Meeting the needs of Mediterranean nations: improving efficiency in laboratory medicine

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Traceability in laboratory medicine: what is it and why is it important for patients?

Graham H. Beastall[1,2]

[1] *University of Glasgow, Mayfield, Birdston, Glasgow, United Kingdom*

[2] *The Joint Committee for Traceability in Laboratory Medicine (JCTLM)*

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Corresponding author:
Graham H. Beastall
University of Glasgow
Mayfield, Birdston
Glasgow G66 1RW
United Kingdom
E-mail: gbeastall@googlemail.com

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ABSTRACT

The between method variability of patient results is a source of uncertainty that can have adverse consequences for patient safety and clinical outcomes. Globalisation requires that laboratory medicine results should be transferable between methods. Traceability in laboratory medicine aims to reduce between method variability so that results are independent of time or location. Application of the metrological traceability chain facilitates a universal approach based around the preparation, adoption and use of higher order international commutable reference materials and reference measurement procedures, supported by expert reference laboratories. Global collaboration is required, involving several different stakeholder groups ranging from international experts to laboratory medicine specialists in routine clinical laboratories.

INTRODUCTION

Laboratory medicine results influence a high percentage of all clinical decisions. Patients expect that different laboratories, using different methods, will give the same result for an analyte measured in a clinical sample. Often this is not the case and an inappropriate clinical decision for a patient may be the consequence. Laboratory medicine specialists have a professional responsibility to provide a high-quality service that is optimised to the needs of the patient [1].

Traceability in laboratory medicine aims to reduce between method variability so that results are independent of time or location [2]. Achieving traceability is a global multi-stakeholder cooperative activity involving metrologists; international standards organisations; scientific and clinical experts from international professional bodies; healthcare regulators; and the in-vitro diagnostics (IVD) industry that is responsible for the manufacture and sale of diagnostic testing systems [3]. The Joint Committee for Traceability in Laboratory Medicine (JCTLM) was established to co-ordinate the activity of these stakeholders, to provide educational support for traceability, and to establish and maintain a database of reference materials, reference methods and reference laboratories [4].

THE IMPORTANCE OF REDUCING BETWEEN-METHOD AND BETWEEN-LABORATORY VARIABILITY

There are several reasons why efforts should be made to reduce between-method and between-laboratory variability [5]. These include:

- Improving patient safety
- Facilitating patient empowerment
- Ensuring public confidence
- Enabling consolidation and networking
- Supporting laboratory accreditation
- Implementing evidence-based clinical guidelines
- Guaranteeing clinical governance
- Adopting common informatics
- Introducing the electronic patient record

TRACEABILITY IN LABORATORY MEDICINE AND THE METROLOGICAL TRACEABILITY CHAIN

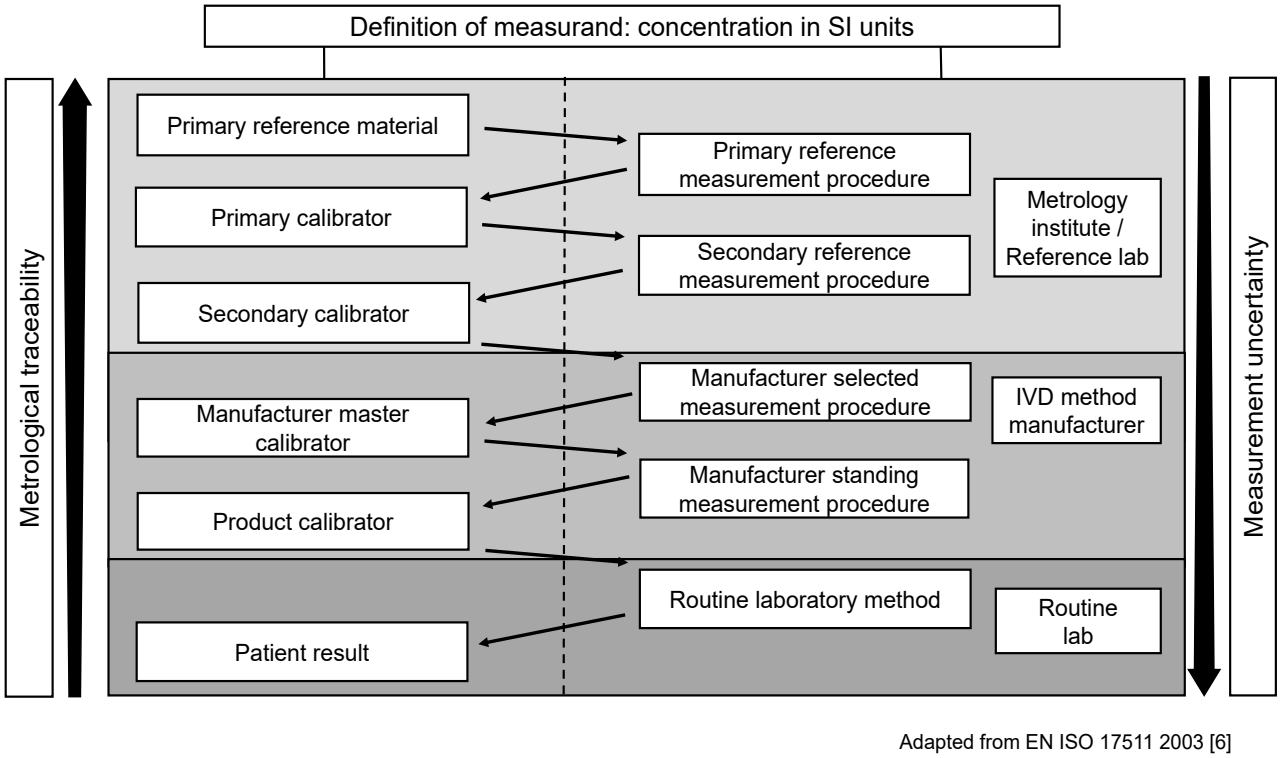
Metrology is the science of measurement. The basics of measurement involve:

- A measurable property, known as a quantity (e.g. concentration)
- Definition of the measurand – the quantity that is intended to be measured. The description of the measurand should include the matrix (e.g. plasma); the component (analyte) of interest, and the amount of substance concentration
- The units in which the measurement will be made. Metrological traceability requires the international system of units (SI) or units with well-established conversions
- The uncertainty with which the measurement can be made

Metrological traceability is the property of a measurement result, which can be related to a reference through a documented unbroken chain of calibrations. The principles of a reference measurement system for establishing metrological traceability are described in the ISO17511:2003 document [6]. The components of a reference measurement system comprise reference materials (calibrators) and measurement procedures (methods), both of which exist at different hierarchical levels.

The inter-relationship between the components of a reference measurement system describes the metrological traceability chain [6]. Figure 1 depicts this traceability chain with higher order

Figure 1 Metrological traceability chain for laboratory medicine



reference materials and measurement procedures at the top and lower order towards the bottom. This hierarchy is depicted by the rising 'metrological traceability' arrow. Descent through the traceability chain is accompanied by increasing measurement uncertainty as depicted by the downward arrow.

The traceability status of an individual measurement result depends on the existence of an unbroken chain to higher order materials and/or measurement procedures. To be effective the unbroken chain requires commutable materials [7] and sufficiently low imprecision at each step. In the case of structurally simple molecules, like many of those measured routinely in clinical chemistry, it is possible to have a complete unbroken chain to primary reference measurement procedures and primary reference materials. Even for some protein molecules it is possible to achieve full metrological traceability by using a unique, signature peptide as the primary reference material. The measurement of serum cholesterol and blood haemoglobin A1c are examples of full metrological traceability where the agreement between methods is excellent [3]. Serum parathyroid hormone and blood haemoglobin A2 are examples where the between-method variability is unacceptably high, causing clinical risk. In both these cases method standardisation/harmonisation initiatives have commenced [3].

For many biological materials, including complex proteins and viruses it is not possible to prepare secondary calibrators. In these circumstances international conventional calibrators are adopted as being the highest order materials available. The global acceptance of such international conventional calibrators can facilitate reduced between method variability.

SOURCES OF REFERENCE MATERIALS AND REFERENCE MEASUREMENT PROCEDURES

The JCTLM maintains a database of reference materials, reference measurement procedures and reference laboratories [8]. Strict criteria are required for inclusion in the JCTLM database, including evidence of commutability of reference materials and measurement uncertainty.

The World Health Organization Expert Committee for Biological Standardization (WHO-ECBS) maintains a catalogue of international conventional calibrators for blood products and biological standards [9].

CHALLENGES IN IMPLEMENTING TRACEABILITY IN LABORATORY MEDICINE AT A GLOBAL LEVEL

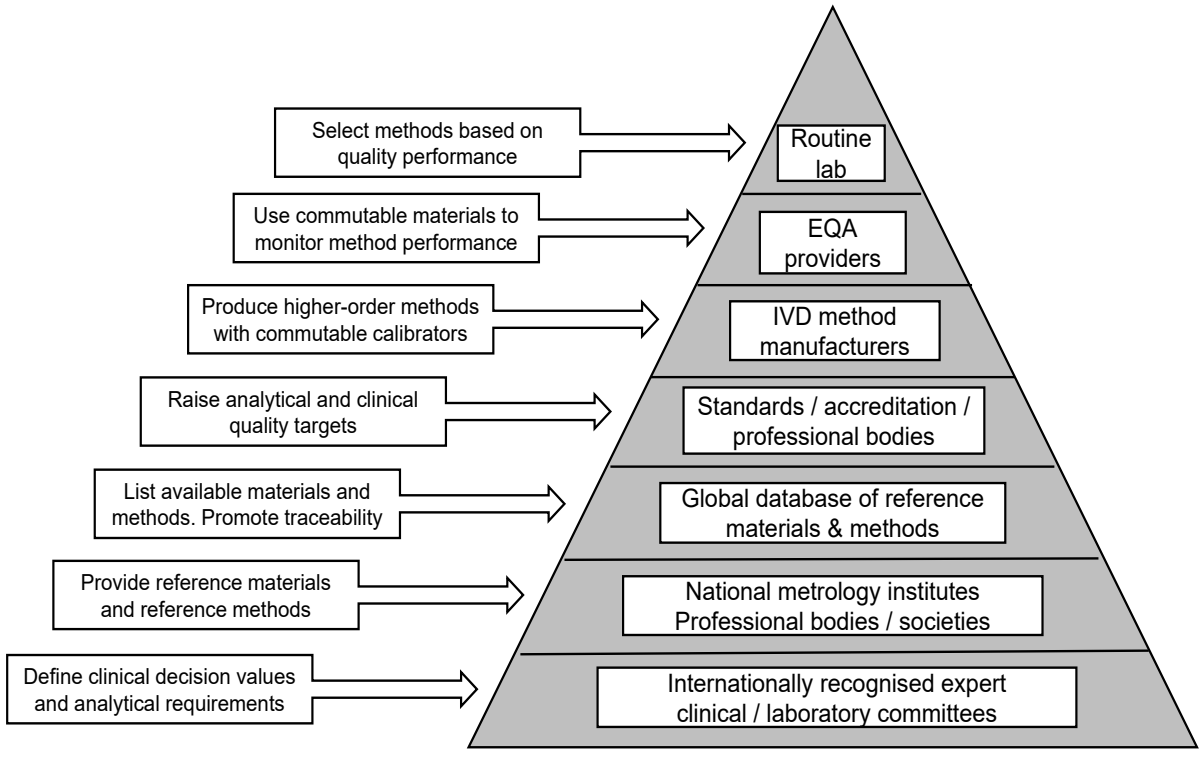
There are several challenges to implementing global traceability [3]. These include:

- Geographical differences
- Lack of uniformity of units
- Complex analytes
- Global coordination

STAKEHOLDERS IN IMPLEMENTING TRACEABILITY IN LABORATORY MEDICINE

The stakeholders involved in delivering traceability in laboratory medicine into routine practice are summarised in Figure 2.

Figure 2 Global stakeholders involved in delivering traceability in laboratory medicine into routine practice



Adapted from Beastall et al. [3]

The initiative begins at the bottom of the triangle with international recognition of the need for traceability for a specific analyte. Thereafter, international and national standards organisations and metrology institutes are responsible for producing and listing the available reference materials and measurement procedures. These are used by the IVD method manufacturers to produce the methods made available for routine use with their performance evaluated through external quality assessment (EQA) schemes based on commutable control materials.

ACTION PLAN TO IMPLEMENT TRACEABILITY IN LABORATORY MEDICINE AT A GLOBAL LEVEL

The implementation of traceability in laboratory medicine at a global level requires a coordinated action plan. This can be derived from Figure 2 by assigning actions to each of the seven stakeholder groups [3].

1. Internationally recognised expert clinical/laboratory committees:

- Develop international consortium for communication and sharing information on the need for traceability
- Prioritise and agree methods that require harmonisation and issue invitations to expert groups to undertake method harmonisation projects [10]

2. National metrology institutes/international professional bodies/societies:

- Develop commutable reference materials and measurement procedures for individual analytes to the highest available order of metrological traceability
- Publish the outcome of harmonisation projects in peer-reviewed scientific literature

3. Global database of reference materials and methods:

- Using freely available lists and catalogues publicise available reference materials and methods that meet agreed standards, including information on commutability and measurement uncertainty
- Provide educational support materials to promote the importance of traceability in laboratory medicine

4. Standards/accreditation/professional bodies:

- Include traceability in laboratory medicine in the training of laboratory medicine specialists and in the standards required for laboratory accreditation
- Provide educational support materials to promote the importance of traceability in laboratory medicine

5. IVD method manufacturers:

- Produce IVD methods that conform with the highest available order of metrological traceability
- Provide details of the traceability status of methods in the information for use documentation

6. EQA providers:

- Promote the use of commutable EQA materials
- Provide educational support about traceability for EQA scheme participants

7. Routine laboratory medicine specialists:

- Know the traceability status of the methods used and understand the measurement uncertainty involved
- Educate staff about traceability in laboratory medicine and its importance to healthcare

Resources for educational support are available from JCTLM [4]. Readers of this article are invited to discuss with their peers how they can contribute to the coordinated action plan.

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