

Programma di “Valutazione Esterna di Qualità”



CARDIAC MARKERS

**United Kingdom
National External
Quality Assessment
Schemes**

**Scheme Manual
2008 - 2009
Versione italiana**

**Distributore per l'Italia:
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INTRODUCTION

In 1997 the requirement for a UK wide EQA scheme for the new cardiac markers Troponin I (cTnI) and Troponin T (cTnT) was recognised and a scheme for these two analytes was proposed. This received recognition and funding as a pilot scheme from CPA in February 1998 and is a CPA (EQA) accredited scheme (Current Accreditation Incorporating ILAC G13:2000, August 2007). The scheme has been a member of UK NEQAS since September 2000. The UKNEQAS Laboratory Numbering System was introduced in September 2003. The material distributed can also be used for CKMB and Myoglobin EQA. Point of Care schemes for Troponins I & T, CKMB and Myoglobin are also available. NT-ProBNP and BNP EQA schemes are now available for both Laboratory based and Point of Care systems.

SCHEME MANAGEMENT

The schemes for Cardiac Markers are run from the Department of Clinical Biochemistry at the Victoria Infirmary, Glasgow. It is managed by Mr. Alan Reid (Scheme Organiser), who will be pleased to provide advice or assistance on any aspect of the scheme or visit our web site at www.ukneqas-cm.org.uk.

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STEERING COMMITTEE

All established UK NEQAS schemes are supported by advice from an appropriate UK NEQAS Steering Committee, accountable to the UK NEQAS Board. The Chairman is normally independent of UK NEQAS operational interests, and membership will include appropriate experts, participants and advisors. Chairmen and members are appointed by the UK NEQAS Board, on the advice of appropriate professionals, and sit in their own right and normally not as representatives of any professional or other group, though some may fulfil an invaluable liaison function with such groups.

Steering Committees do not consider the performance of individual participating laboratories, except in advising on performance criteria or where this may indicate a failure in the operation of the Scheme (and even in such cases the laboratories will not be identifiable).

A Steering Committee may have permanent Specialist Advisory Groups and/or short-term Task Forces to support its work; Specialist Advisory Groups and Task Forces may have members from more than one Steering Committee or discipline. There may be one or more Steering Committee within a discipline (UK NEQAS division), depending on circumstances. A single Committee should assist in promoting harmonisation within the discipline.

The Steering Committee (Clinical Chemistry) meets twice a year and the Specialist Advisory Group (General Clinical Chemistry) four times a year.

STEERING COMMITTEE – TERMS OF REFERENCE

To advise the Scheme Organiser on the overall design and operation of the Scheme(s), including aspects such as:

- Appropriateness of the investigations.
- Surveyed nature of the specimens distributed.
- Number and frequency of specimen distribution.
- Source of target values.
- Data analysis and performance assessment.
- Data presentation.
- Communication with participants, including meetings, newsletters, educational activities.
- Communication with the diagnostics industry.
- Research and development for the Scheme(s).
- In consultation with the Scheme Organiser, to liaise with the relevant National Quality Assurance Advisory Panel in setting performance criteria.
- To consider, and advise the Scheme Organiser(s) on, the need for initiation or termination of EQA services for investigations in the area covered.
- To review Schemes' annual reports.
- To receive any representations, to Chairman, members or Organiser, from participants concerning the Schemes.
- To advise the UK NEQAS Board, and where appropriate other relevant organisations (eg Department of Health, Joint Working Group on Quality Assurance, CPA(UK)Ltd, Medical Devices Agency, Royal College of Pathologists), on any aspect of EQA or quality assurance in the area covered.

MEMBERSHIP OF THE SCHEMES

Participation

Participation is open to all clinical laboratories in the UK and abroad.

Current Participant Numbers for Schemes

Laboratory Based Systems:

Analyte	Total Number of Participants	Number of Participants Overseas
Cardiac Troponin I	212	49
Cardiac Troponin T	130	28
CKMB	71	36
Myoglobin	47	27
NT-proBNP	73	28
BNP	49	12

Point of Care Based Systems:

Analyte	Total Number of Participants (UK Only at Present)
Cardiac Troponin I	8
Cardiac Troponin T	32
BNP	7

Cardiac Troponin I includes Qualitative & Quantitative Methods

Confidentiality

Confidentiality is strictly maintained, with each laboratory identified by a unique code known only to the scheme organiser and participant. The only circumstances under which participation and/or performance records in the scheme might be divulged are where a participant shows poor performance. In this situation there is a formal procedure to address the issues, the final step of which could result in the participating laboratory being referred to the NQA Advisory Panel. Laboratories providing a clinical service in the UK are governed by the conditions of confidentiality determined by the Joint Working Group on Quality Assurance (Ref. 1)(Under Review).



SAMPLES

Manufacture

Samples are prepared from human plasma made available through the Scottish National Blood Transfusion Service. This material, which is surplus to the requirements of the Blood Transfusion Service, has been screened for infective agents. The plasma is treated to remove fibrinogen, citrate and phosphate. Analyte levels are varied by addition of Troponin complex, free Troponin T, CKMB, Myoglobin NT-pro-BNP and BNP to the serum matrix. The serum is lyophilised.

Sample Distribution (Laboratory Based Systems)

There are 12 scheduled monthly distributions per year with three samples per distribution. Occasionally a distribution may have more than three samples if some specific assay parameter (i.e. linearity) is being investigated.

Samples are distributed usually on the second Tuesday of each month by post in accordance with all current postal regulations.

Sample Distribution (Point of Care Based Systems)

There are 12 scheduled monthly distributions per year with two samples and a diluent per distribution. Samples are distributed by post in accordance with all current postal regulations.

Reconstitution and Storage of Samples

Lyophilised samples should be reconstituted by addition of an accurately dispensed 1 ml volume of distilled or deionised water to each vial. Additional plastic vials with diluent are supplied with the BNP scheme. The vials should be allowed to stand for 15 minutes with occasional mixing and then stored at 4°C. The EQA material should be assayed after reconstitution as follows:

- cTnl, cTnT, CKMB, and Myoglobin between 1 and 3 hours
- NT-proBNP between 1 and 2 hours.
- BNP between 45 and 60 minutes.

For the Point of Care based scheme 2 plastic vials containing 1ml of diluent is provided for reconstitution in locations outwith the laboratory.

Instructions on reconstitution of the materials are given on the report form enclosed with the distribution.

Stability

It has been established that at 4°C, troponin (I and T) loss is <2% over 3 hours. CKMB, Myoglobin and NT-proBNP are also stable for this period of time. However BNP is a labile peptide and should be assayed between 30 – 45 minutes post reconstitution.

Analysis

Samples should be treated, where appropriate, in the same manner as clinical sample.

RESULTS

Returning Results

Samples are posted to participants on the 2nd Tuesday of each month and results **must be returned** within three weeks, or two weeks for the Point of Care based system (the final date for receipt of results will be printed on the results sheet). Results should be recorded on the results sheet which is enclosed with each distribution and may be posted, telephoned, faxed or sent via our web site at www.ukneqas-cm.org.uk . For electronic transmission of results please contact the scheme organiser for a user name and password. The date of receipt of results are recorded. If any participant has not returned results by the specified cut-off date a reminder will be faxed to them.

Data Errors and Blunders

Data entry into the Cardiac Marker scheme databases is by double point entry. The data is also checked manually. Any error in data entry will be corrected. If a participant having returned their results identifies an error such as a transcription error which could not have occurred with a patient sample (e.g. transfer of results to the EQA result form), the Scheme Organiser should be informed by letter and the results will be corrected. Other errors will not be amended.

STATISTICAL ANALYSIS AND REPORTS FOR ALL EQA SCHEMES

Assigned Values or Target Values.

- For cTnI, CKMB (Activity), BNP and NT-proBNP values are assigned either as the Method Laboratory Mean (MLM) for <9 laboratories or a Method Laboratory Trimmed Mean (MLTM) for >9 laboratories.
- For cTnT, CKMB (Mass) and Myoglobin values are assigned either as the All Laboratory Mean (ALM) for <9 laboratories or a All Laboratory Trimmed Mean (ALTM) for >9 laboratories.
- Trimming of results takes place by the removal of the top and bottom 5% of the results provided there are more than 9 values.
- At this stage it is still not appropriate to provide an All Laboratory Trimmed Mean (ALTM) for Troponin I due to differences in method calibration within each analyte group.

- Results are considered to be outliers if they fall out-with \pm three standard deviations of the group mean.
- The MLM or MLTM or ALTM is taken as the Assigned or Target Value for that analyte and participants' results are compared with this value.

Performance Parameters are as follows -

- Bias is the percentage deviation from the Target Value and has a sign.
- Cumulative Bias is calculated as the mean of the current and previous 5 months Mean Bias results, taking the sign of the bias into account. Six months were chosen for the calculation to give a reasonably rapid response to changes in bias.
- Variability is calculated by including a sample of the same batch in two or more distributions.

For methods with < 9 laboratories :

$$\text{Variability} = [X_1 - X_2] / [(M_1 + M_2)/2] \times 100.$$

Expressed as a percentage.

For methods with > 9 laboratories :

$$\text{Variability} = [X_1 - X_2] / [(TM_1 + TM_2)/2] \times 100.$$

Expressed as a percentage.

Where X_2 is a replicate of a previously distributed batch (X_1). Signs are ignored.

M = Method Laboratory Mean or All Laboratory Mean.

TM=Method Laboratory Trimmed Mean or All Laboratory Trimmed Mean

- Cumulative Variability is calculated as the mean of the current and previous 5 months results, ignoring sign.
- As an indicator of method performance a coefficient of variation for each sample distributed (expressed as a percentage) is calculated for each method group.

$$\text{Coefficient of Variation} = (\text{SD} / \text{TM or M}) \times 100$$


- Results Summary is printed to provide a rapid overview of the results.


The results summary pages includes the following:


- A performance criteria graphic - plots cumulative bias vs. cumulative variation.
- Graphics indicating cumulative bias and cumulative variation performance over a 12 month period.
- Inclusion of method summaries.
- Method Precision Profiles - a: all levels and b: low levels.

At a glance performance indicator:

- Traffic light Colour Coding to assist participant in assessing performance can be found on the **Address Page** of the report:

 Red indicates a laboratory's cumulative bias and/or variation is outwith current performance criteria limits (this cumulative data is based on the previous five and current distribution data for bias and variation). Action required.

 Amber indicates a laboratory's current distribution bias and/or variation is outwith current performance criteria limits. Warning about distribution performance.

 Green indicates a laboratory is performing within current performance criteria limits.

PERFORMANCE STANDARDS

**PERFORMANCE CRITERIA
FOR LAB BASED EQA SCHEMES**

Limit of acceptable performance from August 2003

ANALYTE	BIAS	VAR
Cardiac Troponin I	±15%	<25%
Cardiac Troponin T	±15%	<25%
CKMB	±20%	<25%
CKMB (Activity)	±25%	<35%
Myoglobin	±20%	<25%

**PERFORMANCE CRITERIA
FOR POINT OF CARE EQA SCHEMES**

Limit of acceptable performance from August 2003

ANALYTE	BIAS	VAR
Cardiac Troponin I	±20%	<25%
Cardiac Troponin T	±20%	<25%
CKMB	±20%	<25%
Myoglobin	±20%	<25%

The following performance criteria have been agreed with the scheme steering committee and NQAAP for Chemical Pathology. They will be implemented by the scheme organiser, and are reviewed annually.

**PERFORMANCE CRITERIA
FOR BNP and NT-proBNP SCHEMES**

ANALYTE	BIAS	VAR
BNP (POC System - Biosite Triage) (B-type Natriuretic peptide)	±20%	<25%
BNP (Lab Based Systems) (B-type Natriuretic peptide)	±20%	<25%
NT-ProBNP (Lab Based Systems) (NT-ProB-type Natriuretic peptide)	±20%	<25%

The following performance criteria have been agreed with the scheme steering committee and NQAAP for Chemical Pathology. They will be implemented by the scheme organiser, and are reviewed annually.

PERFORMANCE STANDARDS

Definitions of Unacceptable Performance

Participants will be defined as **Poor Performers** under the following circumstances:

- a. Failure to make returns for three consecutive distributions.
- b. Having an average cumulative variance greater than the stated performance limits over six distributions.
- c. Having an average cumulative bias of greater than the stated performance limits over six distributions.

If any of these conditions apply the scheme organiser will write to the head of the laboratory concerned drawing attention to the problem and requesting a formal reply within four weeks. This letter will also include an offer of help by way of information, exchange of samples or advice as appropriate. The NQA Advisory Panel will also be informed and at the request of the JWG the UK NEQAS identifier and the name of the laboratory and host hospital will be given to the Panel chair.

Participants will be defined as **Persistent Poor Performers** under the following circumstances:

If a formal reply is not forthcoming a second letter will be sent to the laboratory head, which will indicate that the participant will be referred again to the the NQAAP if no response is forthcoming and that this will lead to identification as a **Persistent Poor Performer**.

If a poor performer as defined by a, b or c, compounds the errors by failing to make more returns or continues with cumulative bias of greater than the stated performance criteria limits for the analyte concerned or variance greater than the stated performance for the analyte concerned over further distributions then they also become classified as a **Persistent Poor Performer**.

NATIONAL QUALITY ASSURANCE ADVISORY PANEL

The Panels are independent bodies of representatives nominated by the professions whose role is to monitor standards of laboratory performance in the UK. The UK NEQAS Cardiac Markers Scheme Organiser will co-operate with the Panel as required. A member of the Panel is represented on the Steering Committee and the Specialist Advisory Group.

COMPLAINTS PROCEDURE

Should a participant have a complaint regarding any aspect of the scheme, they should notify the Scheme Organiser Alan Reid or Bridie Boyle. All complaints are logged and will be formally responded to within 14 days. Should the matter remain unresolved the participant may refer the complaint to the appropriate UK NEQAS Steering Committee/Specialist Advisory Group or the NQA Advisory Panel. The Steering Committee will also monitor and review all complaints.

REGISTRATION AND INVOICING

Application to participate may be made by contacting either Bridie Boyle or Alan Reid at UKNEQAS for Cardiac Markers, Department of Biochemistry Laboratory Division, Victoria Infirmary from whom further information may be obtained. Alternatively visit our web site www.ukneqas-cm.org.uk and electronically register.

References:

1. Conditions of participation by UK Clinical Laboratories in External Quality Assessment Schemes which are under the professional jurisdiction of the Joint Working Group on Quality Assurance. Davidson, John. F and Kilshaw, Dennis. Effective from 1st May 1997.

Membership of Steering Group and Specialist Advisory Groups

UK NEQAS Steering Group (Clinical Chemistry)

Dr. G Beastall (Chairman)
Dr. D G Bullock (Secretary)
Dr. L Sandle (Panel Observer)
Dr W A Bartlett
Dr. G J Beckett
Dr. R Beetham
Dr. R A Braithwaite
Dr. S K Bangert
Dr. C M Dawson
Dr D Isherwood
Dr J Middle
Mr. A Reid
Mr D Ricketts
Mr R Simpson
Dr I D Watson

UK NEQAS Specialist Advisory Group (General Clinical Chemistry)

Dr W A Bartlett (Chairman)
Mr F MacKenzie (Secretary)
Mr B Perry (Panel Observer)
Prof. T. Reynolds
Dr D G Bullock
Mr E Carr
Dr A Duncan
Ms R Goodall
Dr P Hill
Dr J Middle
Mrs J C Powell
Ms J French
Mr A Reid
Dr F Boa

Terminology:

ALTM The All Laboratory Trimmed Mean, which is the geometric mean of the entire set of trimmed results for a specimen.

MLTM The geometric mean of a sub-set of the trimmed results for a specimen. The sub-set is a single manufacturers method.

CUMULATIVE BIAS The geometric mean of the trimmed deviations of your laboratory's results from their targets for all usable specimens for which you have returned results during the current six months.

DEVIATION The difference between your result and the target result, expressed as a percentage of the target.

DISTRIBUTION A group of specimens in a particular scheme that are sent together to each participating laboratory.

GCV The geometric coefficient of variation of the results in a set or sub-set of results for a specimen.

OUTLIER (BETWEEN- LABORATORY, WITHIN- SPECIMEN) A result that is more than three SD's from the appropriate target. These outliers may be of great significance as they demonstrate an inability of a laboratory to agree with their peers.

TRIMMING The effect of aberrant results that, may be present is minimised by trimming the data prior to statistical analysis. The chosen method is that of Healy, which involves trimming of the lowest and highest 5% of results. Note that trimmed results are not necessarily outliers.

VARIATION The GCV of the BIAS or scatter of the deviations of a laboratories' results from target for all usable specimens in the six distributions to date. It reflects your imprecision, but is affected by dose or specimen related bias.