition as a UK NEQAS in 1975. Professor F E Preston was appointed Director in 1992, and organisation of the programme was transferred in November 1993 from the Royal Free Hospital, London, to the Royal Hallamshire Hospital, Sheffield Teaching Hospitals NHS Foundation Hospital Trust. Professor I D Walker was appointed Director from 1st February 2005, on the retirement of Professor Preston.

The purpose of UK NEQAS for Blood Coagulation (BC) is to provide external quality assessment (EQA) for tests of blood coagulation, and other tests of haemostasis, and so promote high standards of performance and practice. EQA, together with internal quality control (IQC) procedures, are seen as vital components of overall laboratory quality assurance. In addition, UK NEQAS BC provides a repeat testing and advisory service to participants together with educational activities, including scientific meetings and articles in peer-reviewed publications.

PROGRAMMES

The following modules are currently administered by UK NEQAS BC in the laboratory programme: Level 1 (screening tests) and Level 2 (factor assays, thrombophilia) programmes.

PARTICIPATION

Participation is open to health care professionals in all areas of clinical and scientific practice, including primary and secondary care centres. Participation by industrial and other laboratories is welcomed. Most participating laboratories are sited within the UK but registration is open to laboratories in all countries, whether Government supported, private or commercial. UK NEQAS BC is operated on a not-for-profit basis under the auspices of UK National External Quality Assessment Service and professional bodies.

Samples for over 30 different tests of blood coagulation are distributed to more than 1,000 participating laboratories in the laboratory-based Level 1 & Level 2 programmes, both within and outside the UK; in addition there are over 5000 participants in the Point-of-Care Testing/Near-Patient Testing (POCT/NPT) programmes.

UK NEQAS for Blood Coagulation ensures the protection of participants' confidential information.

The administration and invoicing for all participants in countries outside the UK are handled by EQUALS (BC) Limited. EQUALS (BC) Limited will issue the invoice and receive the payments. However, we should stress that the performance data for all laboratories will remain strictly confidential within UK NEQAS for Blood Coagulation.

Please note the following requirements of laboratory participation in EQA under ISO15189: *"The laboratory shall not communicate with other participants in the interlaboratory comparison programme about sample data until after the submission date", and " The laboratory shall not refer interlaboratory comparison samples for confirmatory examinations before submission of the data, even if this would be routinely done with patient samples". Where evidence of collusion is found, participant performance will be scored as a fail for that survey.*

PERSONNEL

Professor I D Walker is Director at UK NEQAS for Blood Coagulation, 3rd Floor, Pegasus House, 463A Glossop Road, Sheffield S10 2QD UK.

Members of UK NEQAS for Blood Coagulation personnel include:

Dr I Jennings	Scientific Programme Manager
Dr S Kitchen	Scientific Director
Mrs D P Kitchen	Senior Biomedical Scientist
Mrs S Munroe-Peart	Quality Manager & Biomedical Scientist
Mrs L Brown	Biomedical Scientist
Mrs A Lowe	Biomedical Scientist
Mrs J Foster	PA to Scheme Managers
Mr S Asif	Medical Laboratory Assistant
Mrs J Ogden	EQA Programme Co-ordinator / Deputy Quality Manager
Miss S Shikdar	IT Specialist
Mrs S Burdett	Assistant Clerical Officer
Mrs C Mather	Assistant Clerical Officer
Mr T A Woods	Director (EQUALS BC)
Mrs R L Longden	Assistant Clerical Officer-(EQUALS BC)
Mrs K A Stott	Assistant Clerical Officer-(EQUALS BC)
Mrs S L Lamb	Clerical Officer-(EQUALS BC)
Mrs J Johnson	Company Administrator-(EQUALS BC)

STEERING COMMITTEE MEMBERS

The organisation receives advice from a Steering Committee. Current members of the Steering Committee are as follows:

Professor H Watson (Chair)	Department of Haematology, Aberdeen Royal Infirmary, Foresterhill, Aberdeen
Dr E Gray	Department of Haematology, National Institute for Biological Standards & Control, South Mimms, Herts.
Dr D Harrington	Department of Haemostasis & Thrombosis, St Thomas's Hospital, London
Dr I Jennings	UK NEQAS for Blood Coagulation, 3rd Floor Pegasus House, 463A, Glossop Road, Sheffield
Mrs D P Kitchen (Secretary)	UK NEQAS for Blood Coagulation, 3rd Floor Pegasus House, 463A, Glossop Road, Sheffield
Dr S Kitchen	Coagulation Laboratory, Sheffield Teaching Hospitals, Royal Hallamshire Hospital, Sheffield.
Professor I D Walker (Director)	UK NEQAS for Blood Coagulation, 3rd Floor Pegasus House, 463A Glossop Road, Sheffield

Mrs A Lowe	UK NEQAS for Blood Coagulation, 3rd Floor Pegasus House, 463A, Glossop Road, Sheffield
Ms A Riddell	Haemophilia Centre, Royal Free Hospital, London
Dr W Lester	Haemophilia Unit, Queen Elizabeth Hospital, Birmingham
Dr A Wood	Clinical Haematology, South Tees Hospital
Dr H Lyall	Consultant haematologist, Norfolk and Norwich University Hospital NHS Foundation Trust
Dr R MacLean (UKHCDO)	Sheffield Teaching Hospitals, Royal Hallamshire Hospital, Sheffield
Dr R Alikhan (BSH Thrombosis Haemostasis Task Force)	Cardiff and Vale University Health Board
Dr S MacDonald (NQAAP)	Cambridge University Hospitals NHS Foundation Trust

EQA PROGRAMMES

All EQA Programmes listed below currently have full accreditation status to ISO 17043 with UKAS (United Kingdom Accreditation Service).

SCREENING TESTS (LEVEL 1) AND ASSAYS (LEVEL 2) BLOOD COAGULATION PROGRAMME:

TESTS COVERED IN THIS PROGRAMME

Level 1 (Screening tests):

Prothrombin Time (PT)/INR (Quick and/or capillary methods)
PT (diagnostic)
Activated Partial Thromboplastin Time (APTT)
Heparin Dosage Assessment (HDA)
Heparin Assay (HA)
Thrombin Time (TT)
Fibrinogen evaluation
D-Dimer

Level 2 (Assays):

Factor II assay	Von Willebrand factor antigen assay
Factor V assay	VWF: RiCof (activity) assay
Factor VII assay	Antithrombin antigen assay
Factor VIII: C assay	Antithrombin activity assay
Factor IX: C assay	Protein C antigen assay
Factor X assay	Protein C activity assay
Factor XI assay	Protein S total and free antigen assay
Factor XII assay	Protein S activity assay
Factor XIII screen	Plasminogen assay
Quantitative VIII inhibitor	Activated Protein C Resistance assay

REGISTRATION

The nominated participant, normally the person with overall responsibility for the laboratory, is requested to register for all tests included in UKNEQAS BC, which their laboratory offers as a service. Registration forms are available to download from the UK NEQAS BC website www.uknegasbc.org or by contact with the UK NEQAS BC office.

Completed registration forms are processed by the administration team and a letter of confirmation is sent via email. The letter includes a participant number and password and these must be retained for your records as they allow registered participants to access the data entry system on the UK NEQAS BC website for entry of results and download of reports and other documents. All participants are asked to provide email contact details, as these will be used for alerts about survey distribution and availability of reports. Email addresses alongside other participant information are confidential, and not shared with any third party.

As part of registration, participants in the UK are requested to formally agree to adhere to the Joint Working Group's Conditions of Participation in UK EQA Schemes. With the few exceptions indicated in these Conditions, the Director is obliged to observe strict confidentiality regarding individual performance. All participant details are held in strict confidence and are not shared with any third party. Use of the participant number will assist in maintaining confidentiality in survey correspondence.

The UKNEQAS BC website www.uknegasbc.org provides a range of information about the organisation, programmes and surveys and forthcoming events. Participants can also enter their results on the web; download survey reports, certificates of registration and certificates of performance.

Total number of registrations:	1186
UK	733
Countries outside the UK:	453

SURVEYS

Six survey exercises are distributed each financial year. Each survey includes both screening tests (level 1) and factor assays (level 2), and there are four distributions each of thrombophilia screening exercise. Details of tests to be included in each survey are indicated in survey newsletters three months prior to survey distribution. All samples are of lyophilised plasma, from donors screened for hepatitis B surface antigen (HBsAg) and for antibodies to hepatitis C virus and human immunodeficiency virus types 1 and 2 (anti HIV-1+2). In the majority of cases, samples are from single donations. In addition to six Laboratory programme distributions, relevant supplementary exercises are distributed on an ad-hoc basis to address current issues in haemostasis.

A schedule of the planned surveys can be downloaded from our website www.uknegasbc.org or by request via one of the following methods:

Tel: +44 (0)114 267 3300
Fax: +44 (0)114 267 3309
UK E-mail: negas@coagega.org.uk
Countries outside the UK E-mail: equals@coagega.org.uk

REPORTS

Individual reports for each survey are uploaded to the website within two weeks of the closing date for the respective survey, as pdf documents, and email alerts are sent out to notify participants that these are available. Additionally, some weeks after the individual results, an overall exercise report is made available to registered participants for electronic download from the website (www.uknegasbc.org). This report includes comprehensive analysis of test results by methodology, together with graphically presented data analysis for each test specimen.

PERFORMANCE ANALYSIS

Performance is determined by comparison of individual laboratory results with the target value for each test. Median values determined from participants' results are used as consensus or "target" values against which individual laboratory performance can be assessed. Use of the median avoids the effect of outlying results and the need to perform 'truncation' of data. Where consistent reagent or method-related differences have been identified, participants' results are assessed against their 'peer-groups' provided the number in that group is sufficient to be statistically valid.

Two different approaches are taken to evaluate performance for screening tests and factor assays – both comply with specifications detailed in ISO 13528 *Statistical Methods for use in proficiency testing by interlaboratory comparisons.*

Screening Tests

For PT/INR, PT for diagnosis, and APTT the percentage deviation of each individual laboratory's results from the reagent and overall medians are calculated and the following criteria for performance are applied:-

Performance is considered "*within consensus*" if the deviation is <15% from:

The **reagent median** if the number of users of that reagent is equal to or greater than 10 *or*
The **overall median** if the number of users of the reagent is less than 10.
Results >15% deviation from the median are considered "*outwith consensus.*"

For Heparin Dosage Assessment (HDA) and thrombin times, modified criteria apply. In both cases, results >20% deviation from reagent medians for majority groups is considered *outwith consensus*. Marked differences in the heparin sensitivity of APTT reagents have led to the conclusion that it is inappropriate to assess minority reagent users against the overall median. No performance analysis is applied to minority groups, although % deviation from reagent and overall medians are recorded on individual reports.

For Fibrinogen assay, Clauss method results are assessed against the overall Clauss method median, with results >15% from this median considered outwith consensus. Multifibrin U users are assessed separately.

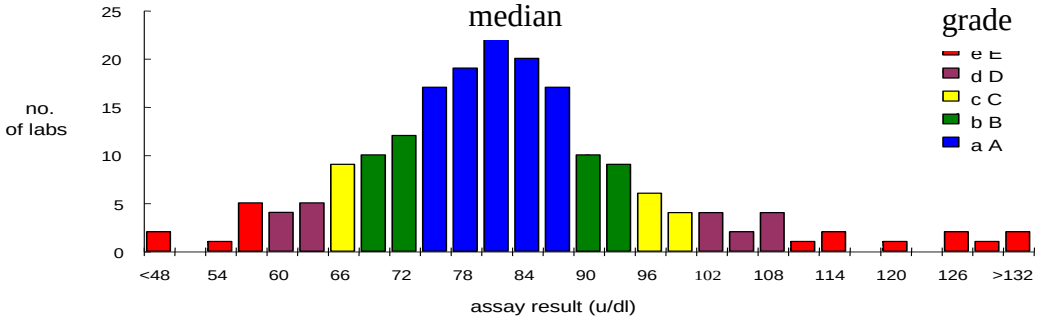
Factor Assays

For factor assays, UK NEQAS BC distributes samples with factor concentrations covering the wide range encountered in clinical practice. For this reason, the percentage deviation from the median cannot be used as a means of defining performance. A ranked grading analysis to evaluate performance was devised by Professor S Thomson, Department of Medical Statistics & Evaluation, Royal Postgraduate Medical School, London.

The overall consensus median is taken as the central reference point or “target value”. Individual results are ranked into five unequal quantiles above and below the median, each quantile being designated by a letter depending on ranked distance from the median:

Group A: *The nearest 25% of results above (A) and below (a) the median (i.e. 50% of results);*
Group B: *The next 10% of results above (B) and below (b) the median (i.e. 20% of results);*
Group C: *The next 5% of results above (C) and below (c) the median (i.e. 10% of results);*
Group D: *The next 5% of results above (D) and below (d) the median (i.e. 10% of results);*
Group E: *The 5% of results furthest from the median, above (E) and below (e) (i.e. 10% of results).*

This is illustrated below:



Grades below the median are shown in lower case, and above the median in upper case, to aid in assessment of bias.
Performance is based on grades obtained in **two consecutive exercises** for any particular test. ***Performance "outwith consensus"*** is defined as a combination of a C (or ‘c’) grade together with an E (or ‘e’) grade, or any combination of D (or ‘d’) and E (or ‘e’) grades (e.g. cE, ec, Dd, de, ED and EE in consecutive distributions of that particular assay).
Persistent "outwith consensus" performance is defined as two consecutive ***"outwith consensus"*** performances, where the order in which the grades were assigned does not affect the overall performance. This will arise from three consecutive performances with the following combinations of grades (upper case only shown):

DDD, DED, ECE, EEC, DDE, DEE, EDD, EED, CEE, EDE, EEE

A non-return for a registered test will be graded as ‘F’ and taken as equivalent to an E grading. Thus, designations which include ‘F’ grades are based on performance over 2 or 3 exercises, respectively.

In some cases, significant differences have been noted between different methodologies. Where this occurs on a consistent basis, separate analysis of the groups is carried out using medians specific to each method group. However, the system is only effective if the number of participants is greater than 20; consequently, grading analysis is not applied to groups of results from fewer than 20 centres. In these cases we recommend that the participant compares their result with the median for users of the same method, alongside the overall assay median and evaluates whether any differences from these results have clinical relevance. We recommend this approach for *all* participants, including those receiving a performance assessment of their results. Advice is always available by making contact with UK NEQAS BC.

At present, the following groups are analysed separately (groupings are regularly reviewed):

D-Dimers Assays	(kit-specific and FEU/non-FEU groups)
Factor VIII: C assay	(1-stage, 2-stage & chromogenic assays)
Antithrombin antigen	(results expressed in u/dl and mg/dl)
Antithrombin activity	(bovine thrombin, human thrombin, factor Xa substrate)
Protein C activity	(clotting and chromogenic assays)
Activated Protein C resistance	(Kit-specific groups)
VWF RiCof (activity)	(Kit-specific groups)

Performance analysis for protein S activity assays is currently suspended.

If results of screening tests are outwith consensus on three consecutive occasions (including failure to return results), or results from factor assays are persistently outwith consensus, a letter of concern with an offer of assistance is sent to the Head of Department by the Scheme Director.

For some analytes, performance criteria cannot be applied to all data – examples include minority reagents for some screening tests, and assays assessed by peer groups where the number of users in a peer group is less than 20. In these cases, reports indicate performance is "not assessed" with a grade of *****. We recommend that the participant compares their result with the median for users of the same method alongside the overall assay median to evaluate whether any differences from these results have clinical relevance. We recommend this approach for *all* participants, including those receiving a performance assessment of their results. Advice is always available by making contact with the Scheme.

ADDITIONAL INFORMATION ABOUT UK NEQAS FOR BLOOD COAGULATION

OTHER PROGRAMMES

UK NEQAS BC also offers EQA for the following programmes:

- Molecular Genetics of Thrombophilia
- Genetics of Heritable Bleeding Disorders
- Homocysteine
- Lupus
- DOAC (Dabigatran, Rivaroxaban, Apixaban, Edoxaban
- FXIII
- ADAMTS13
- Supplementary tests

For further information on any of our programmes, and details of annual fees, please contact us as follows:
Tel: +44 (0)114 267 3300
UK E-mail: neqas@coaguega.org.uk
Countries outside the UK E-mail: equals@coaguega.org.uk

COMPLAINTS

Any complaint about UK NEQAS BC will be treated as serious and will be dealt with as soon as possible by the Director or Manager. If the outcome is not to the satisfaction of the participant, referral may be made initially to the President, UK NEQAS Board and subsequently to the Chairman of the National Quality Assurance Advisory Panel for Haematology.

Address for complaints:
UK NEQAS for Blood Coagulation
3rd Floor, Pegasus House, 463A Glossop Road, Sheffield S10 2QD, UK
Tel: +44 (0)114 267 3300
UK E-mail: neqas@coageqa.org.uk
Countries outside the UK E-mail : equals@coageqa.org.uk

EDUCATIONAL ACTIVITIES

In addition to an advisory role for individual laboratories, UK NEQAS BC also publishes and presents data through a variety of leading journals and meetings.

Well established Annual Scientific Meetings include presentations from nationally and internationally renowned speakers, in addition to data from survey distributions and open debate on EQA issues.

SUPPLEMENTARY EXERCISES

Supplementary exercises are carried out to address topical issues in haemostasis testing. Recent exercises have included post factor-concentrate assays and assays for direct oral anticoagulant drug measurement. Reports are circulated to participating centres and data are presented at national and international meetings.

QUESTIONNAIRES

Questionnaires are distributed to participants on a regular basis to gain feedback on issues of general interest in haemostasis and thrombosis, in addition to specific aspects relating to UK NEQAS BC.

PUBLICATIONS

Data are regularly presented at national and international scientific meetings, including British Society for Haematology, British Society for Haemostasis and Thrombosis, ISTH Scientific Sub-Committee meetings and the World Federation of Haemophilia Congress.

Haemophilia. 2016 Sep; 22(5):806-12. doi: 10.1111/hae.12962. Epub 2016 May 24.

Factor VIII assay variability in post infusion samples containing full length and B-domain deleted FVIII.

Kitchen S[1,2], Jennings I[3], Makris M[3,4], Kitchen DP[3], Woods TA[3], Walker ID[3].

Quality control of point of care INR devices is essential.
Kitchen DP, Kitchen S, Jennings I, Woods TA, Makris M, Walker ID.
BMJ. 2016 Apr 12; 353:i2019. doi: 10.1136/bmj.i2019. No abstract available

Confirmation of genetic testing results in haemostasis and thrombosis - survey of current practice in the field.
Jennings I, Goodeve A, Theophilus B, Hill M, Cumming A, Kitchen S, Walker ID, Perry D.
Haemophilia. 2016 May;22(3):e239-41. doi: 10.1111/hae.12934. No abstract available.

Bridging the gap between point-of-care testing and laboratory testing in haemostasis.
Kitchen DP, Jennings I, Kitchen S, Woods TA, Walker ID.
Semin Thromb Hemost. 2015 Apr; 41(3):272-8. doi: 10.1055/s-0035-1544197.

Stability of coagulation proteins in lyophilized plasma.
Jennings I, Kitchen DP, Woods TA, Kitchen S, Preston FE, Walker ID.
Int J Lab Hematol. 2015 Aug; 37(4):495-502. doi: 10.1111/ijlh.12318.

The UK National External Quality Assessment Scheme for heritable bleeding disorders.
Perry DJ, Cumming T, Goodeve A, Hill M, Jennings I, Kitchen S, Walker I.

Investigation of a prolonged APTT. Different approaches taken by laboratories to achieve the same diagnosis.
Jennings I, Kitchen DP, Kitchen S, Woods TA, Walker ID.

Point of Care INR testing devices: performance of the Roche CoaguChek XS and XS Plus in the UK NEQAS BC external quality assessment programme for healthcare professionals: four years' experience.
Kitchen DP, Kitchen S, Jennings I, Woods TA, Fitzmaurice DA, Murray ET, Walker ID.
J Clin Pathol. 2012 Dec; 65(12):1119-23. doi: 10.1136/jclinpath-2012-201049.