Deliverable D9: Comprehensive catalogue of the EQAS services available for RA

Report version: D9.01

Executive summary

**Project number:** 2008 12 10

**Project Acronym:** ENERCA 3

**Title:** European Reference Network of Expert Centres in Rare Anaemias

**Deliverable:** D9

**Delivery Date:** December 2011

**Short description:**

Deliverable 9 has been developed under WP2 “Quality of patient care” by Working Group 1 “Harmonization of procedures”. Deliverable 9 includes the analysis of the results of questionnaire ENQUE-HARMONIZATION-2 which objective is assess the EQAS available for laboratory test on rare anaemias.
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Partners contributed: UNIMILANO
Made available to: Internal
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Table of Contents

1. Introduction
2. Objective
3. Methodology
4. Results
1. Introduction

Deliverable 9 is the last one deliverable of three related deliverables (Deliverables 7, 8 and 9) which share a common objective, to promote harmonization and the establishment of External Quality Assessment (EQA) Schemes for laboratory procedures for diagnosis of rare anaemias (RA).

There are a number of well established EQA organizations within Europe, and participation in EQA is mandatory or, at least, required for laboratory accreditation in many MS. Some EQA organizations, such as the NEQAS from UK (UK-NEQAS), offer services all over Europe and also for countries outside Europe. Despite this, there is no yet a centralized information service holding a comprehensive catalogue of the EQAS services available for RA.

In the field of RA (with more than 90 different diseases), there are a relatively important number of diagnostic tests but due to the scarce number of clinical laboratories with expertise in their use, the establishment of national EQAS is very difficult. ENERCA 3 by means of WP2 will cover this quality assurance requirement by facilitating the establishment of a centralized European wide EQAS service for RA, accessible to all MS laboratories performing these diagnostic tests. Consequently, the main purpose is to identify the need for additional EQA provision for RA in Europe, to provide the necessary information about existing programmes and where possible, make these programmes easily available to expert laboratories in RA.

For this, two main tasks have been foreseen under WG2- Harmonization of procedures:

**Task H.1: Identify and list the core laboratory tests for the diagnosis of RA**

The purpose of this task is to identify the core laboratory test that are considered essential for the diagnosis of RA and assess the number of laboratories that are currently performing them. **Deliverable 7**
Task H.2: Promotion of quality assurance and accreditation of laboratory systems across Europe for the diagnosis and management of RA

The purpose of this task is to assess the availability of EQAs for the list of core laboratory procedures for the diagnosis of RA Deliverable 8 and elaborate a comprehensive catalogue of the EQAS services available for RA Deliverable 9.

2. Objective

- To present the results of the survey conducted among EQA providers within European Union member states to determine the provision of EQAS for rare and congenital anaemias. This includes the catalogue of available EQAS.
- To analyze the need to develop a new EQA scheme for laboratory test on rare anaemias

3. Methodology

In the previous task WP2-H.1. Deliverable 7, WG-2 established a list of core laboratory tests that are used in the diagnosis of rare and congenital anaemias.

Based on that list, a survey was conducted among EQAS providers between June-September 2011 within Europe and members of EQALM to identify the EQAS provision for tests that are included in this core list Deliverable 8. The results of this survey are presented herein.
ENERCA III PROJECT

Work Package 2
‘Quality of Patient Care’

The Provision of External Quality Assessment Services for the Rare Anaemias

REPORT

Questionnaire ENQUE-Harmonisation 2

Barbara De la Salle, UK NEQAS General Haematology, Watford, UK
Andrea Mosca, University of Milan, Milan, Italy

February 2012
The Provision of EQA Services for the Rare Anaemias

ABSTRACT

The provision of external quality assessment services (EQAS) for rare disorders is a challenge. For many of these conditions, the number of patients in any one European Union member state is very small with only a few laboratories providing diagnostic testing. In these cases, the development of pan-European or cross-border EQAS may be the only means by which standardisation of methods and results can be achieved.

The ENERCA project (the European Network for Rare and Congenital Anaemias; www.enerca.org) has operated for 10 years, as 3 consecutive work projects, with the support of the European Parliament. The aims of the Network are to improve the provision of care for individuals with rare and congenital anaemias, including the haemoglobinopathies, thalassaemia syndromes, red cell enzymopathies, red cell membrane disorders, erythropoietic disorders, metabolic disorders of iron and acquired haemolytic disease. ENERCA has established a list of core laboratory tests that are used in the diagnosis of rare and congenital anaemias, which has formed the basis of a survey of European EQAS providers within the External Quality Assessment in Laboratory Medicine (EQALM) organisation for services in this key area.

EQAS providers have been asked to provide details of their services for the rare and congenital anaemias, including the nature of the survey material, the application of performance criteria, the frequency of distribution and the accreditation status of the service. In addition, EQAS providers have been asked if they are willing or able to accept participants from other member states or regions, and whether they are willing to work with other EQAS providers to establish cross-border services.

In general, the provision of EQAS for rare and congenital anaemias is widely variable with little provision for the very rare disorders. For the more common congenital anaemias, such as the haemoglobinopathies and thalassaemias, provision is better but there is variation in aspects of the scheme design, especially the frequency of distribution.

CONTACT

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SCOPE
This report summarises the findings of the ENERCA ENQUE Harmonisation-2 questionnaire, distributed in 2011 as part of the ENERCA III project, Work Package 2, in collaboration with EQALM.

INTRODUCTION
The European Network for Rare and Congenital Anaemias (ENERCA) was established in 2002 to improve the management of patients with rare anaemias. ENERCA has identified a wide range of disorders categorised into the main areas of the haemoglobinopathies and thalassaemia disorders, red cell enzmopathies, red cell membrane disorders, paroxysmal nocturnal haemoglobinuria (PNH) and other acquired haemolytic disorders, metabolic disorders of iron metabolism and congenital dyserythropoietic anaemias (www.enerca.org). The European Commission’s definition of a rare anemia is one with a prevalence of fewer than 5 per 10,000 individuals in a given community, meaning that there may be relatively few sufferers in any one country. In many cases, diagnosis of these conditions requires the use of specialist laboratory testing, and the number of diagnostic centres providing expert diagnostic services in any one European member state may be very low.

External quality assessment (EQA) in haematology was established in the United Kingdom in the late 1960s (Lewis and Burgess, 1969), as a means of improving interlaboratory performance in laboratory medicine. Since that time it has been widely adopted as a recognised part of laboratory quality management. Participation in EQA is an essential requirement for laboratory accreditation under international standards, such as ISO15189. Within Europe, there are a number of EQA provider organisations; these may be public or commercial enterprises, operated on a national, regional or local basis. Some operate internationally, within Europe and beyond; by the same token, laboratories in European member states may also participate in EQA programmes from providers outside Europe. Determination of the accuracy and comparability of results between testing centres through the use of EQA is essential for the harmonisation of testing procedures and improved patient care, especially where the methodology is largely manual or only semi-automated.

ENERCA has established a core list of laboratory tests that are used for the diagnosis of rare anaemias, including non-specific, general laboratory investigations used in the diagnosis and monitoring of a wide range of conditions and specialist investigations used primarily for the diagnosis of individual diseases. The low prevalence of rare anaemias makes the provision of EQA for the specialist laboratory tests a challenge for national EQA providers in individual member states since good EQA requires a minimum number of participating laboratories for financial and statistical viability.

Questionnaire ENQUE-Harmonisation 2 (ENQUE-H2) was undertaken as part of work package 2 of the ENERCA III project to determine the availability of EQA provision for the investigations in the core list and the willingness of EQA provider organisations to collaborate across national boundaries. The use of higher order reference methods, where available, to determine target values in EQA and to calibrate IVDDs has also been examined as part of the survey.
**METHOD**

EQA providers within Europe were contacted via the European Quality Assessment in Laboratory Medicine (EQALM) organisation. The organiser of each EQA organisation registered with EQALM was sent the questionnaire ENQUE H2, which had been developed with the assistance of the ENERCA Executive Committee.

Each EQA provider was sent a copy of the Core List of Laboratory Tests and the ENQUE-H2 questionnaire. The questionnaire, which is displayed in full in Appendix 1, sought information on the provision of EQA services for each test on the core list, including:

- Analytes covered,
- Frequency of distribution,
- Type of survey material,
- Number of participants,
- Performance monitoring,
- ‘Wishlist’ of new provision,
- Potential for collaboration,
- Accreditation status.

**RESULTS**

**Number and location of responses received**

The questionnaire was distributed to 31 member organisations within EQALM and responses were received from 16 (52%). This included a supplier from Canada. ENERCA and EQALM thank all the EQA organisers who took the time to respond to this questionnaire.

**Table 1. Responses received**

<table>
<thead>
<tr>
<th>Country</th>
<th>EQA provider organisation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canada</td>
<td>QMP-LS</td>
</tr>
<tr>
<td>Croatia</td>
<td>Croatian Society of Medical Biochemists - Committee for External Quality Control</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>SEKK</td>
</tr>
<tr>
<td>Denmark</td>
<td>DEKS</td>
</tr>
<tr>
<td>France</td>
<td>AFSSAPS</td>
</tr>
<tr>
<td></td>
<td>CTCB</td>
</tr>
<tr>
<td>Ireland</td>
<td>Irish EQAS</td>
</tr>
<tr>
<td></td>
<td>RIQAS</td>
</tr>
<tr>
<td>Norway</td>
<td>NOKLUS</td>
</tr>
<tr>
<td>Romania</td>
<td>RoEQALM</td>
</tr>
<tr>
<td>Russia</td>
<td>National Centre for EQA in Laboratory Medicine</td>
</tr>
<tr>
<td>Slovenia</td>
<td>SNEQAS</td>
</tr>
<tr>
<td>Spain</td>
<td>Sociedad Española de Hematología y Hemoterapia</td>
</tr>
<tr>
<td>Sweden</td>
<td>EQUALIS</td>
</tr>
<tr>
<td>Switzerland</td>
<td>CSQC</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>UK NEQAS</td>
</tr>
</tbody>
</table>
EQA provision for ‘General’ tests

The provision of EQA for tests from the General section of the Core Tests list was good amongst the EQA providers that responded to the questionnaire, with 17/22 (77%) of tests covered.

Figure 1. EQAS provision for tests from the General section of the core list of laboratory tests. Key: B12: vitamin B12 assay; Bili: bilirubin; CBC: complete blood count; Fe: serum iron; FOL: serum &/or red cell folate; FTN: serum ferritin; Hapto: haptoglobin; Hburia: Haemoglobinuria; HS: urinary haemosiderin and bone marrow iron stain; LDL: low density lipoprotein; LDH: lactate dehydrogenase; Morph: peripheral blood/bone marrow morphology; RE: reticulocyte count; TFN: transferrin; TIBC: total iron binding capacity.

Five tests not covered by the EQA organisations that responded were: urine ferroxamine iron, serum transferrin receptor, liver iron, myocardial iron and zinc protoporphyrin.

EQA provision for diagnostic tests for haemoglobin disorders

Only 4 of the 16 EQA organisations provided EQA services for diagnostic tests associated with the haemoglobin disorders, and just 3 of these provided their services outside their own countries. The tests covered included sickle solubility; haemoglobin (Hb) variant identification; quantification of Hb A$_2$, Hb F and Hb S; Hb H bodies; newborn sickle screening and molecular haemoglobinopathies.

EQA services were not available for unstable haemoglobins, Heinz bodies, oxygen affinity (p50) or globin chain synthesis among the organisations that responded.
**Figure 2. EQAS provision for tests for the diagnosis of haemoglobin disorders.**

Key: SCT: sickle screening test; Hb Var: Hb variant identification; Hb A2%: quantification of Hb A2; Hb F%: quantification of Hb F; Hb S%: quantification of Hb S; Hb H: Hb H inclusion bodies; NB sickle: newborn sickle screening; DNA: molecular haemoglobinopathies.

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**EQA provision for tests for the diagnosis of red cell enzymopathies, membrane disorders and other rare anaemias**

There is little provision of EQA for the specialist diagnostic tests of other rare anaemias. Of the core list of laboratory tests for red cell enzymopathies, red cell membrane disorders and paroxysmal nocturnal haemoglobinuria (PNH), EQA is only provided amongst the responders to the questionnaire for glucose-6-phosphate dehydrogenase (G6PD) activity, Hb F by flow cytometry, Kleihauer (acid elution) slides, methaemoglobin and PNH by flow cytometry. In all cases, there was a single EQA provider for each test.

**EQA service provision across national borders**

Service provision across national boundaries was available from 10/16 (60%) of EQA service providers. In addition, 11/15 (73%) that responded would be prepared to offer new specialist EQA services in collaboration with other EQA providers.

**Frequency of service provision**

There was a large variation in the frequency and number of specimens provided by different EQA organisations. For full blood count (FBC or CBC), for example, the number of specimens varied from 1 to 26 annually. A similar variation is seen for bilirubin (from 'as requested' to 52 specimens annually) and for Hb A2 quantification (1 to 18 specimens annually).
**EQA providers’ ‘wishlist’**

The EQA providers were asked which tests they thought would most benefit from the development of new EQA services. EQA is available for the majority of the tests on the wishlist, through the organisations within EQALM that responded to the questionnaire. Only 4/16 tests listed did not have EQA provision by an alternative organisation.

Table 2. Diagnostic tests that respondents feel would most benefit from the provision of EQA, and the availability of EQA services from another EQALM member organisation.

<table>
<thead>
<tr>
<th>Tests for which EQA is available within EQALM questionnaire respondents</th>
<th>Tests for which EQA is not available within EQALM questionnaire respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb variant detection</td>
<td>Unstable haemoglobins</td>
</tr>
<tr>
<td>Hb A2, Hb F and Hb S quantification</td>
<td>Heinz bodies</td>
</tr>
<tr>
<td>G6PD activity</td>
<td>Serum transferrin receptor</td>
</tr>
<tr>
<td>Kleihauer</td>
<td>Pyruvate kinase activity</td>
</tr>
<tr>
<td>Flow cytometry for Hb F</td>
<td></td>
</tr>
<tr>
<td>Reticulocyte count</td>
<td></td>
</tr>
<tr>
<td>Red cell folate</td>
<td></td>
</tr>
<tr>
<td>Serum folate</td>
<td></td>
</tr>
<tr>
<td>Cobalamin</td>
<td></td>
</tr>
<tr>
<td>Serum ferritin</td>
<td></td>
</tr>
<tr>
<td>Serum haptoglobin</td>
<td></td>
</tr>
<tr>
<td>Blood Film Morphology</td>
<td></td>
</tr>
</tbody>
</table>

The EQA providers reported the availability of a higher order reference method in less than 5% of analytes tested and this was not consistent between providers.

In nearly all cases, target values were derived from a consensus of participants’ results. For tests such as morphology, a consensus of expert laboratories was also used. Over 90% of tests were subject to performance assessment.

It was encouraging to note that 7/16 of the EQA providers offered accredited services.

**DISCUSSION**

This questionnaire has demonstrated that the provision of EQA for general or routine diagnostic tests utilised in the investigation of rare anaemias is adequate amongst the EQA provider organisations within EQALM. These tests are used in the diagnosis and monitoring of a greater range of disorders than the rare anaemias, are widely available and hence have good EQA provision. The provision of EQA for more specialist tests however is not as good. Although responses to this questionnaire were received from a limited number of EQA providers, it included several large providers with a comprehensive range of services and also reflects the provision listed in other catalogues, such as that provided by the College of American Pathologists (www.cap.org) or the Centre for Disease Control (www.cdc.org).

This relatively poor provision of EQA for RA diagnostic tests reinforces the need for collaborative operation where possible. The choice of EQA programme is made difficult by the differences in the service offered between providers, for example the very wide variation in the frequency of provision. The responsibility for the selection of
an EQA scheme appropriate to the laboratory’s needs lies with the laboratory and this requires a diversity of EQA provision; however, patients have the right to expect that the EQA services conform to a recognised quality standard and that the scope of the EQA programme is clear. For this reason, EQA providers should work to improve their services through accreditation to international standards, such as ISO17043. This is particularly important if EQA services are provided across national boundaries.

Of the EQA wishlist items, ENERCA has identified pyruvate kinase (PK) activity as the investigation for which it is most feasible to develop a pilot EQA scheme. PK deficiency is the commonest cause of hereditary, non-spherocytic, haemolytic anaemia, with an estimated incidence of 51 cases per million in North America (Beutler and Gelbart, 2000), although the exact incidence in Europe is unknown. Relatively few centres may provide qualitative and/or quantitative PK assay within any one EU member state and the interpretation of the results is challenging, meaning that an effective EQA programme would have an impact. The most effective model would be to develop a Europe wide EQAS, using the expertise of a consortium of experts in EQAS provision, laboratory diagnosis and clinical management of PK deficiency. A suggested protocol for a pilot EQA scheme has been developed between ENERCA Executive Committee partners (Appendix 2).

The provision of high quality EQA, coupled with educational support, is an important component of a quality management system by which laboratory performance can be improved and maintained, and key to the development of laboratory services for patients with rare anaemias. The majority of the EQA providers indicated a willingness to provide their services across national borders or to collaborate in the development of new, specialist services. This is important where the EQA programme may only be statistically viable if participants are recruited from a number of countries. However, the availability of sufficient volumes of stable survey material, funding models that restrict the provision of EQA to a single country, the cost of transportation, restrictive customs rules, language and differences in local medical practice all pose barriers to cross border service delivery.

International accreditation standards and support from professional bodies with an international profile, such as ENERCA, the International Federation of Clinical Chemistry (IFCC), the International Council for Standards in Haematology (ICSH) and the World Health Organisation (WHO), will be required to overcome the barriers to the cross-border provision of EQA for RA.

A networking organisation such as ENERCA has a key role in the facilitating collaborative working between experts in the development of EQA services and in publicising their availability to laboratory professionals.

PRESENTATION AT EQALM ANNUAL MEETING IN SZEGED, HUNGARY (2011)

The results of this questionnaire were presented at the 2011 EQALM meeting by Barbara De la Salle. The abstract submitted for this meeting is shown in Appendix 3.

REFERENCES


APPENDIX 1

ENQUE-H2 QUESTIONNAIRE
QUESTIONNAIRE TO EUROPEAN EQA PROVIDERS

ENQUE-Harmonisation-2

Dear Colleague,

At last year’s EQALM meeting, the Haematology Working Group adopted a new project to examine the provision of EQAS and the use of reference methods for the laboratory investigations used in the diagnosis of Rare Anaemias throughout Europe. This work is a collaboration with the European Network for Rare and Congenital Anaemias (ENERCA) with the objective of providing improved patient diagnostics through standardisation and harmonisation.

ENERCA has created a core list of laboratory tests that are used in the diagnosis of haemoglobin disorders, thalassaemia disorders, red cell membrane disorders, enzymopathies and other rare anaemias. This new EQALM project will contribute to the development of a comprehensive database of EQA provision in these areas to improve the quality of laboratory performance and to identify where additional EQA provision is required.

We would like to invite you to complete the attached questionnaire on the services that you provide in this field.

If you have any queries or problems, please contact Barbara De la Salle (barbara.delasalle@whht.nhs.uk).

The results of this survey will be reported at the EQALM 2011 meeting.

Thank you for your time,

Barbara De la Salle, UK NEQAS General Haematology
On behalf of the EQALM Haematology Working Group
June 2011

For information about ENERCA: www.enerca.org
# CORE LIST OF TESTS

PLEASE COPY THE G1 SHEET AND COMPLETE FOR EACH ANALYTHEMEASUREMENT FOR WHICH YOU PROVIDE AN EGA SCHEME

<table>
<thead>
<tr>
<th>Core List of Tests</th>
<th>General Laboratory Tests</th>
<th>Hematological Disorders</th>
<th>Red cell enzyme disorders</th>
<th>RBC membrane disorders</th>
<th>NHL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder film microscopy</td>
<td>Hb variant detection</td>
<td>Chromosomal microarray analysis (CMA)</td>
<td>β-thalassemia</td>
<td>Hb-C</td>
<td></td>
</tr>
</tbody>
</table>
**EXAMPLE QUESTIONNAIRE PART 1 – COMPLETED FOR EACH TEST PROVIDED**

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1 What is the name of the EQA programme or survey provided?</td>
<td>Full Blood Count</td>
</tr>
<tr>
<td>1.2 What tests from the ‘core list of tests’ are covered?</td>
<td>CBC - Hb, WBC, RBC, Hct, MCV, MCHC, MCHC, Platelets</td>
</tr>
<tr>
<td>1.3 How frequently do you distribute specimens?</td>
<td>12 times per year</td>
</tr>
<tr>
<td>1.4 How many specimens are distributed each year?</td>
<td>24</td>
</tr>
<tr>
<td>1.5 What is the type of survey material provided?</td>
<td>Human whole blood - partially fixed</td>
</tr>
<tr>
<td>1.6 How many participants are registered?</td>
<td>1,300</td>
</tr>
<tr>
<td>1.7 Do you accept participants from outside your own country?</td>
<td>Yes x</td>
</tr>
<tr>
<td>1.8 Is there a higher order reference method for this test?</td>
<td>Yes x</td>
</tr>
<tr>
<td>If yes, please give the reference if you can</td>
<td></td>
</tr>
<tr>
<td>Do you use the higher order reference method in your laboratory?</td>
<td>Yes x</td>
</tr>
<tr>
<td>Do you know if IVDD manufacturers use this reference method to calibrate their kits or equipment?</td>
<td>Yes x</td>
</tr>
<tr>
<td>1.9 How do you establish your target value?</td>
<td>Higher order reference method</td>
</tr>
<tr>
<td>Consensus of selected expert laboratories</td>
<td></td>
</tr>
<tr>
<td>Consensus mean or median of participants’ results</td>
<td>x</td>
</tr>
<tr>
<td>Other</td>
<td></td>
</tr>
<tr>
<td>1.10 Do you provide performance assessment?</td>
<td>Yes x</td>
</tr>
<tr>
<td>1.11 Do you have document that describes how this is done?</td>
<td>Yes x</td>
</tr>
<tr>
<td>1.12 Is the programme accredited?</td>
<td>Yes x</td>
</tr>
<tr>
<td>1.13 If yes, please give the name of the accreditation body</td>
<td>CPA</td>
</tr>
<tr>
<td>1.14 Would you agree to your scheme being listed on the European Network for Rare and Congenital Anaemias website (<a href="http://www.enerca.org">www.enerca.org</a>)?</td>
<td>Yes x</td>
</tr>
<tr>
<td></td>
<td>No x</td>
</tr>
</tbody>
</table>
### FUTURE EQAS DEVELOPMENT

2.1 Of the tests that you do NOT provide EQAS for, list the 5 that you think would benefit most from EQAS provision.

<table>
<thead>
<tr>
<th>Test 1</th>
<th>Test 2</th>
<th>Test 3</th>
<th>Test 4</th>
<th>Test 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>PK screen and assay</td>
<td>Transferrin</td>
<td>Flow cytometry for Hb F cells</td>
<td>PNH</td>
<td></td>
</tr>
</tbody>
</table>

2.2 Would you be prepared to offer EQAS for rare anaemias in collaboration with another EQAS provider?

- Yes [x]
- No

2.3 Are there any other tests that should be included in the core tests list?

No

### ABOUT YOUR EQA SCHEME

2.4 Organisation name

UK NEQAS General Haematology

2.5 Nature of the organisation

- Private company
- Government organisation [x]
- Charity
- Other

2.6 Name of the Scheme Organiser/Director

Professor Keith Hyde

2.7 Address

PO Box 14, Watford, WD18 0FJ, UK

2.8 Telephone number

44 1923 217878

2.9 Fax number

44 1923 217879

2.10 Email

haem@uknegas.org.uk

2.11 Website

www.uknegash.org.uk

2.12 Name of the person completing this form

Barbara De la Salle
APPENDIX 2

DRAFT PROPOSAL FOR THE DEVELOPMENT OF A NEW EQA PILOT SCHEME FOR PYRUVATE KINASE ACTIVITY
DRAFT PROPOSAL: A NEW PILOT SCHEME FOR PYRUVATE KINASE ACTIVITY

Introduction

External Quality Assessment (EQA) is a recognised component of laboratory quality management. Determination of the accuracy and comparability of results between testing centres through the use of EQA is essential for the harmonisation of testing procedures and improved patient care, especially where the methodology is largely manual or semi-automated. Within Europe, there is no EQA scheme (EQAS) for PK activity. Because the number of centres providing qualitative and quantitative PK assay within any one EU member state is relatively small, the most effective and cost efficient model is a Europe wide EQAS, utilising the expertise of a consortium of experts in EQAS provision, laboratory diagnosis and clinical management of PK deficiency. Development of a pilot EQAS would comprise three phases of work: firstly, the in-house development of survey material suitable for both qualitative screening and quantitative assay, secondly the initial testing of this material by 3-5 expert centres and finally, the distribution of a pre-pilot exercise to approximately 20 laboratories.

The purpose of these exercises is to test the stability and acceptability of the survey material and to assess the logistical issues associated with the operation of the pilot scheme, not participant performance. The exact procedures for each of the development phases outlined below will be subject to review by the collaborating partners and are for general guidance only.

Collaborating centres and contacts within ENERCA
Barbara De la Salle, UK NEQAS (H)
Richard van Wyck, University of Utrecht
Andrea Mosca, University of Milan

Phase 1: In-house survey material development
1. Normal PK activity material will be sourced from waste patients’ specimens, stabilised and stored at -80°C in Milan. Specimens will be tested, initially for 2 weeks, then for a longer period of storage, to determine the stability of the stored material.
2. PK deficient and normal patients’ material will be sent from Utrecht to Milan under temperature controlled conditions. The material will be stabilised, stored at -80°C and tested.

Phase 2: Pre-pilot exercise 1 with selected expert laboratories
3. Material developed from phase 1 will be dispatched to 3-5 expert laboratories, for testing by qualitative and quantitative methods. The expert laboratories will be recruited from London, Milan, Utrecht and Barcelona.
4. 3 specimens each from one batch of PK deficient and one batch PK normal survey material will be distributed. Material will be dispatched on dry ice.
   a. Each site will be asked to test each specimen (6 in total) in duplicate (total of 12 assays) as soon as possible after receipt.
   b. Data will be returned to UK NEQAS (H) for within and between batch analysis.

Phase 3: Pre-pilot exercise 2
5. Approximately 20 laboratories will be recruited via the ENERCA network. The group will include the expert laboratories used in phase 2. The participant laboratories must offer PK activity as part of their diagnostic repertoire and should be from as wide a range of European member states as possible.
6. 2 batches of survey material (one deficient and one normal) will be distributed by UK NEQAS (H), with 2 samples of each sent to the participating laboratories. Samples will be sent on dry ice.
7. Participants will be asked to test each specimen according to their normal protocol.
8. Participants will also be sent a brief questionnaire to return, on the acceptability of the survey material as an EQA product.
9. Results will be returned to UK NEQAS (H) for analysis.

Once the data from these pre-pilot exercises have been reviewed, other variables will be examined as part of the development of the pilot scheme.
APPENDIX 3

ABSTRACT, EQALM 2011 MEETING, SZEGED, HUNGARY
EXTERNAL QUALITY ASSESSMENT FOR RARE AND CONGENITAL ANAEMIAS

The provision of external quality assessment services (EQAS) for rare disorders is a challenge. For many of these conditions, the number of patients in any one member state is very small with only a few laboratories providing diagnostic testing. In these cases, the development of pan-European or cross-border EQAS may be the only means by which standardisation of methods and results can be achieved.

The ENERCA project (the European Network for Rare and Congenital Anaemias; www.enerca.org) has operated for nearly 10 years, as 3 consecutive work projects, with the support of the European Parliament. The aims of the Network are to improve the provision of care for individuals with rare and congenital anaemias, including the haemoglobinopathies, thalassaemia syndromes, red cell enzymopathies, red cell membrane disorders, erythropoietic disorders, metabolic disorders of iron and acquired haemolytic disease. ENERCA has established a list of core laboratory tests that are used in the diagnosis of rare and congenital anaemias, which has formed the basis of a survey of European EQAS providers for services in this key area.

EQAS providers have been asked to provide details of their services for the rare and congenital anaemias, including the nature of the survey material, the application of performance criteria, the frequency of distribution and the accreditation status of the service. In addition, EQAS providers have been asked if they are willing or able to accept participants from other member states or regions, and whether they are willing to work with other EQAS providers to establish cross-border services. The use of higher order reference methods, where available, to determine target values in EQA and to calibrate IVDDs has also been examined as part of the survey.

In general, the provision of EQAS for rare and congenital anaemias is widely variable with little provision for the very rare disorders. For the more common congenital anaemias, such as the haemoglobinopathies and thalassaemias, provision is better but there is variation in aspects of the scheme design, especially the frequency of distribution.

The results of this survey will be used to collate a catalogue of available EQAS within Europe, in collaboration with the ENERCA project. This catalogue will be an information resource for providers of diagnostic testing for rare anaemias in Europe and will identify the most important areas for EQAS collaboration and development.