

QUALITY MANUAL

This document together with specified procedure manuals represents the Quality Management System of NEQAS Leucocyte Immunophenotyping. It has been compiled to meet the requirements of the Clinical Pathology Accreditation (UK) Ltd (CPA) system and appropriate national and international standards. All procedures specified herein are mandatory within UK NEQAS Leucocyte Immunophenotyping.

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1 GENERAL INFORMATION

1.1 Title of laboratory or department

Location & Administration

The Leucocyte Immunophenotyping EQA Scheme is located on two sites:

Administration is sited at:

**UK NEQAS for Leucocyte Immunophenotyping,
Rutledge Mews,
3 Southbourne Road
Sheffield S10 2QN
United Kingdom**

The laboratories are sited:

**H Floor Room H100D
Royal Hallamshire Hospital
Glossop Road
Sheffield S10 2JF
United Kingdom**

Please note: Any deliveries of results or courier services should be to the administrative site.

The EQA Scheme is administered as part of the laboratory directorate within the Trust, which provides employment and financial services. It operates independently of this Trust's pathology services.

Communications

The postal address is:

**UK NEQAS for Leucocyte Immunophenotyping,
Rutledge Mews,
3 Southbourne Road
Sheffield S10 2QN
United Kingdom**

This address should be used for all postal communications and courier services.

The telephone number is

UK 0114 267 3600 (direct line)

non-UK +44 114 267 3600

This number is manned from 0830 to 1630 Monday to Friday, while a voice mail recording may be obtained at certain times and on official holidays. Callers will be asked to state their *Participant code number*, the nature of their request, or enquiry, and will be transferred to a senior member of staff if appropriate. Urgent messages are given priority and brought to the attention of senior staff as soon as possible. Participants are requested to ALWAYS have their *Participant code number* on hand before calling. All calls and action(s) taken are logged.

The FAX number is

UK 0114 267 3601

non-UK +44 114 267 3601

All fax traffic is logged to enable tracing of receipt of documents and coloured paper is used to distinguish result documents received by fax from those received by post.

E-mail addresses:

All staff have e-mail addresses, and these are provided under the relevant individual's contact details found on the Internet.

World Wide Web site:

<http://www.ukneqasli.org>

This contains specific information relating to UK NEQAS for Leucocyte Immunophenotyping.

These should only be used for messages of a specific nature, which only the individual concerned can answer. Mail may not be scanned each day or during holiday periods.

EQA Programme

a) Immune Monitoring programme

The Immune Monitoring programme issues stabilised whole blood with participants required to determine the lymphocyte subsets within the preparation. Participants are required to return absolute counts and percentage values. Performance scores are generated from this data. The scheme issues a variety of CD4 levels over the year. All the preparations used in the Immune Monitoring Scheme are obtained from routine blood donors and have been screened for HIV I and II, HBV, HCV and syphilis using the latest viral screening methods.

b) Leukaemia Immunophenotyping and Diagnostic Interpretation programme

This will comprise of Leukaemia Immunophenotyping (Part A) and Leukaemia Diagnostic Interpretation (Part B). Part A is purely technical and will involve the detection of cell surface antigens on a leukaemic case. Part B is interpretational and participants are provided with detailed clinical data relevant to the case to enable a diagnosis to be made. Therefore, laboratories that use immunophenotyping as part of the process of diagnosis will be required to participate in both parts. Please note that part B may not necessarily be undertaken by either the same laboratory or the same person who undertook part A. Laboratories that perform immunophenotyping only, but report results to a third party who then undertake the final diagnosis, may wish to register the third party with us to undertake part B. This will need local agreement.

The programme issues stabilised leukaemic whole blood (Part A), which can be successfully analysed using either whole blood lysis or ficoll density centrifugation techniques. This programme will issue and examine a wide variety of haematological malignancies and antigens (up to 20 antigens tested per trial). Part B is entirely web based, no samples will be dispatched, although detailed clinical results and digital morphology are provided via the web site.

c) CD34 Stem Cell Quantitation programme

The CD34+ Stem Cell Quantitation programme issues stabilised peripheral blood obtained from patients, following informed consent, who are undergoing stem cell mobilisation. Laboratories are requested to report both percentage and absolute values, although performance scores are generated using only the absolute values. This material can be used with whole blood lysis techniques and sequential gating strategies. The scheme issues a wide variety of CD34 levels.

d) Low Level Leucocyte Counting programme

The Low Level Leucocyte Counting Scheme issues stabilised peripheral blood and stabilised platelet apheresis samples. Participants are requested to report the absolute count of leucocytes in each sample. Performance monitoring has been introduced and is currently in the "pilot" phase.

e) Paroxysmal Nocturnal Haemoglobinuria (PNH) programme (Pilot Phase)

The PNH programme issues stabilised whole blood using material obtained from cases with a known PNH clone. Participants are required to assay for the PNH clone and return results for red cells and/or granulocytes. This programme is in the “pilot” phase at present and is therefore for educational purposes and is not subject to performance monitoring at present.

f) Molecular Diagnosis of Haematological Malignancies programme (Pilot Phase)

The Molecular Diagnosis of Haematological Malignancies programme comprises five sub-programmes for which participants can register individually. A novel lyophilised cell preparation is issued for *JAK2*, BCR-ABL Quantitation and BCR-ABL + AML (t(8;21), t(15;17) and inv(16)) Translocation Identification programmes, and fresh whole blood samples are issued for Post-SCT Chimerism Monitoring and IgH/TCR Gene Rearrangement programmes. Participating centres are asked to extract DNA and/or RNA as appropriate and carry out molecular analysis using their in-house methodologies. Results are currently submitted by post or fax, however the programme should be web-based within the next 12 months. As this programme is in the “pilot” phase at present it is not subject to performance monitoring.

g) Minimal Residual Disease Detection programme (Pilot Phase)

The Minimal Residual Disease Detection programme currently issues stabilised blood, into which has been seeded stabilised leukaemic whole blood or stabilized bone marrow. Participants are provided with the phenotype of the initial abnormal clone and are requested to assay the level of this clone in the EQA sample provided.

Accreditation & Recognition

We have again been awarded unconditional CPA (EQA) accreditation for all our schemes, Immune Monitoring, CD34 Stem cell Enumeration, Low Level Leucocyte Counting, Paroxysmal Nocturnal Haemagloinuria and Leukiaemia Immunophenotyping&Diasgnostic Interpretation (with the exception of the molecular diagnosis of haematological malignancies pilot scheme and the MRD programme) after an inspection in August 2006.

Further information about the EQA Standards may be obtained from CPA (UK) Ltd at 45 Rutland Park, Botanical Gardens, Sheffield S10 2PB, tel 0114 268 6151, fax 0114 268 6251. CPA have a web site at <http://www.cpa-uk.demon.co.uk>.

1.2 The Quality Manual

This Quality Manual describes the Quality Management System of UK NEQAS for Leucocyte Immunophenotyping. Throughout the text there are references to CPA (UK) Ltd Standards (in brackets) and to procedures (indicated by square brackets) written in fulfillment of these standards.

This Quality Manual fulfills two functions. It describes the Quality Management System for the benefit of UK NEQAS for Leucocyte Immunophenotyping own management and staff, and it provides information for users and for inspection/accreditation bodies.

This Quality Manual can be regarded as the index volume to separate volumes of management, laboratory, clinical and quality procedures. The sections of the Quality Manual are arranged so that they equate with the CPA (UK) Ltd Standards (see table below). Under the title of each standard there is a brief description of the way in which UK NEQAS for Leucocyte Immunophenotyping seeks to comply with the particular standard and references are given to appropriate procedures.

The sections of the standards should be seen to relate to each other in the following manner Section A describes the organisation of UK NEQAS for Leucocyte Immunophenotyping and its quality management system which uses resources (Sections B, C and D) to undertake the organization and operation of the programme, together with communication with participants (Sections E,F and G). The quality management system and the examination processes are continually evaluated and quality assured (Section H). The results feed back to maintain, and where required, improve the quality management process and to ensure that the needs and requirements of users are met.

Page in the Quality Manual	Section of CPA Standards
16	A Organization and quality management system
19	B Personnel
20	C Premises and environment
20	D Equipment, information systems and materials
21	E Organization and design of the EQA scheme
23	F Operation of the EQA scheme
29	G Communication with participants
32	H Evaluation and improvement

2 QUALITY POLICY

The Quality Policy of UK NEQAS for Leucocyte Immunophenotyping is stated overleaf and published as separate controlled document to be displayed within the laboratory (room H100D) and office (3 Southbourne Road).

The Quality Policy of UK NEQAS for Leucocyte Immunophenotyping

UK NEQAS for Leucocyte Immunophenotyping is committed to providing a service of the highest quality and shall be aware and take into consideration the needs and requirements of its users.

In order to ensure that the needs and requirements of users are met, UK NEQAS for Leucocyte Immunophenotyping will:

- Operate a quality management system to integrate the organisation, procedures, processes and resources.
- Set quality objectives and plans in order to implement this quality policy.
- Ensure that all personnel are familiar with this quality policy to ensure user satisfaction.
- Commit to the health, safety and welfare of its entire staff. Visitors to the department will be treated with respect and due consideration will be given to safety while on site.
- Uphold professional values and is committed to good professional practice and conduct.
- Commit to comply with all relevant environmental legislation

UK NEQAS for Leucocyte Immunophenotyping will comply with standards set by CPA (UK) Ltd and is committed to:

- Staff recruitment, training, development and retention at all levels to provide a full and effective service to its users.
- The proper procurement and maintenance of such equipment and other resources as are needed for the provision of the service.
- The collection, transport and handling of all specimens in such a way as to ensure the correct performance of laboratory examinations.
- The use of examination procedures that will ensure the highest achievable quality of all tests performed.
- Reporting results of examinations in way which are timely, confidential, accurate and clinically useful.
- The assessment of user satisfaction, in addition to internal audit and external quality assessment, in order to produce continual quality improvement.

Signed on behalf of UK NEQAS for Leucocyte Immunophenotyping

..... **Date**

3 ORGANISATION, RESPONSIBILITIES AND AUTHORITIES

3.1 Relationship to the Host Organisation and Oversight arrangements

OVERVIEW OF THE UK NEQAS ORGANISATION & ADVISORY STRUCTURES

UK National External Quality Assessment Schemes:

- a charitable company limited by guarantee (charity registration number: 1044013; company registration number: 3012351)
- company membership (guarantor) open to those schemes entitled to use the name UK NEQAS
- Executive committee elected from and by the membership
- UK NEQAS pilot schemes may enjoy associate membership

Board terms of reference:

To provide guidance in the following areas:

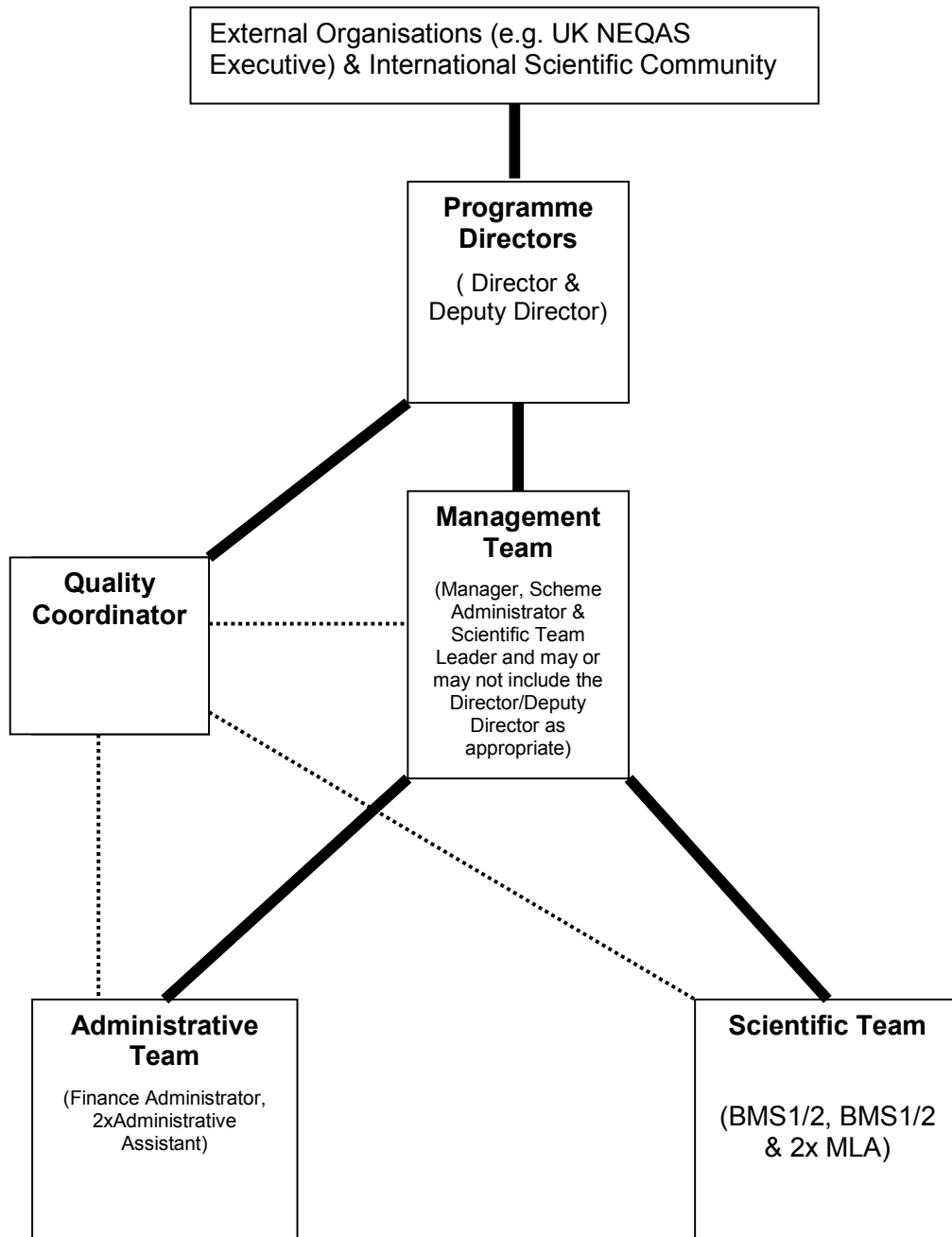
- appointment of UK NEQAS Steering Committee members and Chairmen
- monitoring relevance and appropriateness to patient care of current and projected UK NEQAS activity
- audit of compliance with UK NEQAS Code of Practice (financial and professional)
- approval of UK NEQAS subscription charges (lead purchaser role)

UK NEQAS EXECUTIVE COMMITTEE

The Executive Committee is a group of UK NEQAS Personnel elected by the Consortium to fulfil central co-ordinating and administrative needs. The executive committee has the oversight of full UK NEQAS scheme operation and ensures accountability through Steering Committee appointment to the relevant NQAAP and Joint Working Group. Current membership of the committee is available from <http://www.ukneqas.org.uk>

3.2 Organisation and Responsibilities within UK NEQAS for Leucocyte Immunophenotyping.

UK NEQAS for Leucocyte Immunophenotyping is an independent department. A medical consultant and a consultant clinical scientist are in charge of UK NEQAS for Leucocyte Immunophenotyping. (B1 Professional direction)



Staffing

The Leucocyte Immunophenotyping EQA programme is directed by Professor John T Reilly (Consultant Haematologist) who has worked at the unit since 1987. Professor Reilly is assisted by the programme deputy director, Dr David Barnett (Consultant Clinical Scientist) and programme manager Mr. Liam Whitby. The scheme recruited Mr. Liam Whitby (Biomedical Scientist Team Leader) in 1998 owing to the continuing expansion of the schemes. In 2006, Miss Jane Holden was recruited to develop and oversee the rapidly expanding molecular programme. In 2007 Mrs Alison Whitby (Biomedical Scientist) was recruited to provide a suitable level of qualified staff necessary to ensure the operation of the programmes. In 2009 to ensure a sufficient level of qualified staff the programme recruited Mr Matthew Fletcher (Biomedical Scientist). In 2008 Miss Andrea Jack was recruited as a Medical Laboratory Assistant to assist the scientific staff in the operation of the programmes. Mrs. Joanne Antcliff is the Quality co-ordinator and has worked at UK NEQAS LI since 1998; her duties include quality monitoring of the EQA programmes to ensure current CPA guidelines are met. Miss Sarah Sardinha is the personal secretary to Dr Barnett, she joined the programme in 2007. She is responsible for the production of minutes at steering committee meetings and general administration duties. Further administrative support is provided by Miss Caley Addinall (recruited 2008) and Miss Frances Barnett (recruited 2009). The finance officer is Miss Claire Robinson (recruited 2005) and she is responsible for monitoring of participant subscriptions.

The Sheffield Teaching Hospitals NHS Foundation Trust

Sheffield Teaching Hospitals is managed by the Trust Executive Group who work closely with the Trust Board to make decisions on how the Hospitals should be run. Details of the membership of this group can be found on the Sheffield Teaching Hospitals Website (<http://www.sth.nhs.uk>)

Within the trust management structure UK NEQAS is represented on the monthly meetings of the Directorate of Laboratory Medicine Committee and on the monthly meetings of the Directorate of Laboratory Medicine Management Team.

Local Support

The Leucocyte Immunophenotyping EQA has very close links with the Cell Marker Laboratory (also managed by Dr David Barnett) situated within the Department of Haematology at the Royal Hallamshire Hospital. The scheme also works closely with the National Blood and Transplant Service Centre at Sheffield who kindly provides whole blood samples. The scheme is indebted to all local and regional haematology consultants who allow access to interesting patient material. All material used within the schemes has been approved by the Local Ethics Committee.

External & Professional links

We have close ties with other UK NEQAS operations through the UK NEQAS Consortium (of which Mr. Peter White is currently Chairman). Accountability is detailed in section 3.1 and schemes comply fully with the UK NEQAS Code of Practice appendix 1.

All EQA providers are required to seek advice from, and report to, specialist Steering Committees and Advisory Panels, comprising of expert professionals in appropriate areas of laboratory work, representatives of professional bodies and fellow Directors. The Leucocyte Immunophenotyping EQA schemes currently reports to the Leucocyte Immunophenotyping Steering Committee (SC), which provides advice on overall policy matters. The addresses of SC Panel members are given on the UK NEQAS for Leucocyte Immunophenotyping website (www.ukneqasli.org). Comments or concerns about schemes and their operation are referred to the SC (see complaints procedure section G1). The MDHM Programme also has a specialist Advisory Group providing advise in areas of the molecular genetics of haematological malignancies.

A Organisation and Quality Management System

A1 Organisation and management

The organisation and management of UK NEQAS for Leucocyte Immunophenotyping is detailed in section 3 of this quality manual

A2 Needs of participants

The needs of the participants are kept under constant review. This is actioned by holding participants meetings and staff lecturing at national and international meetings, which always include a forum for feedback on each EQA programmes effectiveness. Meetings of all UK NEQAS for Leucocyte Immunophenotyping staff are held with discussion covering the full range of UK NEQAS for Leucocyte Immunophenotyping activities. They are translated into requirements which form the focus of objective setting and planning (A5 Quality objectives and plans) within the quality management system. Assessment of user satisfaction and complaints (H2 Assessment of user satisfaction complaints) is conducted on a regular basis and consideration of the findings form part of the annual management review (A11 Management review).

A3 Quality policy

The Quality policy of UK NEQAS for Leucocyte Immunophenotyping is detailed in section 2.0 of this quality manual

A4 Quality management system

The components and relationship within the Quality management system are described in section A of this Quality Manual and under standards A5 to A11

A5 Quality objectives and plans

The UK NEQAS for Leucocyte Immunophenotyping Programme Director and Deputy Programme director define the quality objectives of UK NEQAS for Leucocyte Immunophenotyping in consultation with individual staff members and are responsible for ensuring that plans are made to meet these objectives. The management review (see A11 below) which is undertaken on an annual basis determines whether the objectives have been successfully completed and provides an opportunity for revising such objectives and plans and the functioning of the quality management system.

A6 Quality manual

This standard is fulfilled by the production of this Quality Manual

A7 Quality Manager/ Co-ordinator

The Quality Co-ordinator for UK NEQAS for Leucocyte Immunophenotyping is: Mrs Joanne Antcliff who works with the UK NEQAS for Leucocyte Immunophenotyping Team to ensure the proper running of the Quality Management System. Mrs Antcliff reports directly to the Programme Deputy Director and is responsible for highlighting any quality issues. She is also responsible for the implementation of quality systems and she reports

all of her findings to the annual management review. She is also responsible for the auditing of feedback from participants and for ensuring that the service provision is altered to meet any changes in needs that may arise. In addition the quality manager is also responsible for control of Standard operating procedures used within the department

A8 Document control

This standard is fulfilled by the use of the iPassport quality management system. Standard operating procedures are stored in two formats: (1) Electronic copies that are stored the secure iPassport database to prevent unauthorized access and (2) Hardcopy standard operating procedures that are produced by the quality manager from the electronic database. Hardcopy versions are produced from the iPassport system and are identifiable from the unique document ID produced automatically by the iPassport system. All documents have a unique identification numbers and feature their date of issue. As a result all procedures in use are controlled and identifiable. All standard operating procedures are reviewed on a bi-annual basis or sooner if new techniques are introduced. When procedures are updated the expired versions are removed from circulation by the quality manager, the hardcopy is destroyed and the electronic version is automatically held in a secure section within iPassport. A master list is held by the quality manager that contains details of all protocols. This procedure is documented internally by SOP Procedure for the Control of Documents and SOPs.

A9 Control of technical and quality records

This standard is fulfilled by the Quality Co-ordinators role. The technical records ensure that all samples issued by the centre are uniquely identified and the materials they are produced from are also allocated a unique identification code. All reagent batch numbers used in the production of samples, details of staff involved and sample result dotplots are also logged and this information is retained on a rolling 12 month basis. Flow cytometric dotplots from more interesting cases are retained for longer periods for educational purposes. Quality records are also generated in the evaluation of samples for use in the programmes. These records are stored, either as hardcopies or as electronic documents again on a rolling 12 month basis. Access to the records is not restricted as the right to use for all staff is essential to the implementation of the quality management system. This procedure is documented internally by SOP Procedure for the Control of Quality and Technical Records.

A10 Control of clinical material

This standard is fulfilled by the standard operating procedures for containment and safe disposal of clinical material and is overseen by the Deputy Programme Manager and supported by Senior Biomedical Scientists

Materials

Sources of blood - The majority of blood used by the scheme is obtained from the Blood and Transplant Service (NHSBT) under long-standing agreements. The Leukaemia Immunophenotyping (Part 1), CD34 Enumeration, Paroxysmal Nocturnal Haemoglobinuria, Minimal Residual Disease and IgH/TCR gene re-arrangement programmes depend on peripheral blood samples collected from patients after informed consent.

Stability of EQA sample material – Blood samples issued in the CD34 Stem Cell Quantitation Programme, Immune Monitoring Programme, Paroxysmal Nocturnal Haemoglobinuria Programme, Leukaemia Immunophenotyping and Diagnostic Interpretation Programme, Minimal Residual Disease Detection Programme and Low Level Leucocyte Counting Programmes are stabilized using a patented method owned by Sheffield Teaching Hospitals Foundation Trust. The use of the stabilized blood produced by the patented method is reviewed in two key papers.

1. Barnett D., Granger V., Mayr P., Storie I., Wilson G.A., Reilly J.T. (1996) *Evaluation of a novel stable whole blood quality control material for lymphocyte subset analysis: Results from the UK NEQAS Immune Monitoring Scheme. Cytometry (Communications in Clinical Cytometry) 26:216-222*
2. Barnett D., Granger V., Storie I., Peel J., Pollitt R., Smart T., Reilly J.T. (1998) *Quality Assessment of CD34⁺ Stem Cell Enumeration: Experience of the United Kingdom National External Quality Assessment Scheme (UK NEQAS) Using A Unique Stable Whole Blood Preparation. British Journal of Haematology 102:553-565*

Safety - Blood collected by the NHSBT is subject to the same current UK safety testing procedures as blood used for transfusion. Other materials are not tested and participants are regularly informed of this fact. Please heed the safety notice below.

Important Safety Notice

As for clinical specimens, UK NEQAS samples should be handled as if capable of transmitting infection. Appropriate procedures should be used to minimise contact with samples and for their disposal.

Initial analysis & storage - Primary materials should be stored at 4°C . All material should be allowed to attain ambient temperature before breaking any seal and testing (minimum of 1 hour). Where appropriate materials should be thoroughly mixed before use.

Use of residual material - The materials distributed are provided as specimens for the sole purpose of enabling external quality assessment at the recipient's laboratory during the current distribution. They do not constitute in vitro medical diagnostic devices (IVDs), and no claim is made that they may be suitable for any other purpose. Resale or distribution to third parties is strictly prohibited. It is accepted, however, that residual material may be retained by the participant and used for method evaluation, although it is recommended that fresh samples are obtained from us (see below) for this purpose. If materials are to be used in research which is expected to be published, or if participation forms part of contractual agreements with third parties (e.g. in drug trials), written consent must be obtained from the scheme's Director on each and every occasion.

Repeat samples - Single samples or sets from a particular distribution are usually freely available at no charge to participants who may wish to check aberrant results or evaluate new methods. We reserve the right to ask why repeat samples are needed and limit their supply if this would compromise the service to other participants.

A11 Management review

The UK NEQAS for Leucocyte Immunophenotyping senior management conduct an annual review which considers the following items of information

- a) Reports from the Deputy Manager and Senior Biomedical scientists
- b) Assessment of participant satisfaction and complaints (H2)
- c) Internal audit of quality management system (H3)
- d) Internal audit of EQA scheme operation (H4)
- e) Internal audit of quality improvement (H5)
- f) Reports of assessments by outside bodies (CPA)
- g) Status of preventive, corrective and quality improvement actions (H5)
- h) Major changes in organisation and management, resource (including staffing) or process.

Records are kept and key objectives for subsequent years defined and plans formulated for their implementation.

B PERSONNEL

B1 Professional direction

Detailed in organisation chart 3.1

B2 Staffing

Detailed in organisation chart 3.2

B3 Personnel management

This standard is fulfilled by procedure the role of the Deputy Director/ Programme Manager and supported by the Department of Human Resources of Sheffield Teaching Hospitals Foundation Trust.

B4 Staff orientation and induction

Records of staff orientation and induction are kept using Staff Induction record form and kept in the staff record folder (filing cabinet in Deputy Director/ Programme Manager's office). These courses are run by the NHS Training and development at Pegasus house.

B5 Job descriptions and contracts

Each member of staff has a job description prepared and is stored on the central folder of the file server. All members of staff have contracts of employment with Sheffield Teaching Hospitals NHS Foundation Trust.

B6 Staff records

Personal staff records are kept by the Deputy Director/ Programme Manager.

B7 Staff annual joint review

Each member of staff has an annual review by regular staff appraisals.

B8 Staff Meetings

These are scheduled monthly and minutes taken and disseminated to all staff

B9 Staff training and education

Staff training and education is organised by Ms J Holden and each staff member is responsible for the upkeep of their own Continuing Personal Development (CPD) records.

C PREMISES AND ENVIRONMENT

C1 Premises and environment

UK NEQAS for Leucocyte Immunophenotyping has an office located at 3 Southbourne Road and laboratories at the Royal Hallamshire Hospital (Room H100D). We also use molecular analysis facilities at the Sheffield Children's Hospital and cell culture facilities in the Sheffield Medical School.

C2 Facilities for staff

The office at 3 Southbourne Road has facilities for staff to prepare drinks and light meals in a shared separate kitchen. The laboratory (Room H100D) is in close proximity to all the staff facilities provide by The Royal Hallamshire Hospital.

C3 Facilities for storage

Two storage archive areas are located at 3 Southbourne Road, overhead shelving used at the laboratory in room H100D

C4 Health and safety

The Health and Safety co-ordinator is Mrs J Antcliff. All new staff are taught the basics of Health and Safety as part of the Induction course. Established staff are encouraged to keep skills up to date by attending refresher courses. All staff attend monthly Health and Safety meetings held at UK NEQAS in the conference room.

D EQUIPMENT, INFORMATION SYSTEMS AND MATERIALS

D1 Procurement and management of equipment

Overall responsibility for procurement is with the Deputy Director (Dr D Barnett). Management of computer hardware and software and the management of laboratory and office equipment is the responsibility of Mr L Whitby.

D2 Management of data and information

This is the responsibility of Mr. L Whitby, with software support and web service maintenance provided by KPMD Ltd (Sheffield).

Data Processing

Data handling - All data processing is managed by bespoke software produced by KPMD Ltd (written in Microsoft Access VB.net). This system was commissioned in October 2003. The Programme Management system enables handling of all the UK NEQAS for LI programme in operation, with flexible configuration of all parameters, scoring systems and report output. Within the department, a network of workstations and printers enables staff to perform any EQA programme task. New software developments are being planned to enable schedule processing, define special listing and tabulation parameters for non-routine data analysis and reporting.

The telephone, fax or email trial enquiry

All correspondence from participants is recorded electronically in the UK NEQAS for Leucocyte Immunophenotyping database and prioritised with regard the degree of importance. UK NEQAS for LI aim to respond to all enquiries within 24 hours of the initial contact. Numbers of incoming and outgoing telephone calls are automatically logged on the file server.

D3 Management of materials

It is the responsibility of Mr L Whitby to ensure adequate levels of all routinely used reagents and materials are maintained.

E ORGANISATION AND DESIGN OF EQA SCHEME

E1 Organisation, scope and strategy

All information relating to the day to day activities of the EQA schemes, the programmes operated and the staff can be found on the UK NEQAS for Leucocyte Immunophenotyping website at www.ukneqasli.org

E2 External professional advice

There is a formally constituted Steering Committee, membership of which is given on the UK NEQAS for Leucocyte Immunophenotyping website (www.ukneqasli.org). This Steering Committee meets twice a year to advice on the running of the EQA programmes. The programme also has a Specialist Advisory Group providing advice in areas of the molecular genetics of haematological malignancies.

E3 Extent of participation

Participation in the EQA programmes is not limited to any geographical region or laboratory type. Participation from non-UK laboratories is actively encouraged.

E4 EQA scheme design; sample distribution and analysis of results

Trial samples are conveyed to participants using First Class postal service, commercial couriers (e.g. TNT, DHL or FEDEX) and participants are electronically notified of the trial being in transit.

Routine Scheme Operation

- **Distribution cycle** - All schemes operate according to a regular cycle of activity, based nominally on 6 distributions per year. A distribution has a numeric identifier with fixed sample dispatch and results return dates. When the distribution is generated, a 'snapshot' of participation (labs, analytes & methods) is taken for the duration of that distribution cycle. Changes in participation that occur during the current distribution cycle are incorporated before data processing.
- **Pool distribution policy** - It is intended that within any given cumulative performance assessment period a number of different samples will be distributed that assess the range of analytes agreed by our expert groups and advisors to be clinically important. How successfully this policy is delivered in practice also depends on scheme size and availability of material.
- **Distribution dates** - We operate on a rolling 8-week cycle for most schemes. Please be aware that in particular the Leukaemia Immunophenotyping and Diagnostic Interpretation programme is subject to minor changes depending upon material availability and operational circumstances. Generally no distributions will be made in December.
- **Live trial window**. – The Immune Monitoring, CD34 Quantitation, Leukaemia Immunophenotyping (Part 1), PNH are "live" for 15 working days from the issue of the trial until the closing date. The Low Level Leucocyte Counting and Leukaemia Diagnostic Interpretation (Part 2) programmes are "live" for 10 working days from the issue of the trial until the closing date. Currently all molecular programmes (except for BCR-ABL and AML Translocation identification programme) are live for 20 working days from the issue of trial until closing date. The BCR-ABL and AML Translocation Identification is live for 25 working days from the issue of trial until closing date.
- **Participant notification** – Participants who have registered for the web based results entry and report issue service will be informed electronically via the UK NEQAS for LI programme management system when a new trial has been issued.
- **Method classification** - A crucial element of participation for all schemes is the correct notification of method, since performance scoring may be method-based, and the provision of accurate method-related information is an important element of the service. Considerable effort is expended by UK NEQAS staff to ensure the accuracy of method input. Participants are required to co-operate with this process by completing fully and legibly all method questionnaires and informing us of errors, omissions or changes at the earliest opportunity.

Calculation of mean or median target values

Target values are crucial to scheme design and usefulness and are the basis for accurate performance scores. To eliminate the distorting effect of grossly atypical results, outliers are trimmed from both tails of the ranked data set, with a corrected estimate of dispersion (SD or CV) usually by the method of Healy (1979) to allow for the removal of extreme values which are not 'true' outliers. For a full description of each scheme's scoring system

please refer to appendices 3 to 6. The data processing for individual schemes is conducted using individually configured modules within the Core System.

Healy M.J.R. Outliers in Clinical Chemistry Quality-Control Schemes. (1979) Clin. Chem. 25:675 - 677

E5 Assessment and evaluation of performance

Each of the following programmes: Immune Monitoring, CD34+ Stem Cell Enumeration, Leukaemia Immunophenotyping and Diagnostic Interpretation and Low Level Leucocyte Counting have scoring systems. Details of how the scoring systems work and acceptable limits of performance can be found in appendices 3 to 6.

E6 Sub-contractors and collaborators

All work is performed in house.

F OPERATION OF THE EQA SCHEME

F1 Preparation of test items

Stability of EQA sample material – blood samples issued in CD34 Stem Cell Quantitation Programme, Immune Monitoring Programme, Paroxysmal Nocturnal Haemoglobinuria Programme, Leukaemia Immunophenotyping and Diagnostic Interpretation Programme, Minimal Residual Disease Detection Programme and Low Level Leucocyte Counting Programmes are stabilized using a patented method owned by Sheffield Teaching Hospitals Foundation Trust. All blood is obtained following informed consent and in line with local ethical committee procedures. The use of the stabilized blood produced by the patented method is reviewed in two key papers.

1. *Barnett D., Granger V., Mayr P., Storie I., Wilson G.A., Reilly J.T. (1996) Evaluation of a novel stable whole blood quality control material for lymphocyte subset analysis: Results from the UK NEQAS Immune Monitoring Scheme. Cytometry (Communications in Clinical Cytometry) 26:216-222*
2. *Barnett D., Granger V., Storie I., Peel J., Pollitt R., Smart T., Reilly J.T. (1998) Quality Assessment of CD34⁺ Stem Cell Enumeration: Experience of the United Kingdom National External Quality Assessment Scheme (UK NEQAS) Using A Unique Stable Whole Blood Preparation. British Journal of Haematology 102:553-565*

Safety - Blood collected by the NHSBT is subject to the same current UK safety testing procedures as blood used for transfusion. Other materials are not tested and participants are regularly informed of this fact. Please heed the safety notice below.

Important Safety Notice

As for clinical specimens, UK NEQAS samples should be handled as if capable of transmitting infection. Appropriate procedures should be used to minimise contact with samples and for their disposal.

Initial analysis & storage - Primary materials should be stored at 4°C . All material should be allowed to attain ambient temperature before breaking any seal and testing (minimum of 1 hour). Where appropriate materials should be thoroughly mixed before use.

F2 Packaging and accompanying documentation

- Packaging & mailing - Single samples or sets (depending on the scheme) for each distribution are mailed to the registered scheme contact as appropriate. First class mail is used for the UK, and airmail for outside the UK. Packaging complies with current UK , IATA and UN602 legislation for the mailing of pathological material. All tubes are labeled with the scheme, distribution identifier, and sequential sample number. Courier transport can be arranged if required but the cost of this service must be met by the participant.
- Results documents - All schemes have distribution-specific results documents that are individual to each participant. These carry the UK NEQAS laboratory code and in some cases method confirmation, as well as messages about sample handling and return of results. They are available as either paper hard copy with the samples or electronically via the UK NEQAS for LI website for participants who have registered with the web service. They are under constant review to make them easy to understand and use. They may change from time to time to reflect improvements.
- Sample handling - The general rule is that participants should treat EQA samples identically to those from patients. However, it is recognised that some minor adjustment of forward and side scatter gains may be required on some flow cytometers as an inevitable consequence of any stabilization process. Furthermore, the stabilized sample may not be compatible with some haematology analysers. In order that there should be uniformity of handling amongst participants, it is recommended that if an assay is not to be performed on the day of receipt, EQA samples should be stored as defined in section F1. Unless instructed otherwise, participants should ensure that ALL samples in a given distribution are analysed on the same day, with the same batch of reagents, and in the same analytical 'run', batch or calibration cycle, to ensure that unknown additional variability is not introduced.

F3 Receipt of results

Return rate - According to Advisory Panel requirements for acceptable performance, participants must return 75% of all possible results within a cumulative reporting period. Thus, a participant in the immune monitoring scheme receiving 2 samples bi-monthly (all of which are scored) must return results for at least 5 samples during the 6 month assessment period.

Those participants who are registered for web submission can submit results on-line.

Participants who are not registered for web service can post or fax back the trial results on the pro-forma issued with the samples

Overseas participant who return their results by post should allow an appropriate period of time (a minimum of 7 days prior to the closing date) for their results to reach UK NEQAS for LI

Since the introduction of the UK NEQAS for Leucocyte Immunophenotyping web site www.ukneqasli.org participants are actively encouraged to submit their results electronically.

Result reporting procedure for hardcopy or fax returns.

- Results should be entered in the units shown onto the correct results document, taking care to match sample numbers and avoid transcription or transposition errors.
- Figures and decimal points should be unambiguous and bold enough to be easily read by data entry staff, especially after faxing.
- Avoid obscuring results documents with sample or bar code labels.
- It is advisable to fax results from within the UK followed by a postal hardcopy, fax transmission is essential for non-UK participants at all times.

We recommend that any participants returning results by fax confirm the results have been received by telephoning **UK NEQAS for LI**.

- Late results may be accepted after the return by date but before the reports are mailed. These will be incorporated into cumulative analysis for the next distribution. Results received after mailing of reports will not normally be accepted.
- Participants should always check the method, where this is printed on their results document, and make a correction if a change has occurred, marking whether this is for the current distribution only or a permanent change. Retrospective changes should give the start date of the change, with UK NEQAS distribution number.

Amendments prior to data processing - Participants who discover an error in their reported results before the reporting deadline should contact us immediately by telephone or fax. Amended copies of already faxed or posted results documents should be clearly marked 'Amended Copy' with the change unambiguously highlighted.

As each distribution is processed, UK NEQAS staff check the resulting data for integrity and consistency of results, and any unexpected shifts in method-related values which might signal a clinically-important shift in diagnostic products. If any are identified, the manufacturer is contacted so that the findings can be discussed and a preliminary brief report can be made.

F4 Data entry and statistical analysis

Result data for trials are either entered into the UK NEQAS system via the web entry system or are entered locally by UK NEQAS staff.

For web entry the participant is directly responsible for ensuring accurate data entry prior to submission of results. For local results the data is entered into the NEQAS system by clerical staff and then cross-checked by senior scientific staff to ensure accuracy of data entry.

All data is validated by senior scientific staff prior to generation of trial statistics and any grossly erroneous data is excluded from the statistical analysis, although a performance score will still be generated.

Details of the statistical procedures used to generate target values and performance scores can be found in appendices 3 to 6.

For all UK participants results received after the closing date will not be entered into the database and the corresponding report will highlight the nil-return. For non-UK participants

late results can be received in exceptional circumstances, such as postal delays, by prior arrangement only.

F5 Reports to participants

Participants who have registered for the UK NEQAS for Leucocyte Immunophenotyping web service are electronically contacted and informed that the trial report is completed. Participants can then view their own individual report via the UK NEQAS for Leucocyte Immunophenotyping web site and print a copy. These participants will have the trial report available for downloading within 5 working days of the trial closing date and will not receive a printed report directly from UK NEQAS for LI. This applies to all programmes with the exception of the Leukaemia Diagnostic Interpretation and Paroxysmal Nocturnal Haemoglobinuria programmes which is extended to 30 days from closing date as these reports are written with the assistance of external experts.

Reports and their interpretation

Reports - Schemes' reports are the main interface with participants, and a great deal of effort has gone into making these informative and easy to interpret. Report production will be within 7 working days of a trial closing date, to ensure rapid feedback to participants of any potential problems. All schemes use laser-printed A4 sheet that display the data in a number of discrete tabular and graphic formats shared across related schemes. Examples are available on request, but all reports share most of the following features:

- Distribution summary (tabular)
- Overall performance summary (tabular & graphical)
- Current performance scores and limits of acceptable performance
- Individual results obtained (tabular)
- Histogram of all results (individual results marked)
- Table of method-related results (means, SDs, CVs or median and centile ranges where appropriate)
- Graphical or tabular interpretation of cumulative performance score where appropriate.
- Tabular indication of method-related performance scores
- Interpretation of routine scheme reports & performance scores -

Guidance documents are available on request for schemes using the principal types of report format and scoring systems employed. These should be studied carefully, and our staff consulted if clarification is needed. All are under continuous review with the intention to extend harmonisation of both aspects of scheme design throughout our schemes and in collaboration with other UK NEQAS centres. The principal components of report interpretation may be summarised as follows:

Method comparisons

- Reports may include tables of all methods with >5 users. Included will be an estimate of the central tendency of the method group (e.g. median) and its dispersion (e.g. inter quartile range) if appropriate. It is often useful for participants to compare the performance of their method in relation to others.

Result validation

- Participants should check that they have received the correct report for their laboratory. Mistakes do occur though these are very rare. Telephone us immediately and give the code number of the report actually received and your own, then destroy the incorrect report. A new report will be issued to both laboratories immediately.
- The results for that distribution should be checked to ensure that they are the ones returned by your laboratory. Mistakes can occur if figures are misinterpreted (especially if faxed). UK NEQAS for LI should be informed immediately so that the necessary corrections can be made and a new report issued.
- It is crucially important that participants' methods (and sub-methods, instruments, reagents, calibrants where appropriate) are accurately identified. Any apparent discrepancies should be reported immediately.

Current distribution

- Use the distribution summary pages to examine the deviation of your results from the mean (or median). If deviations are consistent with usual overall or method-related bias and cumulative scores remain stable and within acceptable limits, then it may not be necessary to examine analyte-specific pages in detail. If, however, there are unusual deviations for certain analytes or types of material which appear not to be shared by other users of the method, then detailed examination of the problem area will be required. If these are very large, then non-analytical errors should be suspected.
- When examining analyte-specific pages, participants should relate their results to the overall and method-related distribution of results for each sample as indicated by the histogram and table of method means and CVs. Apparent discrepant results that lie in the tails of the distribution might signify a non-analytical error, others that lie just within the distribution may simply reflect atypical, but not abnormal, variation.

Cumulative performance

- One of the main purposes of a cumulative performance score is to 'smooth out' the natural variation in deviations from target values over a number of distributions, by trimming extreme values and deriving the overall bias. Thus, when interpreting the cumulative elements of reports, it is important to note that (a) a small number of atypical results is unlikely to affect overall scores, and (b) aberrant results which are numerous enough to affect performance scores will take some time to work their way out of the scoring 'window'.
- The principle concern of EQA is the overall bias of participant results and the consistency (variability) of this bias over time with different materials and different

analyte concentrations. Only Internal Quality Control (IQC) can give a clear assessment of analytical imprecision.

- When interpreting cumulative scores, participants should look first for atypical results in a single isolated distribution (as above) and relate these to IQC data on the day of analysis, and then for shifts or trends over a number of distributions that might indicate a method- or instrument-related problem. Attempts should be made to correlate trends and/or shifts in bias with IQC data, which in turn should indicate whether changes in personnel, data reduction, procedures, calibration, reagent batches or instruments are implicated

Acceptable performance criteria (for UK laboratories only)

As previously described, schemes are required to provide information on persistent unsatisfactory performers **in the UK** from clinical NHS or clinical private sites to the National Quality Assurance Advisory Panel (NQAAP) for Haematology and Immunology. Limits for acceptable performance scores are set by the NQAAP after due deliberation and consultation with the Scheme Director and Steering Committee (SC), to reflect the state of the art of analysis and encourage improvement. Special procedures are used to identify those laboratories that have breached these limits on a set number of occasions within the cumulative reporting period. Current limits for our schemes are given in Appendix 3 to 6. Action taken on unsatisfactory performers is described in section F5 "Performance surveillance and Advisory Panel liaison".

Performance Problems

Non-analytical errors

These are defined as 'blunders' made by participants which appear as anomalous results (which may or may not be classified as outliers), and may fall into the following categories:

- Assaying the wrong samples
- Assaying the right samples in the wrong order
- Incorrectly transcribing laboratory results from computer systems or worksheets to results documents
- Use of incorrect units and/or conversion factors
- Technical errors, e.g. incomplete mixing, faulty sampling/pipetting, double addition etc

It is important to note that atypical results that derive from assay failures that are recognised as such only after receipt of the UK NEQAS report (i.e. were not detected by IQC procedures) are not blunders.

Performance surveillance and Advisory Panel liaison (for UK laboratories only)

We are obliged to report to the NQAAP for Haematology or Immunology (as appropriate), any **UK** participant whose cumulative performance score moves outside acceptable limits on a set number of occasions within a cumulative scoring period, or who fail to return sufficient results. The UK NEQAS for LI programme management system is used to

generate a list of such laboratories for each scheme or analyte. The performance of each laboratory identified is then reviewed in association with any correspondence between Director/Manager and the participant, and a decision made on further action. This may be just to monitor, to stimulate dialogue between Director/Manager and participant and monitor improvement in performance, or to suggest that the Panel Chairman should make contact.

The latter course of action is relatively rarely undertaken and begins with a first Panel letter on an anonymous basis (usually sent via our centre using the participants code only) inviting the participant to make contact to discuss action to correct the poor performance. If a satisfactory response is made and improvement in performance ensues, no further action is taken. If poor performance persists or no response is made, then a second Panel letter (direct from Panel Chairman to Head of Department with lab code disclosed) is written requesting that decisive action is taken to re-establish satisfactory performance; this may include a site visit by Panel members. If this fails the Joint Working Group may take further action as detailed in appendix 2 (which gives the full conditions of participation). Where poor performance is purely method-related (e.g. all users have a high BIAS), Directors will normally work directly with manufacturers to assist with correction of any problem.

G COMMUNICATION WITH PARTICIPANTS

G1 Arrangements for participation

The UK NEQAS for Leucocyte Immunophenotyping website (www.uknegasli.org) and this quality manual are designed to be used in combination as a participants' manual.

The terms and conditions of participation and responsibilities of participants can be found in appendix 2 of this quality manual.

In addition there is the following guidance for participants:

- **Eligibility** - UK NEQAS services are designed principally for UK public and private sector clinical laboratories serving clinicians and patients. Non-UK clinical laboratories, those with purely research or industrial roles, manufacturers of diagnostic instruments and reagents, and other laboratories are also welcome to participate. All UK clinical service laboratories must agree in writing to current Joint Working Group (JWG) Conditions of Participation (Appendix 2).
- **Participation period** - Participation in all Leucocyte Immunophenotyping EQA schemes is deemed to be continuous with automatic annual renewal and invoicing for subscription fees for each NHS financial year (1st April to 31st March), unless we are advised to the contrary in writing in advance of annual renewal. However, at the commencement of each year all participating laboratories are required to fill in an update form and sign an agreement for continued participation under the terms and conditions stated in the UK NEQAS Directory. Participation may begin at any time during the year with pro rata charges made.

- Enrolment procedure - Participation begins following receipt of correctly completed enrolment pro forma sent in response to a formal request to participate. The pro forma will gather full details of the participating laboratory. As indicated above, enrolment may take place at any time.
- UK NEQAS Participants code - On enrolment, each participant is given a unique UK NEQAS laboratory code (common across all schemes operated by the UK NEQAS for Leucocyte Immunophenotyping), which remains associated with that participant indefinitely. Participants may register with more than one analytical area (e.g. two flow cytometers). Laboratories at multiple sites but administered by a single department may receive separate codes. Re-attribution of codes and data can be accomplished where laboratories close, merge or de-merge.
- Charges - Annual subscription charges are based on the full actual costs of providing EQA services according to the not-for-profit terms of the UK NEQAS Code of Practice. As such they are subject to continuous review with any increase justified to the UK NEQAS Board before they can be implemented. Current charges are available on request.
- Refunds - No refunds of subscription charges can be made.
- Confidentiality - The fact of participation, raw data and performance scores are confidential between the individual participant and UK NEQAS staff. Performance scores (and some relevant raw data) may be shared by UK NEQAS with the relevant Advisory Panel under defined circumstances (section F5 Performance surveillance and Advisory Panel liaison) as part of the routine reporting of persistent unsatisfactory performance. This data may be shared with local management, regional QA officers, accrediting bodies, and suppliers of equipment and reagents where appropriate and necessary, but only with the participant's explicit permission. UK NEQAS reports are copyright and may not be copied, distributed, published or used for publicity and promotion in any form without the written consent of the scheme Director on each and every occasion, though the participant may share performance data with individual clients (e.g. GPs, clinicians, pharmaceutical companies) without consultation. UK NEQAS participant codes should not be disclosed to third parties.

The UK NEQAS code of practice to which this programme adheres can be found in appendix 1.

Details of scheme design for all of the programmes operated by this centre are freely available via the website (www.ukneqasli.org)

Participants are able to contact UK NEQAS for Leucocyte Immunophenotyping via any of the following methods: telephone, fax, written, email or VOIP. Full contact details for all staff are provided on the website. All communications between participants and UK NEQAS are logged in the UK NEQAS database and electronic images of all hardcopy communication are also retained. Details of any actions taken resulting from communications are also logged.

Complaints

Most queries received by UK NEQAS consist of minor misunderstandings or problems with specimens and reports that can usually be resolved over the telephone by any member of staff. If difficulties persist, then participants with continued justified cause for complaint about any aspect of the service should communicate their concerns immediately to the relevant member of senior staff, preferably in writing. A feedback form is available for this purpose from the publications section of the UK NEQAS LI website. However a preliminary telephone call may assist in clarifying the issue and establishing the requisite action. Where the complaint is about scheme logistics, then the Scheme Manager is the appropriate point of first contact. Where the matter is related to performance assessment and scheme design, the Scheme Director is more appropriate. If the complaint concerns the conduct of a member of UK NEQAS staff, then the Director should be contacted.

It is essential that when a complaint is lodged by whatever communication route that the participant states in the communication that they wish to complain.

Complaints are logged, and the action taken recorded and audited by the Quality Coordinator.

If matters remain unresolved, or the action taken by us is not satisfactory to the complainant, the next step is to refer the complaint to the Chairman of the Steering Committee. If the issue concerns performance assessment, the Chairman of the Advisory Panel may also be contacted.

Where lack of compliance with CPA (EQA) Standards is suspected by the complainant, then the Chief Executive of CPA (EQA) may be contacted. Similarly, where the UK NEQAS Code of Practice itself is the issue of concern, the Chairman of the UK NEQAS Board may be appropriate. In all cases, UK NEQAS staff will provide the names and addresses of the appropriate individuals

G2 Communication procedures and participant feedback

Participants are able to contact UK NEQAS for Leucocyte Immunphenotyping to discuss any issues related to the programmes. All calls of this nature will be transferred to a senior scientific member of staff. Alternatively a feedback form is available for feedback from the publications section of the UK NEQAS LI website.

Details of the contact and complaints procedures can be found in G1.

The trial reports issued to participants may feature conclusions designed to highlight any relevant scientific or technical issues to participants.

H EVALUATION AND IMPROVEMENT

H1 Assessment and improvement processes

This is actioned by having an annual Participants meeting, which always include a forum for feedback on each EQA programmes effectiveness. Regular meetings of all UK NEQAS for Leucocyte Immunophenotyping staff are held, with discussion covering the full range of UK NEQAS for Leucocyte Immunophenotyping activities. Correspondence from participants is discussed.

There is an internal audit procedure in place to assess both the quality management system and the EQA scheme operation. These findings are made available to all staff and are discussed at the management review.

H2 Assessment of participant satisfaction and complaints

All complaints and major comments made by participants are regularly reviewed at staff and steering committee meetings. All actions resulting from these reviews are logged.

UK NEQAS for Leucocyte Immunophenotyping performance targets for the number of trials issued and the time to issue reports to participants are regularly monitored.

The clinical relevance of the EQA programmes are regularly reviewed at steering committee level and the programme designs may be altered accordingly.

H3 Internal audit of quality management system

The UK NEQAS for Leucocyte Immunophenotyping senior management, in conjunction with the Quality Coordinator conduct regular internal audits of the quality management system. All audits are documented by the Quality Coordinator and details of non-conformities and deficiencies are highlighted. Any appropriate corrective action(s) are recommended and the implementation of these is monitored.

H4 Internal audit of EQA scheme operation

The UK NEQAS for Leucocyte Immunophenotyping senior management, in conjunction with the Quality Coordinator conduct regular internal audits of the EQA scheme. All audits are documented by the Quality Coordinator and details of non-conformities and deficiencies are highlighted. Any appropriate corrective action(s) are recommended and the implementation of these is monitored.

H5 Quality improvement

All staff engaged in the operation of the UK NEQAS for Leucocyte Immunophenotyping EQA programme are encouraged to seek ways of improving the quality of the EQA service for the benefit of participants and staff.

Systems are in place for staff to report any non-conformities, and these are then investigated by the quality coordinator and appropriate actions implemented.

Working practices are under constant review to reduce the incidence of non-conformities occurring

APPENDIX - 1

THE UK NEQAS CODE OF PRACTICE FOR MEMBER SCHEMES

A. Definitions

A1. The Association is the United Kingdom National External Quality Assessment Service - a company limited by guarantee and a registered UK Charity.

A2. Members of the Association are defined as EQA Schemes or groups of EQA Schemes which have been accepted for membership of the Association.

A3. The UK NEQAS Consortium comprises representatives of member Schemes when they meet as a collective body.

A4. The UK NEQAS Executive Committee means those persons appointed to perform the duties of the Executive Committee as defined in the Memorandum and Articles of the Association. Those that are appointed Directors of the UK NEQAS company are responsible for complying with UK company law; those that are appointed Trustees of the UK NEQAS UK Registered Charity are responsible for complying with UK Charity law.

A5. The Executive Committee is accountable to the Consortium for implementation of the strategy for member Schemes, as agreed by the Consortium at its General Meetings.

A6. The term Organiser means the individual designated by the Executive Committee to be responsible for the design and direction of the member Scheme and accountable to the Executive Committee for its compliance with the UK NEQAS Code of Practice. The term 'Director' may be used by member Schemes to mean Organiser if this is their tradition, provided that there is no confusion in understanding. For example, the distinction must be clear between the Director (head of service) of a department which hosts a Scheme, and the designated Director (Organiser) of the member Scheme, if they are separate individuals.

A7. Scheme Participants may be laboratories or individuals.

B. Membership Procedures

B1. Schemes shall be admitted to membership of the Association by the Executive Committee in accordance with the Memorandum and Articles of Association. Applications for membership shall be made to the Executive Committee on an application form available from the UK NEQAS Company Secretary and shall be accompanied by a signed statement from the Organiser that the Scheme or Schemes complies with this Code of Practice.

B2. Pilot Schemes intended to become member Schemes shall be admitted to Associate membership in accordance with the Memorandum and Articles of Association and will comply with all relevant conditions of this Code of Practice, including E3 where a subscription is charged.

B3. Only those Schemes admitted to full or associate membership of the Association by the Executive Committee shall be entitled to use the service mark "UK NEQAS" and associated logo. Use of the UK NEQAS service mark and logo by member Schemes and third parties is regulated.

B4. A Scheme that fails to comply with this Code of Practice shall be reminded by the Executive Committee of its obligation as a member of the Association and required to rectify the non-compliance. Where a Scheme still fails to comply with this Code of Practice, the Executive Committee may prepare a written case for that Scheme to cease to be a member of the Association. In response, the member shall be offered three months in which to prepare a written case for remaining as a member of the Association. The documents shall be circulated to all members, who will determine, by a majority vote of the Association in General Meeting, whether the member should be expelled from the Association, provided that any member to be so expelled shall also have the opportunity to make representation to the meeting at which the decision is to be made. Any decision to expel a member shall have immediate effect.

C. Member Scheme Management

C1. Participation in the Scheme shall be open to all UK laboratories offering a clinical service for analytes or investigations covered by the Scheme.

C2. The analytes or investigations covered by the Scheme shall be selected on the basis of their clinical relevance.

C3. Schemes shall be independent of any manufacturing and marketing interests in equipment and reagents in the field in which they operate, and any interests in the provision of analytical or other services shall be declared.

C4. The staff involved in directing and operating the Scheme shall be appropriately qualified.

C5. The conditions of participation for UK laboratories providing a direct or indirect clinical service shall be those currently defined by the Joint Working Group for Quality Assurance.

C6. The Organiser of the Scheme shall liaise with a UK NEQAS Steering Committee and/or Specialist Advisory Group comprising appropriate experts, participants and clinical advisers approved by the Executive Committee. Agendas, Minutes and lists of attendees at Steering Committee/Specialist Advisory Group Meetings shall be copied to the UK NEQAS Office.

C7. The Organiser shall monitor those participants failing to maintain acceptable levels of performance and present reports to the appropriate division's National Quality Assurance Advisory Panel (NQAAP), which comprises nominees of the appropriate professional societies and is recognised by the Joint Working Group for Quality Assurance.

C8. The full, realistically calculated costs of operating the Scheme shall be fully recovered from participants' subscriptions. Schemes shall be non-profit making and any operating surplus shall be reinvested in the Schemes.

C9. Management arrangements shall enable continuity of the EQA service to participants.

D. Member Scheme Design

D1. The Scheme's aim shall be to promote optimal patient care by facilitating the availability of reliable laboratory investigations, through provision of objective information on laboratory performance and professional advice and assistance where appropriate.

D2. Schemes shall enable the detection of inadequate performance by participants. The standard of participants with apparent performance difficulties should be improved by education rather than penalty.

D3. Material for investigation shall be distributed regularly at an appropriate frequency and in appropriate numbers, guided by advice from Steering Committee or Specialist Advisory Group.

D4. Evidence shall be available to demonstrate the appropriateness, stability and uniformity (homogeneity) of the material distributed.

D5. The Scheme shall provide rapid turnaround of results and performance data to participants.

D6. A "correct" or target result should be identified and an appropriate (usually quantitative) evaluation of results be presented to allow comparison of individual participants' results with overall results.

D7. The Scheme shall conform to relevant safety standards and transport regulations.

D8. Confidentiality of individual participants' results and performance data shall be maintained except under circumstances specified in the Joint Working Group for Quality Assurance Conditions of Participation for UK clinical laboratories.

D9. The Scheme should share a common participant identification code with other UK NEQASs and co-operate fully with the development and maintenance of a unified participant identification code database. Information in the database shall not be used by member schemes to the detriment of other member schemes.

E. Obligations and Responsibilities of Member Schemes and their Organisers

E1. Organisers of member schemes shall keep the UK NEQAS Office informed of changes in schemes' details and activities. This shall include completion of an Annual Return and mid-year update as appropriate. Changes to scheme details and other information for publication (eg enhancement services and notice of participants meetings) shall be made promptly to the UK NEQAS Office and these amendments checked by Schemes after publication.

E2. Financial returns including annual accounts shall be submitted as required to the Executive Committee. These shall be in a standard format and validated by appropriate supporting documentation indicating agreement and acknowledgement by the budget holder. Full disclosure of all sources of UK NEQAS Scheme income shall be made. In addition, any additional income which supports the viability of the Scheme shall also be stated.

E3. The Scheme shall contribute to the operating costs of the Association's Office and the costs of the services provided by the Office, as determined by the Association and administered by the Executive Committee. This shall include costs of developing and maintaining the UK NEQAS website and unified laboratory code database.

E4. The Organiser of the Scheme shall uphold, support and promote the underlying principles of the Association as embodied in the Memorandum of Association, Code of Practice and policies agreed by the Consortium at Annual General Meetings and Conferences. Organisers shall play a full part in ensuring UK NEQAS is a harmonised, participant-responsive service and shall not damage the reputation of the UK NEQAS organisation as a whole through inappropriate action or inaction.

E5. Organisers shall achieve appropriate accreditation for their Schemes.

E6. All aspects of the work of a member Scheme shall be open to audit conducted by or on behalf of the Association. The purpose of any such audit shall be to assess the management of

the Scheme in its ability to provide a service that complies with the stated aims and Code of Practice of the Association.

E7. Where Organisers of member Schemes also operate other services including non-member Schemes, other than pilot Schemes intended to become member Schemes, the other services shall be financially independent of the member Schemes.

E8. Organisers and staff of member Schemes and members of Steering Committees or Specialist Advisory Groups shall neither operate nor advise any EQA schemes which are in competition with member Schemes.

APPENDIX – 2

Joint Working Group for Quality Assurance : Conditions of EQA Scheme Participation

The Joint Working Group for Quality Assurance (JWG) is a multidisciplinary group accountable to the Royal College of Pathologists for the oversight of performance in external quality assurance schemes (EQA) in the UK. Membership consists of the chairs of the National Quality Assurance Advisory Panels (NQAAPs), the Institute of Biomedical Sciences, the Independent Healthcare Sector, the Department of Health and CPA (UK) Ltd.

1. The Head of a laboratory is responsible for registering the laboratory with an appropriate accredited EQA scheme.
2. The laboratory should be registered with available EQA schemes to cover all the tests that the laboratory performs as a clinical service.
3. EQA samples must be treated in exactly the same way as clinical samples. If this is not possible because of the use of non-routine material for the EQA (such as photographs) they should still be given as near to routine treatment as possible.
4. Changes in the test methodology of the laboratory should be notified in writing to the appropriate scheme organiser and should be reflected in the EQA schemes with which the laboratory is registered.
5. The criteria for *poor performance* and *persistent poor performance* are proposed by the EQA scheme Steering Committee in consultation with the Scheme Organiser and approved by the relevant NQAAP.
6. The identity of a persistently poor performing laboratory will be made available to members of a NQAAP. Normally management of such laboratories will be undertaken by the NQAAPs. However, it may be escalated to the JWG if not resolved by the NQAAP.
7. Samples, reports and routine correspondence may be addressed to a named deputy, but correspondence from Organisers and NQAAPs concerning persistent poor performance will be sent directly to the Head of the laboratory or, in the case of the independent healthcare sector, the Hospital Executive Director.
8. The EQA code number and name of the laboratory and the assessment of individual laboratory performance are confidential to the participant and will not be released by Scheme Organisers without the written permission of the Head of the laboratory to any third party *other than* the Chairman and members of the appropriate NQAAP *and* the Chairman and members of the JWG. The identity of a participant (name of laboratory and Head of Department) and the tests and EQA schemes for which that laboratory is

registered (but *not* details of performance) may also be released by the Scheme Organiser on request to the Health Authority, Hospital Trust/Private Company in which the laboratory is situated after a written request has been received.

9. When a laboratory shows poor performance the Organiser will generally make contact with the participant in accordance with the Scheme Standard Operating Procedure for poor performance. Within 2 weeks of a laboratory being identified as a *persistent poor performer* the Organiser will notify the Chairman of the appropriate NQAAP together with a resume of remedial action taken or proposed. The NQAAP Chairman should agree in writing any remedial action to be taken and the timescale and responsibility for carrying this out. Advice is offered to the Head of the laboratory in writing or, if appropriate, following a visit to the Laboratory from a NQAAP member or appropriate agreed expert.

10. A NQAAP may, with the written permission of the Head of a laboratory, correspond with the Authority responsible for the laboratory, about deficiencies in staff or equipment which, in the opinion of the NQAAP members, prevent the laboratory from maintaining a satisfactory standard.

11. If persistent poor performance remains unresolved, the NQAAP Chairman will submit a report to the Chairman of the JWG giving details of the problem, its causes and the reasons for failure to achieve improvement. The Chairman of the JWG will consider the report and, if appropriate, seek specialist advice from a panel of experts from the appropriate professional bodies to advise him/her on this matter. The Chairman of the JWG will be empowered to arrange a site meeting of this panel of experts with the Head of the department concerned. If such supportive action fails to resolve the problems and, with the agreement of the panel of experts, the Chairman of the JWG will inform the Chief Executive Officer, or nearest equivalent within the organisation of the Trust or Institution of the problem, the steps which have been taken to rectify it and, if it has been identified, the cause of the problem. The Chairman of the JWG also has direct access and responsibility to the Professional Standards Unit of the Royal College of Pathologists.

12. Problems relating to EQA Schemes, including complaints from participating laboratories, which cannot be resolved by the appropriate Organiser, Steering Committee or NQAAP, will be referred to the Chairman of the JWG.

July 2008 A J Howat

Chairman, Joint Working Group for Quality Assurance

APPENDIX – 3

UK NEQAS Immune Monitoring Programme- Calculation of Performance Score

The Immune Monitoring Scheme monitors individual laboratory performance using percentage and absolute values.

The trimmed mean and trimmed standard deviation are calculated from the results returned using the method described by Healy, (1979).

For percentage values all results are used, but for absolute values only single platform results are used to derive the scoring ranges – all participants are then scored against these values.

Individual values are then compared directly with these calculated values.

The performance is based on an accumulated running score obtained from the last six specimens and uses values obtained from the following analytes: percentage and absolute CD3+, CD3+ CD4+ cells and CD3+ CD8+ cells.

Scores awarded for each analyte will be as follows:

Values within 1 trimmed SD value of the trimmed mean will be assigned 2 points.

Values outside 1 trimmed SD value but within 2 trimmed SD values of the trimmed mean will be assigned 1 point.

Values outside 2 trimmed SD values will be assigned 0 points.

Nil returns will be assigned 0 points.

Therefore, using the above criteria the maximum number of points attainable for each antigen over 6 trials is 12 points. Any new laboratory joining the scheme will only be subject to performance monitoring once six specimens have been issued.

The total score attained will determine overall laboratory performance:

Unsatisfactory <5

Satisfactory 5-12

These target values are subjected to periodic review.

APPENDIX – 4

UK NEQAS Leukaemia Immunophenotyping and Diagnostic Interpretation Programme - Calculation of Performance Score

UK NEQAS Leukaemia Immunophenotyping (Part 1)- Calculation of Performance Score

The UK NEQAS for Leucocyte Immunophenotyping Steering Committee has approved the following scoring system for use in the Leukaemia Immunophenotyping Programme.

1. Each of the core and recommended antigens will be scored separately.
2. Any optional antigens tested by a participant will not be performance scored.
3. The overall median will be used to determine if a given antigen is to be scored as positive, or negative, based upon the BCSH 20% cut-off point acute case and 30% cut-off point for chronic cases for immunofluorescent techniques (i.e. a median value of 70% then the antigen deemed to be positive; a median value of 5% then the antigen is deemed to be negative).
4. A laboratory's analytical result for a given antigen will be compared directly with the median value. For example, if a laboratory returns a result of 10% when the median value is 70% (i.e. positive) then that result is out of consensus.
5. Should an out of consensus result occur then a laboratory would attract 50 points for that antigen.
6. In contrast, where a laboratory's result is in agreement with the consensus classification then points will be awarded based upon the identification of the median and the 5th, 10th, 25th, 75th, 90th and 95th centiles.

N.B. Performance scoring will only occur where the 25th and 75th centile values both fall in the positive or negative results category. If both fall in the same category i.e. both are positive or negative then performance points will be awarded.

7. The scores assigned are as follows and are based on where an individual laboratory's value lies in relation to the defined centile ranges:
 - < 5th Centile 40 points
 - > 5th - 10th Centile 20 points
 - >10th - 25th Centile 10 points
 - >25th - 75th Centile 0 points
 - >75th - 90th Centile 10 points
 - >90th - 95th Centile 20 points
 - >95th Centile 40 points

8. The running score for each antigen will reflect the LAST THREE TIMES THE ANTIGEN WAS REQUESTED. For example out of consensus results in CD3 expression for each of the last three occasions will, therefore, result in a score of 150. The participant may however, have correctly identified CD19 expression in the same three specimens and therefore would score 0 points for CD19. The participant would only be identified as an Unsatisfactory Performer for CD3 antigen determination.
9. In accordance with UK NEQAS for Leucocyte Immunophenotyping Steering Committee recommendations, a Persistent Unsatisfactory Performer (PUP) for any antigen is defined as a running score > 100 points on three occasions within a 12 month period. Thus it is quite possible to be a good performer for CD5 but poor for CD3.
10. Nil returns will be monitored. A nil return for ANY of the core antigens will result in 50 points being awarded. Nil returns for recommended antigens will not be penalized. A running score for each individual antigen will be kept and if a participant scores > 100 points, for any antigen, this will be deemed an Unsatisfactory Performer. A running score for returns will be kept independently of the antigen scoring system, and will similarly cover the last three specimens issued.
11. The programme will have the discretion not to score a given antigen if it is felt that the analyte was unsatisfactory i.e. unexplained bi-modal distribution of data.
12. Performance within this programme will ultimately be reported to the Haematology National Quality Assurance Advisory Panel.
13. Overseas laboratories will not be reported to the UK committees for unsatisfactory performance.

UK NEQAS Leukaemia Diagnostic Interpretation (Part 2)- Calculation of Performance Score

The UK NEQAS for Leucocyte Immunophenotyping Steering Committee has approved the following scoring system for use in the Leukaemia Diagnostic Interpretation Programme. Please Note: It is important that if your laboratory only undertakes immunophenotyping but diagnostic interpretation is performed elsewhere then the laboratory/centre that ultimately performs the diagnostic interpretation completes the Leukaemia Diagnostic Interpretation (Part Two) section.

1. The diagnosis returned by all participants will be used to produce a consensus diagnosis.
2. A performance score will be produced on the basis of comparing the diagnosis returned to the consensus diagnosis depending upon the following categories:
Correct 0 points
Minor Error 20 points
Major Error 50 points
3. These categories are defined as:
Correct – in total agreement with the consensus diagnosis

Minor Error – differs from consensus diagnosis but would not have any significant diagnostic and/or therapeutic implications

Major Error – differs from consensus diagnosis but would have significant diagnostic and/or therapeutic implications

4. The running score will reflect the LAST THREE TRIALS. Out of consensus results in diagnosis for each of the last three trials will, therefore, result in a score of 150.
5. In accordance with UK NEQAS for Leucocyte Immunophenotyping Steering Committee recommendations, a Persistent Unsatisfactory Performer (PUP is defined as having a running score > 100 points on three occasions within a 12 month period.
6. Nil returns will be monitored. A nil return will result in 50 points being awarded. A running score will be kept and if a participant scores > 100 points they will be deemed an Unsatisfactory Performer. To avoid nil returns it is important that if your laboratory only undertakes immunophenotyping but diagnostic interpretation is performed elsewhere then the laboratory/centre that ultimately performs the diagnostic interpretation completes the Leukaemia Diagnostic Interpretation (Part Two) section.
7. The programme will have the discretion not to score a given trial if it is felt that the results were unsatisfactory i.e. unexplained bi-modal distribution of data.
8. Performance monitoring within this programme is currently in pilot phase and as such no participants will be reported to the National Quality Assurance Advisory Panel.
9. Overseas laboratories will not be reported to the UK committees for unsatisfactory performance.

APPENDIX – 5

UK NEQAS CD34+ Stem Cell Quantitation Programme - Calculation Of Performance Score

1. The scoring system is based upon the identification of the median and the 5th, 10th, 25th, 75th, 90th and 95th centiles and scores for absolute values only. The scoring ranges are derived using only single platform results and all users are compared to these values.
2. The assignment of relevant scores is based on how a participant performs in relation to the median and centile ranges defined and will identify 5.29% of participants as being poor performers.
3. A Persistent Poor Performer is defined as a participant with a total score of 100 points or more over 3 surveys on more than one occasion. The score is a running cumulative score over the last 3 samples, thus the latest trial score will replace the oldest score of the three.
4. The scores assigned are as follows and is based on where an individual laboratory's absolute CD34+ value lies in relation to the defined centile ranges:
Result falling on Score or within/outside Assigned

< 5th Centile	50 points
>5th - 10th Centile	35 points
>10th - 25th Centile	20 points
>25th - 75th Centile	0 points
>75th - 90th Centile	20 points
>90th - 95th Centile	35 points
>95th Centile	50 points

the three samples stated below will score as:

Sample 10 = Result falls less than 5th Centile therefore 50 points scored

Sample 11 = Result falls within the 5th - 10th Centile range therefore 35 points scored.

Sample 12 = Result falls within the 90th - 95th Centile range therefore 35 points scored.

Total scored = 120 points therefore classified as a Poor Performer.

5. Any laboratory who fails to return a result by the closing date will be regarded as a nil return and will attract 50 points for each sample.

APPENDIX – 6

UK NEQAS Low Level Quantitation programme - Calculation Of Performance Score

(Pilot)

1. The scoring system is based upon the identification of the median and the 5th, 10th, 25th, 75th, 90th and 95th centiles and scores for absolute values only.
2. The assignment of relevant scores is based on how a participant performs in relation to the median and centile ranges defined and will identify 5.29% of participants as being unsatisfactory performers.
3. A Persistent Unsatisfactory Performer (PUP) is defined as a participant with a total score of 100 points or more over 2 surveys on more than one occasion. The score is a running cumulative score over the last 6 samples, thus the latest trial score will replace the oldest score of the six.
4. The scores assigned are as follows and is based on where an individual laboratory's absolute Low Level value lies in relation to the defined centile ranges:

Result falling on or within/outside	Score Assigned
< 5th Centile	25
> 5th - 10th Centile	15
>10th - 25th Centile	5
>25th - 75th Centile	0
>75th - 90th Centile	5
>90th - 95th Centile	15
>95th Centile	25

5. Thus a laboratory who returns an absolute Low Level Leucocyte value for the six samples stated below will score as:
 - Sample 10 = Result falls less than 5th Centile therefore 25 points scored
 - Sample 11 = Result falls within the 5th - 10th Centile range therefore 15 points scored.
 - Sample 12 = Result falls within the 90th - 95th Centile range therefore 15 points scored.
 - Sample 13 = Result falls over 95th centile therefore 25 points scored.
 - Sample 14 = Result falls within the 5th – 10th centile range therefore 15 points scored.
 - Sample 15 = result falls within the 75th – 90th centile range therefore 5 points scored. Total scored = 100 points therefore classified as an unsatisfactory Performer

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6. Any laboratory who fails to return a result by the closing date will be regarded as a nil return and will attract 25 points. This will be scored independently of the analytical score and is identified on the front sheet as such.

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