ERNDIM
QUALITY ASSURANCE IN LABORATORY TESTING FOR IEM

ERNDIM Administration Office
Manchester Centre for Genomic Medicine
6th Floor, St Mary's Hospital, Oxford Road,
Manchester M13 9WL, United Kingdom.
Tel: +44 161 276 6741
Fax: +44 161 850 1145
Email: admin@erndim.org

Special Assays in DBS Pilot Scheme 2017

Scientific Advisor
Prof Jim Bonham
Dept of Clinical Chemistry
Sheffield Children's NHS Foundation Trust, Western Bank
Sheffield, S10 2TH
United Kingdom
Tel: +44(0)114 271 7000
Fax: +44(0)114 276 6205
Email: jim.bonham@sch.nhs.uk

Scheme Organiser
Dr. C.W. Weykamp
Queen Beatrix Hospital
MCA Laboratory
P.O. Box 9005
NL – 7100 GG Winterswijk
The Netherlands
e-mail :
c.w.weykamp@skbwinterswijk.nl

ERNDIM Dried Blood Spot EQA Pilot 2017 Report

There is an increasing use of dried blood spots to measure the metabolites used when monitoring patients with inherited metabolic disorders.

The measurement uncertainty intrinsic to this approach is poorly appreciated and results from both analytic and pre-analytic factors. It is possible that this variability has important clinical significance when establishing and interpreting effective dietary control.

To help assess this and the current state of practice, ERNDIM began a pilot scheme in 2017 by circulating dried blood spot samples containing: phenylalanine, tyrosine, leucine, isoleucine, valine, allo-isoleucine and homocysteine – typical compounds used when monitoring patients with PKU, MSUD and homocystinuria.

Samples were distributed by SKML on 11th September 2017 to 109 laboratories who expressed an interest in the scheme with a deadline for results of 3rd November 2017. Responses were obtained from between 30 laboratories for homocystine measurement to 88 laboratories for phenylalanine.

When the results were interpreted it showed that recovery ranged between 78% - 124% and was considered acceptable. Linearity was also acceptable with a range of, r=0.869 – 0.997. Within laboratory precision, measured as CV%, was perhaps better than anticipated for a method of this type and ranged from 5.9% – 11.6%.

The clear analytical challenge was seen by the dispersion revealed when assessing inter-laboratory precision which ranged from a CV% for phenylalanine and tyrosine of 21% to an inter-lab CV = 65% for homocysteine. These findings are characteristic of variably standardised assays.

These results suggest that while, within a given centre assay imprecision may be acceptable eg the range for phe at 360 µmol/L (the recommended upper control limit at 0 – 5 years of age) is 316 – 404 µmol/L; the between laboratory range at this concentration is 208 – 512 µmol/L and may fall below the precision needed to monitor patients effectively. These results do question the clinical reliability of internationally set treatment targets as they apply to individual centres.

To help address this issue the pilot scheme for 2018 is circulating samples alongside the usual EQA samples that will be used as virtual standards by participants reporting the results that will then be pooled and used as means of re-calculating the EQA responses based common standard. If this significantly reduces the laboratory to laboratory variability then the need for consistent use of a traceable reference material, in line with ISO 15189 requirements, will be compelling for those laboratories who undertake these investigations.

This scheme is a good example of one of the key founding principles of ERNDIM to help evaluate and support the application of international clinical guidelines in the area of inherited metabolic disorders and to improve the performance of analytical methods used to investigate and monitor these patients.

J R Bonham, 5th March 2018