Public Health England

NHS

NHS Newborn Blood Spot Screening Programme

Specification for analytical equipment capable of supporting the CF and CHT screening programmes

Introduction

The measurements of TSH and IRT are fundamental to the screening programmes for cystic fibrosis (CF) and congenital hypothyroidism (CHT). The principle for the measurement of thyroid-stimulating hormone (TSH) and immunoreactive trypsinogen (IRT) is immunoassay and currently all laboratories in the UK use Fluoroimmuno assay (FIA). With the advent of emerging alternative methodologies and hence differing analytical platforms, it would seem appropriate to develop a specification that will support laboratory personnel to make an informed decision on the most appropriate analyser for their laboratory and ensure open competition within the market place.

Aims

This document aims to provide guidance for laboratories that provide newborn screening for CF and CHT by defining a specification framework to support the newborn screening analytical process requirements.

Overall system specification

Any system available for procurement must offer an innovative solution for new born screening in line with the needs of the service which may be different between individual laboratories. However, there are fundamental requirements that any system must be capable of including the following:

- undertake analysis on appropriate sample type(s)
- positive patient identification through barcoding or other suitable technologies
- utilise barcodes for reagent identification and audit
- utilise barcodes for Calibrator and Quality control identification
- the analyser must be easy to use and maintain within the laboratory environment
- the analyser must enable timely and appropriate analytical processing of samples based against workload
- a capability to handle workload fluctuations as defined by each laboratory
- robust audit of sample and reagents used throughout the process
- data handling is available to ensure robust data manipulation and audit
- availability of reagent packs sizes to meet the needs of the laboratory
- intuitive reagent handling system with minimum user intervention
- robust maintenance procedures with limited downtime
- appropriate training and refresher training of staff as required

- timely application support must be provided
- IT support to ensure robust data processing, maintenance and auditing
- fit for purpose in adhering to health and safety requirements
- the system must be future proof to meet future demands either in sample number or test repertoire
- meet the criteria set by UKAS under ISO 15189
- walk away technology for 24/7 operation

Maintenance procedures

- daily, weekly and monthly maintenance procedures must be simple to perform and appropriate documentation must be available to all staff electronically in close proximity to the analyser
- time to complete maintenance must be minimal and where possible automatically scheduled
- the instrument software should record all maintenance procedures performed
- supplier preventative maintenance schedules must be clearly defined and kept to a minimum to maximise analyser usage, typically 98% uptime. Consideration must be given to these visits occurring out of hours
- robust maintenance contracts must be offered to include engineer and software support. Same day support should be available
- suppliers must state the number of field engineers employed and the location of base engineer responsible for the laboratory

Sample requirements

- the supplier must demonstrate that the analyser throughput is sufficient to handle the workload
- the system must be able to use dried bloodspot sampling. The volume of sample required must be minimal for each analysis. Current expectation is that analysis can be performed on a 3-5mm blood spot disc. Future expectation may be for smaller volume per test as additional newborn screening programmes are introduced
- the system must be able to accommodate positive patient identification

Reagents

- the functionality of the analyser should ensure that reagents can only be placed in the appropriate section on the analyser
- reagent loading must be simple and straight forward
- the analyser should have reagent level detection and real time inventory
- reagent expired or low flags must be available
- the reagents should be uniquely identified for complete audit purposes
- differing reagent pack size should be available to meet the needs of individual laboratories to ensure maximum return In terms of reagent usage against cost
- where possible reagents used should have a long shelf life but not less than three months
- the expected stability of reagents on board should be given
- reagent should be supplied where possible in large batches to minimise lot changes throughout the year

- reagent lot to lot variation should be less than 8% and ideally less than 5%
- special reagent storage condition must be highlighted and appropriate stability data available
- guidance on reagent handling must be available to ensure compliance with national legislation e.g. COSHH, Health and Safety at Work Act
- it must be CE marked

Calibration and Quality Control overlay

- guidance on the storage, preparation and use of Calibrators and Quality Control must be supplied
- it would be desirable for the analyser to store multiple calibrations for each assay and information on the curve fitting algorithms must be available. It would also be beneficial to be able to overlay calibration curves
- a warning or Indication for the requirement to re-calibrate should be available
- quality control data must be clearly identifiable
- manipulation of QC data must be available
- all QC and calibration data outside range must be flagged to alert the operator

Analyser performance

The analyser must be simple to use, with minimal interventions to mitigate against human error. It should have the capacity to deal with current and expected increases in workload as defined by the individual laboratory.

Data must be available to demonstrate acceptable analytical performance:

- analytical accuracy
- analytical imprecision
- acceptable linearity range for each assay
- analyte recovery
- limit of quantitation
- measurement of uncertainty
- assay Specificity in terms of cross reaction
- highlighting potential interfering substances e.g. EDTA
- evidence of NEQAS or other external assurance body participation

Please see appendix 1 for performance characteristics that the equipment must be able to deliver.

Information technology

- the instrument must be capable of bidirectional interfacing to the host system to ensure the transfer of relevant information is available to the analyser and host system including patient, test and result data
- the supplier must provide evidence of interfaces in operation with their equipment
- any software updates must be readily available throughout the contract life, incurring minimal costs or free of charge

- transmission of data should be easy with the ability to re transmit to host computer following downtime
- the analyser should have automatic flags to alert the user of potential problems with the system e.g. Calibration, QC limit failure or short sample or missing sample. The limits where appropriate for these must be user definable
- the analyser must be able to flag patient data that exceeds limits set by the laboratory. It would be desirable if this may triggered some element of reflex testing defined by the user
- the IT solution must support report generation when the host system is unavailable in line with the laboratories business continuity strategy
- the software must be able to compile large amounts of data into a useable format, to minimise user intervention. This data must be exportable to a suitable database e.g. Excel
- the system should be able to assimilate calibration data to support result extrapolation
- the system must be able to compile internal quality assurance information into “real time” reports to support the analytical validation processes within laboratories. These reports should be easily accessible for further review
- the system must be able to offer a complete audit trail against each sample or quality control analysed with appropriate real time flags available to the operator to assist in the analytical validation phase of the process
- the system should be capable of storing at least 25000 data sets (3 months) including any appropriate demographic data
- the data stored must be able to be uploaded for long term storage
- it would be desirable for the analyser to have on board electronic maintenance procedures e.g. video clip or electronic operating procedure
- the PC software and analyser must be protected against power interruption
- it would be desirable for raw data to be available to the user for the purposes of troubleshooting assays and analyser diagnostics

Audit capabilities

The expectation is that the whole process from sample identification to result production can be audited in line with ISO 15189 standards. Data must be available on any analysis undertaken to demonstrate:

- reagent lot used
- calibrators lot used
- calibration information
- quality assurance data at the time of the analysis
- system function e.g. Running temperature, diagnostic flags
- operator information

Training and support

- the manufacturers must have a proven record in training and analyser support for their instrumentation. The laboratory must have access to application specialists
- the training requirements should be defined on an individual laboratory basis. This training must be specified in terms of numbers of staff requiring training, duration, and level e.g. basic, advanced or update training

Health and safety

- the analyser must conform to laboratory health and safety standards set by the Trust, UKAS and current national legislation
- it must conform to electrical, mechanical and biological safety
- the supplier must conform with all current regulations regarding shipping and COSHH
- COSHH data must be available from the supplier
- the supplier must recommend how “high risk” samples are handled
- a decontamination protocol must be available
- disposal of waste must be controlled to meet appropriate guidance e.g. Waste electrical and electronic equipment (WEEE) regulations

Appendix 1

Guidance for undertaking an evaluation of equipment (measurement verification is available on the Association of Clinical Biochemistry Website: www.acb.org.uk).

Assessment of accuracy

EQA samples of known concentrations should be analysed and a comparison against ALTM and method group should be undertaken. With new instrumentation coming to market, it is possible that the results obtained may be different from established ALTM values. It is for individual laboratories to make informed judgements on the potential impact the instrumentation would have on decision limits.

Assessment of imprecision – Intra and Inter Assay CV

Intra Assay and Inter Assay coefficient of variation should be established for each assay. Following review of existing data from published EQA data and from Internal Quality Control from a newborn screening laboratory the following guidance is given with respect to acceptable performance.

Please note that this assumes that the samples used were prepared in a consistent manner or provided commercially. For information the tables show the concentrations ranges that were reviewed on an individual basis. However no differences were observed for either Intra or Inter CV across the whole range shown here.

TSH

Analyte Concentration (mU/l)	Intra Assay CV (%)	Inter Assay CV (%)
5 – 10	Less than 10%	Less than 15%
10 – 20	Less than 10%	Less Than 15%
20 – 50	Less than 10%	Less than 15%
>50	Less than 10%	Less than 15%

IRT

Analyte Concentration	Intra Assay CV (%)	Inter Assay CV (%)
15 – 35	Less than 10%	Less than 15%
40 – 70	Less than 10%	Less than 15%
71 -170	Less than 10%	Less than 15%

Assay working range

It is important that data is acquired to ensure the assays perform across an analytical range appropriate for the screening programme. Precision profiling will ensure that there is an acceptable imprecision across the working range of an assay that ensures appropriate patient classification minimising false positive and negative results purely due to poor analytical performance (imprecision) at critical decision limits.

Patient comparisons

Patient comparisons should be performed to ensure that the new instrumentation is appropriately aligned with the outgoing equipment. Therefore a good correlation should be obtained. Where there is good correlation but the results are different then the user will have to assign cut off values appropriate to their needs.

Other factors to consider

1. An assessment should be made of the analytical impact potential Interfering substances may have. This is most certainly to be method dependent e.g. EDTA.

2. It may be necessary to assess the impact of cross reaction within assays. This will be highly dependent on the analyte in question and methodology.

3. Measurement of uncertainty to conform with ISO 15189 standards.

4. Traceability in order to conform with ISO 15189 standards.

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