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***OUTLINE OF THE CALIBRATION
AND MEASUREMENT HIERARCHY
IN LABORATORY MEDICINE
- QUALITY POLICY AND
DEFINITIONS***

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PROCEDURE / DOCUMENT

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2. Outline of the Calibration and Measurement Hierarchy in Laboratory Medicine

The implementation of the concept of traceability results in a hierarchical measurement infrastructure consisting of distinct measurement services (see also the flow chart in the attachment to this document):

- National Metrology Institutes provide calibration and measurement services which have been internationally reviewed and verified via the CIPM MRA process. These measurement services and the uncertainties with which they are offered are listed in Appendix C of the BIPM Key Comparison Data Base (KCDB), and are often used in the value assignment of certified reference materials, including primary and secondary calibrators (e.g. for NIST-SRM 909 Human Serum or IRMM certified reference materials). In addition, National Metrology Institutes may also undertake comparative measurements with Reference (Calibration) Laboratories that are required to demonstrate compliance with ISO 17025 and ISO 15195, or provide reference values for ring trials. This link to the Reference Laboratories is essential for the entire calibration and measurement infrastructure since it enables the demonstration of equivalence of measurements internationally. Reference measurement services of National Metrology Institutes which have been approved via the CIPM-MRA, are deemed to fulfil the JCTLM criteria and may also be published in the JCTLM database.

- The second group of laboratories in the hierarchical infrastructure is that of Reference (Calibration) Laboratories. As outlined in the P-03 section of this document, in principle, Reference Laboratories applying for inclusion of their Reference Measurement Services in the JCTLM data base have to fulfill the following requirements:

- a) Use of a Reference Method that has been approved and listed by JCTLM WG-1.
- b) Accreditation as Calibration Laboratory according to ISO 17025 and ISO 15195.

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c) Regular Participation in Intercomparisons (Ring Trials for Reference Laboratories)
The JCTLM process provides a mechanism for the review and listing of these laboratories' measurement services.

Typically, such Reference Measurement Service providers will offer their capabilities to

- Diagnostic Kit Manufacturers
- Regulatory Bodies
- Proficiency Testing Organizations by providing target values for Ring Trials of Testing Laboratories.

Thereby, reference laboratories establish the link to the basic routine laboratories which are requested to demonstrate traceability to higher order reference materials and/or procedures.

National Metrology Institutes which are listed in the BIPM KCDB according to the CIPM MRA may also provide the same service as the Reference Laboratories. In view of their double function they will then be listed in the JCTLM list of reference measurement service providers.

- Routine (Testing) Laboratories form the third group of laboratories in the hierarchical infrastructure. They provide the daily measurement service for medical purposes. Such laboratories usually demonstrate their competence by accreditation according to relevant standards (e.g. ISO 15189) and by participation in proficiency testing ring trials. The approval of these laboratories (e.g. by national Regulatory Bodies) is outside the scope of JCTLM.

3. Purpose

The purpose of JCTLM Working Group 2 (WG2) is to implement the JCTLM Framework for the international recognition of Reference Measurement Services provided by Laboratories. This process is intended to identify and encourage reference measurement laboratories to participate in the processes required to achieve greater comparability of laboratory measurements. This goal will be achieved by assigning traceable values to calibrator and control materials through the use of reference materials and reference measurement procedures identified in the lists provided by JCTLM Working Group 1 (WG1) as compliant with the standards ISO 15193 and ISO 15194. The JCTLM Framework facilitates the implementation of traceability to higher order materials and reference measurement procedures as required by the European IVDD.

It is the policy of WG1 and WG2 to make all evaluations of materials, measurement procedures and reference measurement laboratory services by an openly distributed, transparent process that is known to all interested parties. The processes for identifying reference laboratory services are described in this procedure manual.

4. Scope

The scope of this document is all procedures that describe the activities of JCTLM Working Group 2; procedures pertaining to Working Group 1 are found in the corresponding WG1 Quality System Manual.

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5. Acronyms

BIPM.....	International Bureau of Weights and Measures, website: http://www.bipm.org
CIPM.....	International Committee for Weights and Measures
CIPM-MRA.....	CIPM- Mutual Recognition Arrangement
CRM.....	Certified Reference Material, a “reference material, accompanied by a certificate, one or more of whose property values are certified by a procedure which establishes its traceability to an accurate realization of the unit in which the property values are expressed, and for which each certified value is accompanied by an uncertainty at a stated level of confidence” (VIM: 1993, 6.14)
IFCC.....	International Federation of Clinical Chemistry and Laboratory Medicine, website: http://www.ifcc.org
ILAC.....	International Laboratory Accreditation Cooperation
ISO.....	International Standardization Organization
IVD.....	<i>In Vitro</i> Diagnostic
IVDD.....	IVDD Directive (Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on <i>in vitro</i> diagnostic medical devices)
JCTLM.....	Joint Committee for Traceability in Laboratory Medicine
JCTLM Executive ..	Committee of the JCTLM comprising representatives of the IFCC, BIPM and ILAC and Working Group chairholders.
JCTLM Secretariat .	Secretariat maintained by the BIPM, email address: jctlm@bipm.org
KCDB.....	Key Comparison Data base
RM.....	Reference Material, material, sufficiently homogeneous and stable with reference to specified properties, which has been established to be fit for its intended use in measurement or examination of nominal properties (VIM 2007, 5,13)
RMP.....	Reference Measurement Procedure, measurement procedure accepted as providing measurement results fit for their intended use in assessing measurement trueness of measured quantity values obtained from other measurement procedures for quantities of the same kind, in calibration, or in characterizing reference materials (VIM 2007, 2.7)
RML	Reference Measurement Laboratory, a laboratory that meets the requirements specified in ISO 15195 as a calibration laboratory. Reference measurement laboratories should implement reference measurement procedures and produce results of measurement that are accurate and traceable to national or international primary reference materials when such are available. Whenever possible, traceability

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should be established to a reference material which forms an embodiment of the SI unit (ISO 17511).

This International Standard may form a basis for the accreditation of a reference measurement laboratory that applies for official recognition of the performance of a reference measurement procedure. Reference measurement laboratories are usually accredited by national accrediting bodies.

- RSP Reference Service Provider, a laboratory that for commercial purposes provides measurements according to their individual procedures and uncertainty specifications. Compliance with ISO 17025 as calibration laboratory and/or ISO 15195 may not be required for designation as a RSP.
- SI International System of Units, the metric system
- VIM International Vocabulary of Basic and General Terms in Metrology
- QUAM EURACHEM / CITAC Guide, Quantifying Uncertainty in Analytical Measurement, 2nd Edition
- WG1 Working Group 1 of the JCTLM, is responsible for Reference Materials and Reference Measurement Procedures
- WG1 Chair(s) Leader(s) of WG1, during some time periods the Chair position may be held by more than a single individual to facilitate WG1 activities
- WG1RT Working Group 1 Review Team
- WG1RTL Working Group 1 Review Team Leader
- WG2 Working Group 2 of the JCTLM, is responsible for Reference Laboratory Networks

6. Definitions

- Analyte component indicated in the name of a measurable quantity. (ISO 18153, 3.1, 2002)
- Commutability Property of a given reference material, demonstrated by the closeness of agreement between the relation among the measurement results for a stated quantity in this material, obtained according to two measurement procedures, and the relation obtained among the measurement results for other specified materials (ISO 15194:2009, 3.8).
- Comparability A measure of the equivalence of values of the same quantity assigned to two or more CRMs that are used for calibrating or validating a specified measurement process. CRM comparability can be estimated from the extent of overlap between certified (expectation with uncertainty) and measured values (expectation with uncertainty), using a specified process under repeatability conditions. Comparability among CRMs with any given measurement process does not assure commutability of any CRM across different measurement processes.

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- Competency..... Demonstrated ability of a reference measurement laboratory to perform reference measurement procedures within a predefined uncertainty. For a reference measurement laboratory the competency is demonstrated from concordance of measurement results obtained during inter-laboratory testing schemes.
- Consensus..... Group solidarity in sentiment and belief; the phrase consensus of opinion (which is not actually redundant) has been so often claimed to be a redundancy that many writers avoid it. You are safe in using consensus alone when it is clear you mean consensus of opinion, and most writers in fact do so. (From Miriam Webster – Online Dictionary)
- Higher Order The term “higher order” was left undefined in the IVDD; however, ISO 15193 and ISO 15194 describe the essential requirements for higher order reference materials and methods.
- Listing order Order in which certified reference materials or reference measurement procedures are presented on lists produced by the JCTLM. (presented here to be a part of a sequence “listed—recognized—leading to preferred—creation of a basis for this progression”)
- List I The list of CRMs and RMPs evaluated by JCTLM WG1 and maintained by the JCTLM Secretariat, website: <http://www.bipm.org/jctlm/>
Certified reference materials and reference measurement procedures for well-defined chemical entities with determined values traceable to SI units, and internationally recognized reference procedure-defined measurands; e.g. enzymes are placed in List I.
- List II..... The list of materials evaluated by JCTLM WG1 and maintained by the JCTLM Secretariat, website: <http://www.bipm.org/jctlm/>
Reference Materials that are value-assigned using an internationally agreed upon protocol; e.g., WHO reference materials for Blood Typing, Coagulation Factors, Microbial Serology, Nucleic Acids, and some Proteins. The values of the measurands in the reference materials on this List are not SI-traceable and/or no internationally-recognized reference measurement procedures exist that are applicable to patient samples. List II also contains a group of purified substances which due to the absence of reference measurement procedures should not be directly used for calibration unless commutability is established.
- List III..... The list of materials evaluated by JCTLM WG1 and maintained by the JCTLM Secretariat, website: <http://www.bipm.org/jctlm/>
Certified Reference Materials for nominal properties
- Measurand Quantity intended to be measured (VIM 2007. 2.3)

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Procedure-defined

measurand..... A measurable quantity which is defined by a measurement process rather than a primary reference material. Examples are the catalytic concentrations of enzymes which are defined by the 'Primary IFCC Reference Measurement Procedures'

Measurement

uncertainty..... non-negative parameter characterizing the dispersion of the quantity values being attributed to a measurand, based on the information used (VIM 2007, 2.26)

7. Related documents

- 7.1. BIPM. The International System of Units (SI), 7th Edition. Paris, France (1998).
Website: http://www1.bipm.org/en/si/si_brochure/
- 7.2. BIPM/IEC/IFCC/ISO/IUPAC/IUPAP/OIML. International vocabulary of basic and general terms in metrology, 2nd Edition. ISO, Geneva, Switzerland (1993).
- 7.3. Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices.
Website: <http://www.fxtrans.com/medical/IVD98-79-EC.pdf>
- 7.4. ILAC –G17:2002, Introducing the Concept of Uncertainty of Measurement in Testing in Association with the Application of the Standard ISO/IEC 17025
- 7.5. ISO 17025, General requirements for the competence of testing and calibration laboratories, ISO, Geneva, Switzerland (Date)
- 7.6. ISO 15195, Laboratory medicine - Requirements for reference measurement laboratories, ISO, Geneva, Switzerland (2003)
- 7.7. ISO 15193:2009(E). In vitro diagnostic medical devices – Measurement of quantities in samples of biological origin – Requirements for content and presentation of reference measurement procedures. ISO, Geneva, Switzerland (2009). Website: <http://www.iso.org>.
- 7.8. ISO 15194:2009(E). In vitro diagnostic medical devices – Measurement of quantities in samples of biological origin – Requirements for certified reference materials and content of supporting documentation. ISO, Geneva, Switzerland (2009). Website: <http://www.iso.org>.
- 7.9. ISO 17511. In vitro diagnostic medical devices -- Measurement of quantities in biological samples -- Metrological traceability of values assigned to calibrators and control materials. ISO, Geneva, Switzerland (2003).
- 7.10. ISO 18153. In vitro diagnostic medical devices -- Measurement of quantities in biological samples -- Metrological traceability of values for catalytic concentration of enzymes assigned calibrators and control materials. ISO, Geneva, Switzerland (2003).
- 7.11. Joint Committee for Traceability in Laboratory Medicine, PREAMBLE (2004).
Website: <http://www.bipm.org>

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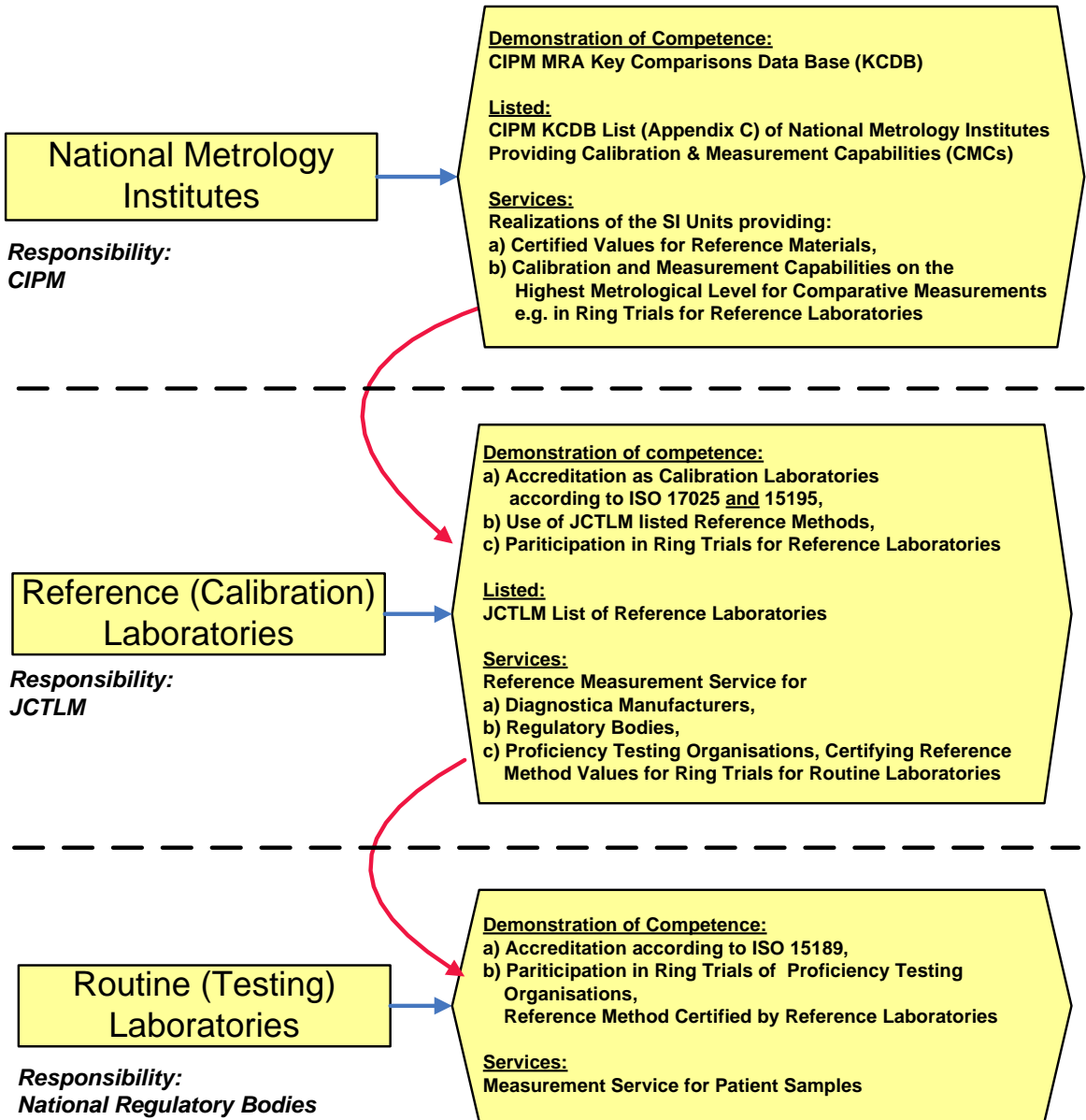
8. Revision History

Version number	Date of Issue/Review	Summary of change
1.0	05/20/2005	Initial issue of WG2 Quality System Procedures
1.1	22/03/2010	Modifications for compliance with VIM (2007)
2.0	27/01/2011	Corrections made in version 1.1 accepted

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Attachment: Flowchart

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Metrology Institutes, listed in Appendix C of the BIPM KCDB according to CIPM MRA may also act as Reference Measurement Service providers; they will be listed by JCTLM without further review.