

Joint Committee for Traceability in Laboratory Medicine

PREAMBLE

The goal of obtaining comparability of laboratory diagnostic test results will be possible only when common reference systems can be established for worldwide use. A critical step in reaching this goal is achieving traceability of reference measurement procedures and reference materials to a universally recognized and accepted reference point such as the International System of Units (SI). Recently, traceability requirements for medical devices marketed within the European Community have been codified. The European Community In Vitro Diagnostic Directive (EC IVDD) states that "**The traceability of values assigned to calibrators and/or control materials must be assured through available reference measurement procedures and/or available reference materials of a higher order.**" (98/79/EC, Annex 1 (A) (3) 2nd paragraph).

The Joint Committee for Traceability in Laboratory Medicine (JCTLM) was created to meet the need for a worldwide platform to promote and give guidance on internationally recognized and accepted equivalence of measurements in Laboratory Medicine and traceability to appropriate measurement standards. These are embodied in ISO 17511 and 18153. The JCTLM created two working groups:

- WG1 Reference Materials and Reference Procedures
- WG2 Reference Laboratory Networks

The Declaration of Cooperation between the International Committee of Weights and Measures (CIPM), the International Federation for Clinical Chemistry and Laboratory Medicine (IFCC), and the International Laboratory Accreditation Cooperation (ILAC) for establishment of the JCTLM can be found at <http://www.bipm.org/en/committees/jc/jctlm/declaration.html>.

JCTLM WG1 was charged with establishing a process for identifying, reviewing against agreed upon criteria, and publishing List(s) of Higher Order Certified Reference Materials and Reference Measurement Procedures required for industry compliance with the EC IVDD regarding *in vitro* diagnostic medical devices.

Nominated reference materials and measurement procedures were categorized according to the criteria described in ISO 15194 and ISO 15193. Two Lists of Higher Order Reference Materials and Reference Measurement Procedures are published:

- List I. Certified Reference Materials and Reference Measurement Procedures for well-defined chemical entities or internationally recognized reference method-defined measurands. Reference Materials and Measurement Procedures included in this category are those that provide values that are traceable to the SI units; e.g., Electrolytes, Drugs, Metabolites and Substrates, Non-Peptide Hormones, Enzymes and some Proteins.
- List II. Reference Materials (e.g. reference materials for Blood Typing, Coagulation Factors, Microbial Serology, Nucleic Acids, and some Proteins) that are value-assigned using an internationally agreed upon protocol. 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. List II also contains a group of purified substances that due to the absence of reference measurement procedures should not be directly used for calibration unless commutability is established.

As medical knowledge and measurement science are advanced to the point that a measurand present in JCTLM List II has been clearly defined and/or internationally-recognized reference measurement procedures have been developed, that are applicable to patient samples, such reference materials should be nominated for listing in JCTLM List I. At present, only about 100 internationally-recognized reference measurement procedures and/or 150 certified reference materials are available for the hundreds of chemical or biochemical entities that are routinely measured in the clinical laboratory.

Measurands cannot be included in either List I or List II if they are not traceable to a material or procedure of higher metrological order. Commonly such measurands are traceable only to a manufacturer's proprietary internal value-assignment process and thus cannot be candidates for listing.

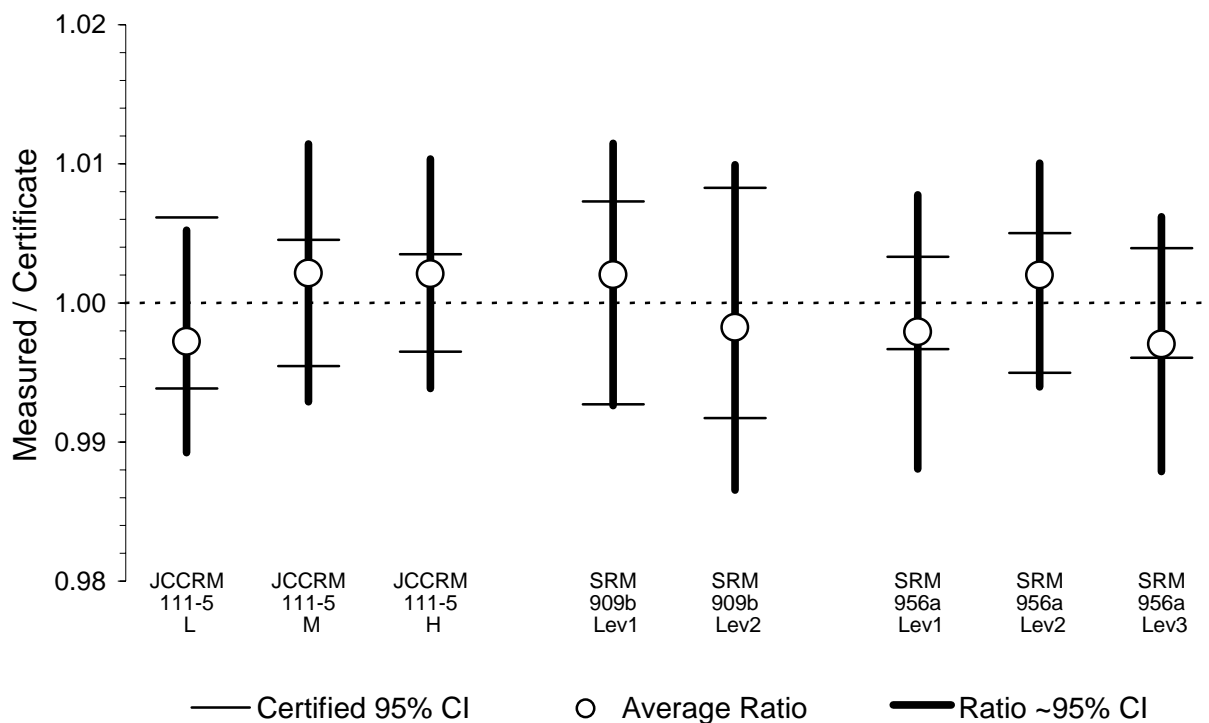
The general procedures by which reference materials and reference measurement procedures have been evaluated for listing and are provided in the JCTLM Quality Systems Document which is available on the BIPM websites at <http://www.bipm.org/en/committees/jc/jctlm/jctlm-db/> and <http://www.ifcc.org> respectively.

JCTLM List I contains multiple Reference Material and Reference Measurement Procedure entries for some measurands. Where multiple entries occur for Reference Materials, the users must determine which material is most appropriate to their needs. Comparison studies, such as the one shown in Figures 1 and 2 for potassium, are planned to demonstrate the equivalence of different Reference Materials for the same measurand. Since internationally-recognized reference measurement procedures do not exist for the measurands in the materials on JCTLM List II, such comparisons can not be made. However, the basis for traceability for each material will be provided.

JCTLM WG2 is establishing criteria and processes for assessing the competencies required by ISO 15195 for Reference Measurement Laboratories to be included on the JCTLM lists. These Reference Measurement Laboratories will be required to participate in formal inter-laboratory comparisons to allow assessment of their competence in the implementation of Reference Measurement Procedures on a measurand-by-measurand basis. Data from the inter-laboratory comparisons will also be used to assess the comparability of different higher order Reference Measurement Procedures for the same measurand. The initial list of Reference Laboratories identified through this process should be available in 2005.

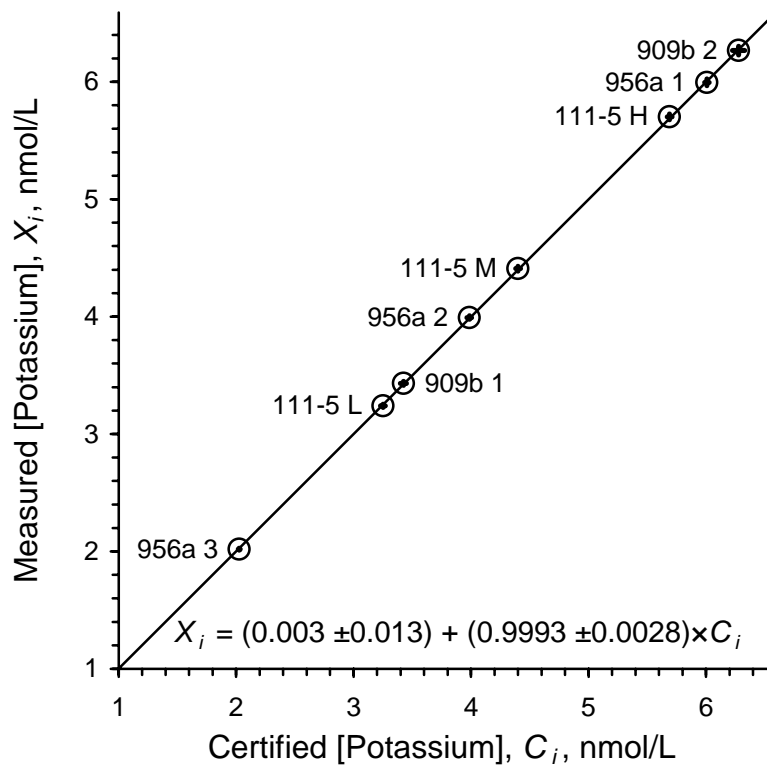
New materials and procedures will be considered for listing annually. Listed materials are expected to be available for at least eighteen months after initial posting. However, because usage rates for listed materials cannot be predicted accurately, producers must be contacted to determine availability of the current materials and projected times for production of new lots. It is the responsibility of the producer to notify the JCTLM Secretariat if a material ceases to be available.

Figure 1A. Comparability Assessment for Potassium in Human Serum CRMs on JCTLM List I: Ratio Display



Potassium in Human Serum CRMs on provisional JCTLM List 1 was assessed for comparability by a single laboratory using a reference measurement procedure under repeatability conditions. The horizontal axis reports the CRMs evaluated. The vertical axis reports the ratio between the measured and certified values of each CRM, X_i/C_i . The open circles denote these ratios; the dark vertical lines represent the approximate 95% confidence interval (95% CI) about the ratios. The light horizontal lines represent the certified 95% CIs. The dotted line represents the expected ratio for the suite of all materials given the observed identity between the measured and certified values. (CI = Confidence Interval)

Figure 1B. Comparability Assessment for Potassium in Human Serum CRMs on JCTLM List I: Scatter gram Display



The data demonstrate that these CRMs are comparable over a wide concentration range. The horizontal axis reports the certified values, C_i ; the vertical reports the average measured values, X_i . Each level of each CRM is displayed as approximate 95% CIs along both axes. The intersection of these intervals is bounded by an open circle to aid visual inspection.

TITLE QUALITY POLICY AND DEFINITIONS			
Author: C. M. Jackson	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG1-P-00

QUALITY POLICY AND DEFINITIONS

CRAIG M. JACKSON

PROCEDURE / DOCUMENT

JCTLM WG1-P-00

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SIGNATURE	SIGNATURE

TITLE QUALITY POLICY AND DEFINITIONS			
Author: C. M. Jackson	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG1-P-00

QUALITY POLICY AND DEFINITIONS

Chapter 1 Contents

PARAGRAPH	TITLE	PAGE
CHAPTER 1 CONTENTS.....		2
CHAPTER 2 PURPOSE.....		2
CHAPTER 3 SCOPE.....		2
CHAPTER 4 ACRONYMS		2
CHAPTER 5 DEFINITIONS.....		3
CHAPTER 6 RELATED DOCUMENTS		4
CHAPTER 7 REVISION HISTORY		5

Chapter 2 Purpose

The purpose of JCTLM Working Group 1 (WG1) is to implement the JCTLM Framework for the international recognition of reference measurement procedures and reference materials of a higher metrological order. The JCTLM Framework facilitates the implementation of traceability to higher order materials and reference measurement procedures as required by the European IVDD. Nominated reference procedures and reference methods are reviewed by WG1 for compliance with the standards, ISO 15193 and ISO 15194.

It is the policy of WG1 to make this evaluation by an openly distributed, transparent process that can be and is known to all interested parties.

The procedures provided in this Quality System document are those by which the evaluations are made.

Chapter 3 Scope

The scope of this document is all procedures that describe the activities of JCTLM Working Group 1.

Chapter 4 Acronyms

BIPM.....	International Bureau of Weights and Measures, website: http://www.bipm.org
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

TITLE QUALITY POLICY AND DEFINITIONS			
Author: C. M. Jackson	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG1-P-00

- IVDD IVDD Directive (Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on *in vitro* diagnostic medical devices)
- JCTLM Joint Committee for Traceability in Laboratory Medicine
- SI International System of Units, the metric system
- VIM International Vocabulary of Basic and General Terms in Metrology
- 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

Chapter 5 Definitions

- List I 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 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.
- Commutability Commutability of a material - ability of a material to yield the same numerical relationships between results of measurements by a given set of measurement procedures, purporting to measure the same quantity, as those between the expectations of the relationships obtained when the same procedures are applied to other relevant types of material (ISO 15194, 3.5)
- 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.

TITLE QUALITY POLICY AND DEFINITIONS			
Author: C. M. Jackson	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG1-P-00

Comparability among CRMs with any given measurement process does not assure commutability of any CRM across different measurement processes.

- 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)
- 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)
- 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.
- JCTLM Executive .. Committee of the JCTLM comprising representatives of the IFCC, BIPM and ILAC
- JCTLM Secretariat . Secretariat maintained by the BIPM, email address: jctlm@bipm.org
- List I The list of CRMs and RMPs evaluated by JCTLM WG1 and maintained by the JCTLM Secretariat, website:
<http://www.bipm.org/en/committees/jc/jctlm/jctlm-db/>
- List II..... The list of materials evaluated by JCTLM WG1 and maintained by the JCTLM Secretariat, website:
<http://www.bipm.org/en/committees/jc/jctlm/jctlm-db/>
- Measurand a “particular quantity subject to measurement” (VIM 1993, 2.6)
- RM..... Reference Material, material or substance one or more of whose property values are sufficiently homogeneous and well established to be used for the calibration of an apparatus, the assessment of a measurement method, or for assigning values to materials (VIM 1993, 6.13)
- RMP Reference Measurement Procedure, “a thoroughly investigated measurement procedure shown to have an uncertainty of measurement commensurate with the intended use, especially in assessing the trueness of other measurement procedures for the same quantity and in characterizing reference materials.” (ISO 15195 2003)

Chapter 6 Related documents

BIPM. The International System of Units (SI), 7th Edition. Paris, France (1998).
Website: http://www1.bipm.org/en/si/si_brochure/

TITLE QUALITY POLICY AND DEFINITIONS			
Author: C. M. Jackson	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG1-P-00

BIPM/IEC/IFCC/ISO/IUPAC/IUPAP/OIML. International vocabulary of basic and general terms in metrology, 2nd Edition. ISO, Geneva, Switzerland (1993).

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>

ISO 15193. In vitro diagnostic systems – Measurement of quantities in samples of biological origin – Presentation of reference measurement procedures. ISO, Geneva, Switzerland (2002).

ISO 15194. In vitro diagnostic systems – Measurement of quantities in samples of biological origin – Description of reference materials. ISO, Geneva, Switzerland (2002).

ISO 15195. Laboratory medicine – Requirements for reference measurement laboratories. ISO, Geneva, Switzerland (2003).

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).

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).

Joint Committee for Traceability in Laboratory Medicine, PREAMBLE (2004).

Website: <http://www.bipm.org>

Chapter 7 Revision History

Version number	Date of Issue/Review	Summary of change
1.0	23/02/2004	Initial issue of WG1 Quality System Procedures

TITLE Outline of JCTLM Procedures For Evaluating Certified Reference Materials And Reference Measuremen Procedures			
Author : C. M. Jackson	Date : 09/15/2004 Version: 1.0	Authorized :	JCTLM WG1 P-01

**OUTLINE OF JCTLM PROCEDURES
FOR EVALUATING CERTIFIED
REFERENCE MATERIALS AND
REFERENCE MEASUREMENT
PROCEDURES TO BE LISTED AS
BEING OF HIGHER
METROLOGICAL ORDER**

CRAIG M. JACKSON

PROCEDURE

JCTLM WG1-P-01

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TITLE Outline of JCTLM Procedures For Evaluating Certified Reference Materials And Reference Measurement Procedures			
Author : C. M. Jackson	Date : 09/15/2004 Version: 1.0	Authorized :	JCTLM WG1 P-01

OUTLINE OF JCTLM PROCEDURES FOR EVALUATING CERTIFIED REFERENCE MATERIALS AND REFERENCE MEASUREMENT PROCEDURES TO BE LISTED AS BEING OF HIGHER METROLOGICAL ORDER

1. Contents

PARAGRAPH	TITLE	PAGE
1.	CONTENTS	2
2.	PURPOSE	2
3.	SCOPE	2
4.	ACRONYMS	2
5.	DEFINITIONS	2
6.	PROCEDURES	3
7.	RELATED DOCUMENTS	3
8.	ATTACHMENTS	3
9.	REVISION HISTORY	3
	ATTACHMENT 1 FLOWCHART	4

2. Purpose

This outline procedure provides an overview of the process by which JCTLM WG1 and its review teams make recommendations for listing of materials and processes as being of higher metrological order.

3. Scope

The processes described apply to all CRMs and RMPs nominated for inclusion by the JCTLM in its lists of available higher order materials and procedures as described in the Preamble to this Quality System Manual.

4. Acronyms

Acronyms used in these procedures are defined in the document JCTLM WG1-P-00, Quality Policy and Definitions.

5. Definitions

Definitions for the terms used in these procedures are given in the document JCTLM WG1-P-00, Quality Policy and Definitions.

TITLE Outline of JCTLM Procedures For Evaluating Certified Reference Materials And Reference Measurement Procedures			
Author : C. M. Jackson	Date : 09/15/2004 Version: 1.0	Authorized :	JCTLM WG1 P-01

6. Procedures

The procedure for the evaluation of materials and procedures to be listed by the JCTLM as being of higher metrological order is segmented into five processes. The details of each process are presented in the individual procedures of this quality system. The attached flowchart indicates how the detailed processes are interconnected.

7. Related documents

JCTLM WG1-P-00	Quality Policy and Definitions
JCTLM WG1-P-02	Process for Requesting and Accepting Nominations for Certified Reference Materials and Reference Measurement Procedures
JCTLM WG1-P-03	Process for Review and Approval of Nominated Certified Reference Materials and Reference Measurement Procedures
JCTLM WG1-P-04	Process for the Demonstration of the Comparability of Certified Values of the Same Measurand in Multiple Materials Having the Same Nominal Matrix
JCTLM WG1-P-05	Process for the Removal of Entries from the JCTLM Lists of Available Higher Order Reference Materials and Reference Measurement Procedures

8. Attachments

Attachment 1	Flow chart, Outline of JCTLM Procedures for Evaluating Certified Reference Materials and Reference Measurement Procedures to be listed as Being of Higher Metrological Order
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9. Revision History

Version number	Date of Issue/Review	Summary of change
Version 1.0	01/08/2004	Initial issue of WG1 Quality System Procedures

TITLE Outline of JCTLM Procedures For Evaluating Certified Reference Materials And Reference Measurement Procedures

Author : C. M. Jackson

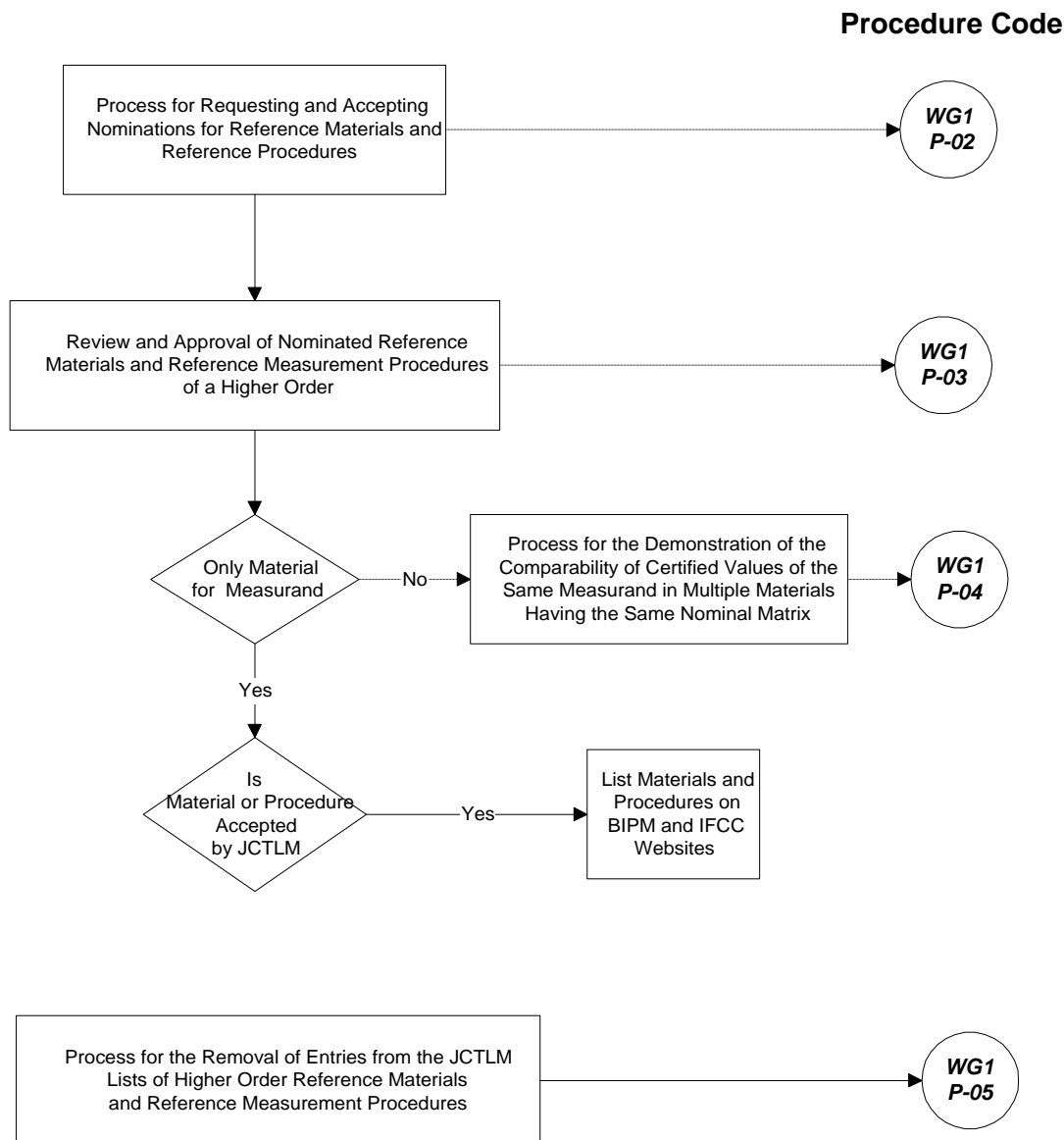
Date : 09/15/2004
Version: 1.0

Authorized :

JCTLM WG1
P-01

Attachment 1 Flowchart

OUTLINE OF JCTLM PROCEDURES FOR EVALUATING MATERIALS AND PROCEDURES TO BE LISTED AS BEING OF HIGHER METROLOGICAL ORDER WG1-P-01



TITLE Nominating Certified Reference Materials and Reference Measurement Procedures			
Author : C. M. Jackson	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG 1 P-02

PROCESS FOR REQUESTING AND ACCEPTING NOMINATIONS FOR CERTIFIED REFERENCE MATERIALS AND REFERENCE MEASUREMENT PROCEDURES

CRAIG M. JACKSON

PROCEDURE

JCTLM WG1-P-02

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SIGNATURE	SIGNATURE

TITLE Nominating Certified Reference Materials and Reference Measurement Procedures			
Author : C. M. Jackson	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG 1 P-02

PROCESS FOR REQUESTING AND ACCEPTING NOMINATIONS FOR CERTIFIED REFERENCE MATERIALS AND REFERENCE MEASUREMENT PROCEDURES

Contents

PARAGRAPH	TITLE	PAGE
CONTENTS.....		2
1. PURPOSE.....		2
2. SCOPE.....		2
3. ACRONYMS.....		3
4. DEFINITIONS.....		3
5. RESPONSIBILITIES AND AUTHORIZATIONS.....		3
6. PROCEDURE.....		3
7. RELATED DOCUMENTS.....		6
8. ATTACHMENTS.....		6
9. REVISION HISTORY.....		7
ATTACHMENT 1 FLOWCHART.....		8
ATTACHMENT 2 REFERENCE MATERIAL / REFERENCE MEASUREMENT SOLICITATION	9	
ATTACHMENT 3 JCTLM WG1-P-02-F-01 REFERENCE MATERIAL NOMINATION FORM, MICROSOFT EXCEL SPREADSHEET.....		15
ATTACHMENT 4 JCTLM WG1-P-02-F-02 REFERENCE METHOD PROCEDURE NOMINATION FORM, MICROSOFT EXCEL SPREADSHEET.....		15

1. Purpose

This procedure describes the processes to be followed for soliciting, receiving and reviewing nominations of materials and procedures for recommendation by the JCTLM for listing as being of higher metrological order and transferring the nominated materials and procedures to WG1 for review.

2. Scope

This procedure will be applied to all materials and procedures of a higher metrological order as described in ISO 15194 and ISO 15193, respectively.

TITLE Nominating Certified Reference Materials and Reference Measurement Procedures			
Author : C. M. Jackson	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG 1 P-02

3. Acronyms

Acronyms used in these procedures are defined in the document JCTLM WG1-P-00, Quality Policy and Definitions.

4. Definitions

Definitions for the terms used in these procedures are given in the document JCTLM WG1-P-00, Quality Policy and Definitions.

5. Responsibilities and Authorizations

- 5.1. Oversight responsibility and authority for the operations of WG1 resides with the WG1 Chair or the designee of the Chair.
 - 5.1.1. Communicating recommendations to the JCTLM Secretariat for listing CRMs and RMPs of higher metrological order is the responsibility of the WG1 Chair.
 - 5.1.2. Communicating recommendations of nominated materials and procedures to the WG1 Chair is based on their fulfillment of the criteria specified by ISO 15194 and ISO 15193 as indicated on the nomination forms from JCTLM for consideration by WG1 and is the responsibility of the expertise-based team leaders of WG1RTs.
- 5.2. Oversight responsibility for the WG1 and WG2 Chairs resides with the JCTLM Executive.
- 5.3. Authority for deciding recommended CRMs and RMPs to be placed on List I and List II resides with the JCTLM Executive.
- 5.4. Responsibility for the maintenance of procedures employed by WG1 and authority to appoint *ad hoc* teams to perform the procedure maintenance resides with WG1 Chair.
- 5.5. Responsibility for the maintenance of procedures employed by WG2 and authority to appoint *ad hoc* teams to perform the procedure maintenance resides with the WG2 Chair.

6. Procedure

- 6.1. The process for nominating and reviewing materials and procedures of a higher metrological order for recommendation by the JCTLM for listing will occur annually.
- 6.2. Solicitation of Nominations from producers of CRMs and developer/owners of RMPs:
 - 6.2.1. The WG1 Chair announces an open solicitation for nominations of CRMs and RMPs for inclusion in the JCTLM lists of higher metrological order materials and procedures. The announcement occurs in the first quarter of each year. The solicitation announcements will found on the websites of the BIPM, the IFCC, and other professional organizations with interests in *in vitro* diagnostic

TITLE Nominating Certified Reference Materials and Reference Measurement Procedures			
Author : C. M. Jackson	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG 1 P-02

devices. The opening of nominations will also be announced in professional and trade journals by the WG1 Chair.

- 6.2.2. A fixed date for receiving completed nominations will be specified in the announcement. Nominations received after the date specified in the annual announcement will be held for consideration in the subsequent annual cycle.
- 6.3. Suggesting Needed Materials and/or Procedures by Interested Parties who are **not** producers or developer/owners:
 - 6.3.1. This process is outside the activities of JCTLM and **must** occur independently of it or its working groups.
 - 6.3.2. Suggestions for new CRMs and RMPs from interested parties who are not themselves producers or developer/owners **must** be made to individuals or organizations responsible for the development of such materials or procedures, not to the WG1 Chair.
 - 6.3.3. Contact information for currently active producers and developer/owners can be obtained from the current list of recommended CRMs and RMPs on the BIPM or IFCC websites.
 - 6.3.4. Submission of suggestions to several producers is recommended, even if materials or procedures in the categories of interest may not be currently on the lists or provided by the particular producers.
 - 6.3.5. Producers will communicate directly with interested parties regarding needs and specifications for new materials and/or procedures.
 - 6.3.6. Producers are encouraged to respond to outside interested parties according to the producer's interests. CRM producers and RMP developer/owners submit nominations based on this mechanism for identification of needs as they deem to be in their interests using the procedure described in this document.
- 6.4. Obtaining Nomination Forms:
 - 6.4.1. Providers of CRMs and developer/owners of RMPs can obtain nomination forms as described in 7.3.2. The name, address and email address of the WG1 Chair will be listed on the BIPM and IFCC websites.
 - 6.4.2. Forms can be obtained by:
 - 6.4.2.1. Downloading from the BIPM or IFCC websites.
 - 6.4.2.2. Email request to the WG1 Chair.
 - 6.4.2.3. Letter request to the WG1 Chair.
- 6.5. Submitting Nomination Forms for Consideration by WG1:
 - 6.5.1. Nominating forms must be submitted to the WG1 Chair **only**. Contact information is found on the BIPM or IFCC websites.
 - 6.5.2. Only nominations submitted from producers of CRMs or developer/owners of RMPs will be accepted by the WG1 Chair.

TITLE Nominating Certified Reference Materials and Reference Measurement Procedures			
Author : C. M. Jackson	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG 1 P-02

- 6.5.3. Producers of reference materials and developer/owners of RMPs acknowledge that a submitted nomination constitutes consent to include the material or procedure on the JCTLM List I of CRMs or RMPs or List II.
- 6.5.4. Only materials for which the requisite information for evaluation is publicly available can be candidates for listing.
- 6.5.5. Only materials from producers who are willing to provide the JCTLM nominated laboratories with sufficient samples of the material free of charge in order to undertake comparability studies can be candidates for listing.
- 6.5.6. Materials can be listed only if the producer consents to comparison studies with other materials of the measurand, when such materials are already listed or are being nominated.
- 6.5.7. Only procedures for which the requisite information for performing the RMP is publicly available can be considered for listing.
- 6.5.8. Nominations for CRMs or RMPs are to be made by completing in full the following forms:
- 6.5.8.1. Spreadsheets that identify the information required for a submission as determined by the requirements of ISO 15194 and ISO 15193.
- 6.5.8.2. Materials nomination spreadsheet (Microsoft Excel) forms (WG1-P-02-F-01 Reference Material Nomination Form) are referenced to ISO 15193.
- 6.5.8.3. Reference procedures nomination spreadsheet (Microsoft Excel) forms (WG1-P-02-F-02 Reference Measurement Procedure Nomination Form) are referenced to ISO 15193.
- 6.5.9. Submission may be by any of the following means:
- 6.5.9.1. An attachment to an email message to the WG1 Chair.
- 6.5.9.2. Electronic medium, diskette or CD ROM sent to the WG1 Chair.
- 6.6. Preliminary Review of submitted nominations for completeness by WG1 Chair:
- 6.7. The WG1 Chair or the Chair's designee reviews nominations within one week of their receipt.
- 6.7.1. The preliminary review is only concerned with completeness and is NOT a review of the qualification of the nominated material or procedure.
- 6.7.2. Incomplete forms will be returned to the individual making the nomination.
- 6.7.3. Returned nomination forms that are incomplete **can** be amended and resubmitted.
- 6.7.4. Acceptance of resubmission after the initial review for completeness is at the discretion of the WG1 Chair.
- 6.7.5. Resubmissions must be received by the date specified on the solicitation (7.4 *et seq.*)
- 6.7.6. Nominations or resubmissions which are received after the date specified may be held until the next review cycle.

TITLE Nominating Certified Reference Materials and Reference Measurement Procedures			
Author : C. M. Jackson	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG 1 P-02

6.8. Distributing Nominations to WG1RTs

6.8.1. The WG1 Chair distributes nominations to the team leaders of the WG1RTs with the appropriate expertise to perform the review

6.8.2. Any WG1RT member affiliated with a nominating organization will not participate in the evaluation of that material or procedure if a potential conflict of interest exists or is perceived to exist.

6.9. The distributed nominations are reviewed by the WG1RTs according to JCTLM WG1-P-03 “Process for Review and Approval of Nominated Certified Reference Materials and Reference Measurement Procedures.”

7. Related documents

ISO 15193	In vitro diagnostic systems – Measurement of quantities in samples of biological origin – Presentation of reference measurement procedures
ISO 15194	In vitro diagnostic systems – Measurement of quantities in samples of biological origin – Description of reference materials
JCTLM WG1-P-00	Quality Policy and Definitions
JCTLM WG1-P-01	Outline of JCTLM Procedures for Evaluating Materials and Procedures to be listed as Being of Higher Metrological Order
JCTLM WG1-P-02-A-00	Solicitation Announcement, Reference Material and Reference Measurement Procedure
JCTLM WG1-P-02-F-01	Reference Material Nomination Form, Microsoft Excel Spreadsheet
JCTLM WG1-P-02-F-02	Reference Measurement Procedure Nomination Form, Microsoft Excel Spreadsheet
JCTLM WG1-P-03	Process for Review and Approval of Nominated Certified Reference Materials and Reference Measurement Procedures

8. Attachments

Attachment 1	Flow chart, Process for Requesting and Accepting Nominations for Certified Reference Materials and Reference Procedures
Attachment 2	Example Reference Material / Reference Measurement Procedure Solicitation Announcement from a previous solicitation – Author Willie E. May
Attachment 3	JCTLM WG1-P-02-F-01 Reference Material Nomination Form, Microsoft Excel Spreadsheet
Attachment 4	JCTLM WG1-P-02-F-02 Reference Measurement Procedure Nomination Form, Microsoft Excel Spreadsheet

TITLE Nominating Certified Reference Materials and Reference Measurement Procedures			
Author : C. M. Jackson	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG 1 P-02

9. Revision History

Version number	Date of Issue/Review	Summary of change
1.0	01/08/2004	Initial issue of WG1 Quality System Procedures

TITLE Nominating Certified Reference Materials and Reference Measurement Procedures

Author : C. M. Jackson

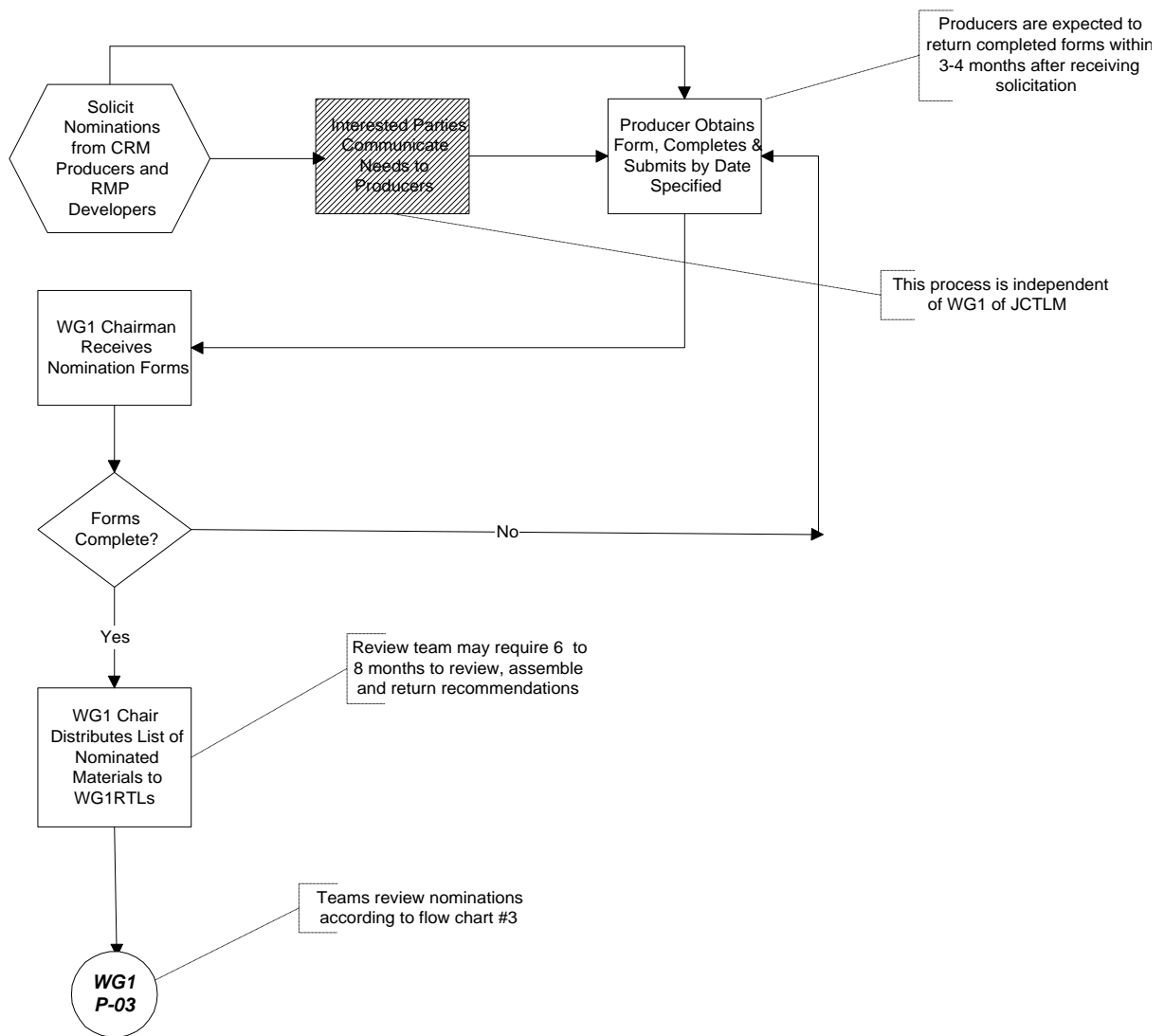
Date : 09/15/2004
Version : 1.0

Authorized :

JCTLM WG 1
P-02

Attachment 1 Flowchart

PROCESS FOR REQUESTING AND ACCEPTING NOMINATIONS FOR REFERENCE MATERIALS AND REFERENCE PROCEDURES WG1-P-02



TITLE Nominating Certified Reference Materials and Reference Measurement Procedures			
Author : C. M. Jackson	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG 1 P-02

Attachment 2 Reference Material / Reference Measurement Solicitation

Dear Colleagues:

The European Directive 98/79/EC on *In Vitro Diagnostic* Medical Devices (IVD MD) requires, among other things, that “the traceability of values assigned to calibrators and/or control materials must be assured through available reference measurement procedures and/or available reference materials of a higher order.” The definition of the term “higher order” was left undefined in the directive. There are, however two ISO standards (ISO/FDIS 15193 and 15194) that describe the essential requirements for higher order reference materials and methods.

To facilitate the identification of the “higher order” Certified Reference Materials (CRMs) and Reference Measurement Procedures that are currently available, **the Joint Committee on Traceability in Laboratory Medicine (JCTLM) was created at a meeting held at the International Bureau of Weights and Measures (BIPM) in early June 2002.** The JCTLM Executive, which oversees the activities of the Joint Committee, is made up of representatives from the International Bureau of Weights and Measures (BIPM), the International Federation for Clinical Chemistry and Laboratory Medicine (IFCC) and the International Laboratory Accreditation Cooperation (ILAC). Professor Joseph H. H. Thijssen, The Netherlands and representing IFCC, is the current Chairman of JCTLM. The secretariat of the JCTLM is maintained by the BIPM.

The JCTLM created two working groups:

- JCTLM WG-I, Reference Materials and Reference Procedures
- JCTLM WG-II, Reference Laboratory Networks

The primary function of the working groups is to provide practical support to the worldwide IVD industry in establishing metrological traceability for values assigned to calibrators and/or control materials as required by the forthcoming European Directive on *in vitro* diagnostics and by comparable regulations in other countries.

JCTLM WG-I is charged with establishing a process for identifying, reviewing against agreed upon criteria, and publishing a list of “higher order” certified reference materials and reference measurement procedures required for IVD industry compliance with the EC IVD directive regarding *in vitro* diagnostic medical devices. The first provisional list of higher order reference materials and reference measurement procedures will be published in April 2004. **The nomination process for cycle II is about to begin. If you wish to nominate a human serum or urine-based reference material or reference measurement procedure for inclusion on the list, please use the attached excel file containing:**

- Template illustrated with examples for Reference Materials and Reference Measurement Procedures
- Blank Reference Materials Template to be completed with your nominations
- Blank Reference Measurement Procedures Template to be completed with your nominations.

Nominations for Reference Materials for high purity substances are also solicited.

TITLE Nominating Certified Reference Materials and Reference Measurement Procedures			
Author : C. M. Jackson	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG 1 P-02

The schedule for this Cycle II nomination and review process is as follows:

- Completed Nomination Spreadsheets to be returned to wem@nist.gov by 01 May 2004.
- Information provided on spreadsheets will be sorted and provided to the Review Teams in early May 2004.
- Approved nominations will be added to the JCTLM List of Higher Order Reference Materials and Reference Measurement Procedures in January 2005.

The Templates are intended to solicit most of the information that will be required for the Review Teams to make their assessments. However, the Review Teams may need to request additional information for some or all of your nominations, so please make sure to complete the “Contact Information for Additional Details” field of each Template.

In order to facilitate the review process, JCTLM WG-I has agreed on thirteen high priority analyte categories listed below and established Review Teams for each. To the extent possible, each Review Team has representation from IVD manufacturers, National Metrology Institutes, accreditation organizations, and professional societies from the US, Europe, and the Asia Pacific Region.

Analyte Category

Review Team Chair

(With representative examples)

Blood Gases

Susan Blonshine, TechEd Consultants

Blood Groupings

Sue Thorpe, NIBSC

British Standard for anti-D (Rho) antibodies, human

British Minimum Potency Reference Preparation for anti-A blood grouping reagents

Coagulation Factors

Elaine Gray, NIBSC

WHO 2nd International Standard for Antithrombin Plasma, Human

WHO 1st International Standard for Beta Thromboglobulin Human Purified

Drugs [therapeutic and “of abuse”] Andre Henrion, PTB

Digoxin/Digitoxin

Theophylline

Cocaine

THC-COOH

Electrolytes

Richard Miller, Dade Behring

Calcium

Potassium

Sodium

TITLE Nominating Certified Reference Materials and Reference Measurement Procedures			
Author : C. M. Jackson	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG 1 P-02

Enzymes Mauro Panteghini, Azienda Ospedaliera “Spedali Civili”
 AMYLASE
 CK
 GGT

Metabolites and Substrates Michael Welch, NIST
 Cholesterol
 Creatinine
 Glucose

Microbial Serology Morag Ferguson, NIBSC
 Hepatitis B surface antigen (HBsAg)
 Antibodies to hepatitis A virus
 Antibodies to toxoplasma

Non-Electrolyte Metals Lee Yu, NIST
 Arsenic
 Cadmium
 Lead

Non-Peptide Hormones Heinz Schimmel, IRMM
 Cortisol
 Estradiol - 17 β
 Thyroxine

Nucleic Acids Helen Parkes, LGC
 Hepatitis A Virus RNA
 Hepatitis B Virus DNA

Proteins David Sogin, Abbott Laboratories
 Albumin
 Troponin-I
 PSA

Vitamins and Micronutrients Katherine Sharpless, NIST
 Retinol (Vitamin A)
 Alpha Tocopherol (Vitamin E)
 Beta Carotene

The “higher order” Reference Materials and Reference Measurement Procedures identified through the Cycle I review process [Reference Measurement Procedures for ~40 analyte-matrix combinations (measurands) and Reference Materials for ~100 measurands] will be published in a database that will be publicly available on the BIPM, IFCC and other relevant websites. There will be two Lists of Higher Order Reference Materials and Reference Measurement Procedures:

TITLE Nominating Certified Reference Materials and Reference Measurement Procedures			
Author : C. M. Jackson	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG 1 P-02

- I. Certified Reference Materials and Reference Measurement Procedures for well-defined chemical entities or internationally recognized reference method-defined measurands, such as enzymes. Reference Materials included in this category are those that are traceable to the SI units. [*Electrolytes, Enzymes, Drugs, Metabolites and Substrates, Non-Peptide Hormones, some Proteins*] This List will be published in April, 2004.
- II. International Conventional Reference Materials, i.e. where the measurand(s) is/are not completely defined and/or no internationally recognized reference measurement procedure is available [e.g. WHO reference materials for Coagulation Factors, Nucleic Acids, some Proteins]. This List will be published by the last quarter of 2004.

As measurement science is advanced to the point that List II measurands can be clearly defined and/or internationally-recognized reference measurement procedures are developed, reference materials could move from List II to List I. Measurands that cannot be included in either List I or List II are not traceable to a higher metrological order. These measurands are traceable only to a manufacturer's internal value assignment process.

Each List will be preceded by a preamble that clearly explains its contents and provides a brief explanation of the process used to determine which Reference Materials and Reference Measurement Procedures are included. The examples below are drawn from the First Provisional List to be published April 2004:

Reference Measurement Procedures for Cholesterol

Reference Measurement Procedure					
Procedure Name and/or ID #	Analyte Name	Applicable Matrices	Measurement Principle	Reference Procedure Citation(s) or Document(s)	Reference Procedure Comparability Assessment Studies
NIST definitive method for serum cholesterol	cholesterol	lyophilized, fresh, or frozen serum	ID/GC/MS	Anal Chem 61, 1718-1723 (1989)	CCQM-K6; http://kcdb.bipm.org/appendixB/appbr esults/ccqm-k6/ccqm-k6_final_report.pdf ; Clin Chem 36, 370-375 (1990)
U. Of Ghent reference method for cholesterol	cholesterol	lyophilized, fresh, or frozen serum	ID/GC/MS	Clin Chem 39,1001-6 (1993) [=part II of Clin Chem 39,993-1000 (1993)]; Eur J Clin Chem Clin Biochem 34, 853-60 (1996); Clin Chem 42, 531-5 (1996)	EUROMET 563
DGKC definitive Method for Serum Cholesterol	cholesterol	lyophilized, fresh, or frozen human serum or plasma	ID/GC/MS	Siekman et al., Z. anal. Chem. 279, 145-146 (1976)	PTB - National Key Comparison for Accreditation
CDCAbell-Kendall method for cholesterol	cholesterol	lyophilized, fresh or frozen human serum	Spectrophotometry	Cooper, GR, et al, Clin Chem 32: 921-929, 1986	Clin Chem 36, 370-375 (1990)

TITLE Nominating Certified Reference Materials and Reference Measurement Procedures

Author : C. M. Jackson Date : 09/15/2004 Authorized : JCTLM WG 1 P-02
 Version : 1.0

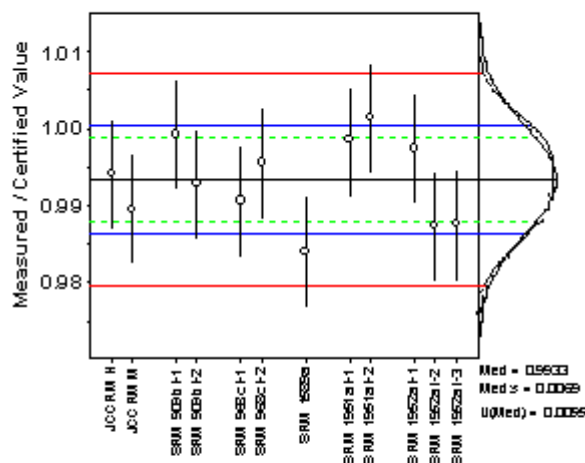
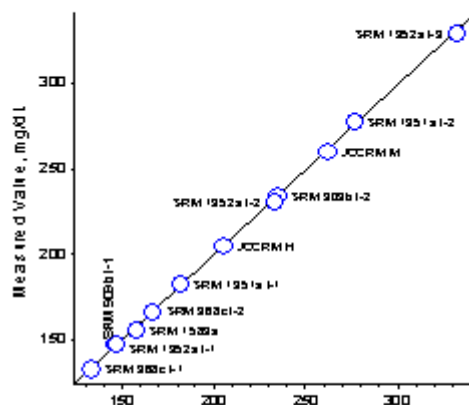
Certified Reference Materials for Cholesterol

Reference Materials					
Information about Material				Contact Information	
Analyte	Matrix	Material Name and/or ID #	Estimated * Availability (months, as of Jan 2004)	- Producer - Country - Website - Email Address - Phone Number - Fax Number	Commutability Study Information and/or Citations
cholesterol	cholesterol	GBW09203b	60	NRCCRM, China Tel: 086-10-64221811 Fax: 086-10-64213149 Email: crmservice@nrccrm.com.cn	Primary calibrator for higher order reference methods
cholesterol	cholesterol	SRM 911b	21	NIST, USA http://ts.nist.gov/ts/htdocs/230/232/232.htm Email: srminfo@nist.gov Tel: (301)975-6776 Fax: (301)948-3730	Primary calibrator for higher order reference methods
cholesterol	human serum	JCCRM 211	12	HECTEF, Japan http://www.in8.co.jp/hectef/starte.htm Tel: 81-44-813-0055 Fax: 81-44-813-0224	
cholesterol	human serum (frozen)	SRM 1951b	60	NIST, USA http://ts.nist.gov/ts/htdocs/230/232/232.htm Email: srminfo@nist.gov Tel: (301)975-6776 Fax: (301)948-3730	Material prepared following NCCLS Document C37-A "Preparation and Validation of Commutable Frozen Human Serum Pools as Secondary Reference Materials for Cholesterol Measurement Procedures; Approved Guideline" Method used for certification: Anal Chem 61, 1718-1723 (1989)
cholesterol	human serum (lyophilized)	SRM 1952a	60	NIST, USA http://ts.nist.gov/ts/htdocs/230/232/232.htm Email: srminfo@nist.gov Tel: (301)975-6776 Fax: (301)948-3730	
cholesterol	human serum (lyophilized)	SRM 968c	38	NIST, USA http://ts.nist.gov/ts/htdocs/230/232/232.htm Email: srminfo@nist.gov Tel: (301)975-6776 Fax: (301)948-3730	
cholesterol	human serum (lyophilized)	SRM909b	60	NIST, USA http://ts.nist.gov/ts/htdocs/230/232/232.htm Email: srminfo@nist.gov Tel: (301)975-6776 Fax: (301)948-3730	

TITLE Nominating Certified Reference Materials and Reference Measurement Procedures			
Author : C. M. Jackson	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG 1 P-02

A laboratory-based quality assurance audit program will also be initiated to provide measurement results that demonstrate the comparability of multiple “higher order” Reference Materials for the same measurand on the list as well as to verify the veracity of the review process. Results from a study for Cholesterol in Serum CRMs where NIST measurement results are plotted vs. CRM certified values are shown below. The error bars represent 95% confidence intervals ($k=2$).

Comparison of “higher order” Cholesterol in Serum CRMs



⇒ CRM comparability independent of analyte level

The measured/certified ratios for this set of CRMs are:

- ~ normally distributed
- with a standard deviation of ~0.7%

If there are questions about JCTLM WG-I activities in general or any particulars about the Reference Method and/or Reference Materials review process, please contact:

Dr. Willie E May
National Institute of Standards and Technology (NIST)
Chemical Science and Technology
Laboratory/Analytical Chemistry Division
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Gaithersburg, Maryland 20899-8390
UNITED STATES
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Fax: +1 301 926 8671
E-mail: wem@nist.gov

Dr. Heinz Schimmel
Institute for Reference Materials and Measurements (IRMM)
European Commission - Directorate General JRC
Retieseweg
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BELGIUM
Tel: +32 14 571 720
Fax: +32 14 590 406
E-mail: Heinz.SCHIMMEL@cec.eu.int

TITLE Nominating Certified Reference Materials and Reference Measurement Procedures			
Author : C. M. Jackson	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG 1 P-02

Attachment 3 JCTLM WG1-P-02-F-01 Reference Material Nomination Form, Microsoft Excel Spreadsheet

JCTLM WG1-P-02-F-01 Reference Material Nomination Form, Microsoft Excel Spreadsheet is a separate item and is not included within this procedure document.

Attachment 4 JCTLM WG1-P-02-F-02 Reference Method Procedure Nomination Form, Microsoft Excel Spreadsheet

JCTLM WG1-P-02-F-02 Reference Method Procedure Nomination Form, Microsoft Excel Spreadsheet is a separate item and is not included within this procedure document.

	A	B	C	D	E	F	G	H	I	J	K	L	M
4		JCTLM Identificati on Number for Reviewing Purposes	Analyte/Parameter		Basis for Traceability		Matrix		RM				
5	Nominated by:		Analyte Category	Analyte Name	Traceable to SI?	Procedurally- defined (if so, name/cite procedure)	Matrix Category	Matrix	Identifier/ Number	Name	Certifying Organization	Mode/approach used for value assignment (if not clearly stated in certificate)	Comments
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4	Concentration or Concentration Range of Analyte Certified/Assigned Value			Range of Expanded Uncertainty for Analyte Certified/Assigned Value				Information for Assessing Commutability						Congruent with other crit			
5	Issued by NMI with Certificate	Certificate from Other RM provider?	RM listed in BIPM Database?	From	To	Unit	From	To	Unit	Lev. of confidence (%)	Physical form of RM matrix	RM fortified with analyte or naturally incurred	Applicable analyte characteristics (e.g., isoform(s); free/bound, total)	Other relevant factors (list)	Citation of specific publication/reference if available	Expression of Uncertainty	Justification of source of reference material
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4	Additional factors in ISO 15194 (list other relevant factors)?				Additional Comments	Contact Information for Additional Details				Is there a sustainable source for the material?
5	Are intended use and instructions for use available?	Are dates of authorization and revision given?	Are safety precautions listed?	Validation report available?		Name	Email address	Phone number	How to obtain certificate	
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4		JCTLM Identificati on Number for Reviewing Purposes	Analyte/Parameter		Basis for Traceability		Matrix		RM				
5	Nominated by:		Analyte Category	Analyte Name	Traceable to SI?	Procedurally- defined (if so, name/cite procedure	Matrix Category	Matrix	Identifier/ Number	Name	Certifying Organization	Mode/approach used for value assignment (if not clearly stated in certificate)	Comments
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4				Concentration or Concentration Range of Analyte Certified/Assigned Value			Range of Expanded Uncertainty for Analyte Certified/Assigned Value				Information for Assessing Commutability					Congruent with other crit	
5	Issued by NMI with Certificate	Certificate from Other RM provider?	RM listed in BIPM Database?	From	To	Unit	From	To	Unit	Lev. of confidence (%)	Physical form of RM matrix	RM fortified with analyte or naturally incurred	Applicable analyte characteristics (e.g., isoform(s); free/bound, total)	Other relevant factors (list)	Citation of specific publication/reference if available	Expression of Uncertainty	Justification of source of reference material
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4	Additional factors in ISO 15194 (list other relevant factors)?				Additional Comments	Contact Information for Additional Details				Is there a sustainable source for the material?
5	Are intended use and instructions for use available?	Are dates of authorization and revision given?	Are safety precautions listed?	Validation report available?		Name	Email address	Phone number	How to obtain certificate	
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4		JCTLM Identificati on Number for Reviewing Purposes	Analyte/Parameter		Basis for Traceability		Matrix		RM				
5	Nominated by:		Analyte Category	Analyte Name	Traceable to SI?	Procedurally- defined (if so, name/cite procedure	Matrix Category	Matrix	Identifier/ Number	Name	Certifying Organization	Mode/approach used for value assignment (if not clearly stated in certificate)	Comments
100													

	N	O	P	Q	R	S	T	U	V	W	X	Y	Z	AA	AB	AC	AD
4				Concentration or Concentration Range of Analyte Certified/Assigned Value			Range of Expanded Uncertainty for Analyte Certified/Assigned Value				Information for Assessing Commutability				Congruent with other crit		
5	Issued by NMI with Certificate	Certificate from Other RM provider?	RM listed in BIPM Database?	From	To	Unit	From	To	Unit	Lev. of confidence (%)	Physical form of RM matrix	RM fortified with analyte or naturally incurred	Applicable analyte characteristics (e.g., isoform(s); free/bound, total)	Other relevant factors (list)	Citation of specific publication/reference if available	Expression of Uncertainty	Justification of source of reference material
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	AE	AF	AG	AH	AI	AJ	AK	AL	AM	AN
4	Additional factors in ISO 15194 (list other relevant factors)?				Additional Comments	Contact Information for Additional Details				Is there a sustainable source for the material?
5	Are intended use and instructions for use available?	Are dates of authorization and revision given?	Are safety precautions listed?	Validation report available?		Name	Email address	Phone number	How to obtain certificate	
100										

Information Needed for Evaluation of Nominated Reference METHOD PROCEDURES by JCTLM Review Teams

Blue columns or items listed as essential in ISO 15193		Orange Columns are Critical attributes										
Nominated by:	JCTLM Identif. No. for reviewing purposes	Analyte/Parameter		Method capable of traceability of analyte to SI or defined procedure?	Matrix		Method/ Procedure					
		Analyte Category	Analyte Name		Matrix Category	Applicable Matrices	Identifier/ Number	Name	Organization that developed/validated method	Measurement Technique(s) Used	Comments 1	Comments 2

Applicable Method Concentration Range			Method Expanded Uncertainty Range			Method/Procedure Documentation				C	
From	To	Unit	From	To	Unit	Peer Reviewed Publication	How to obtain copy of method if literature publication is not available	CCQM Key Comparison Report	Non-CCQM Interlaboratory Comparison Report	Other means of validation used?	Credentialed by a professional organization?

Congruent with other critical factors in ISO 75193 (list factors)				Additional Comments	Contact Information for Additional Details		
Measurement clearly defined?	No known patent issues	Multiple testing sites not required to obtain a single value	Method instructions do not contain all of the required items (list missing items from checklist)		Name	Email address	Phone number

TITLE – Process for Review and Approval of Nominated Certified Reference Materials and Reference Measurement			
Author : R. R. Miller	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG1 P-03

PROCESS FOR REVIEW AND APPROVAL OF NOMINATED CERTIFIED REFERENCE MATERIALS AND REFERENCE MEASUREMENT PROCEDURES

RICHARD R. MILLER

PROCEDURE

JCTLM WG1-P-03

AUTHOR	AUTHORIZED
NAME RICHARD R. MILLER	NAME
FUNCTION MEMBER, JCTLM WG1	FUNCTION
SIGNATURE	SIGNATURE

TITLE – Process for Review and Approval of Nominated Certified Reference Materials and Reference Measurement			
Author : R. R. Miller	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG1 P-03

PROCESS FOR REVIEW AND APPROVAL OF NOMINATED CERTIFIED REFERENCE MATERIALS AND REFERENCE MEASUREMENT PROCEDURES

Contents

PARAGRAPH	TITLE	PAGE
CONTENTS.....		2
1. PURPOSE.....		2
2. SCOPE.....		2
3. ACRONYMS.....		2
4. DEFINITIONS.....		3
5. RESPONSIBILITIES AND AUTHORIZATIONS.....		3
6. PROCEDURE.....		3
7. RELATED DOCUMENTS.....		5
8. ATTACHMENTS		6
REVISION HISTORY		6
ATTACHMENT 1 FLOWCHART.....		7
ATTACHMENT 2 JCTLM WG1-P03-F-01 REFERENCE MATERIAL REVIEW SUMMARY FORM		8
ATTACHMENT 3 JCTLM WG1-P03-F-02 REFERENCE MEASUREMENT PROCEDURE REVIEW SUMMARY FORM.....		9

1. Purpose

This procedure describes the process of reviewing nominated CRMs and RMPs to assure they meet the quality requirements of the JCTLM for inclusion in its lists of available higher order materials and procedures.

2. Scope

This procedure will be applied to all complete nominations received by the WG1 Chair for inclusion in the JCTLM lists of higher metrological order CRMs and RMPs.

3. Acronyms

Acronyms used in these procedures are defined in the document JCTLM WG1-P-00, Quality Policy and Definitions

TITLE – Process for Review and Approval of Nominated Certified Reference Materials and Reference Measurement			
Author : R. R. Miller	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG1 P-03

4. Definitions

Definitions for the terms used in these procedures are given in the document JCTLM WG1-P-00, Quality Policy and Definitions.

5. Responsibilities and Authorizations

- 5.1. The WG1 Chair has the responsibility to periodically solicit nominations of CRMs and RMPs according to procedure JCTLM WG1-P-02 “Process for Requesting and Receiving Nominations for Certified Reference Materials and Reference Measurement Procedures” and routing them to the appropriate WG1RTLs.
 - 5.1.1. The WG1 Chair is responsible for routing received nominations to the appropriate WG1RTs.
 - 5.1.2. The WG1 Chair is responsible appointing the Leaders of the WG1RTs and for assuring their compliance to this procedure.
- 5.2. WG1RTs have responsibility for reviewing materials and procedures for a given class of measurand for which they have expertise.
- 5.3. The WG1RTLs are responsible for nominating the Members of a WG1RT. Each team will consist of experts who are expected to review nominations. World-wide representation will be sought for members of RTs. The WG1RT membership will be drawn from representatives of:
 - 5.3.1. national metrology institutes,
 - 5.3.2. clinical laboratories,
 - 5.3.3. manufacturers of IVD devices,
 - 5.3.4. reference measurement laboratories,
 - 5.3.5. others as deemed needed.
- 5.4. The WG1 Chair approves nominations for WG1RT members.
- 5.5. It is the responsibility of the JCTLM Secretariat to receive the recommendations of the WG1RTs from the WG1 Chair and request the inclusion of new CRM and RMP nominations to the JCTLM list of Certified Reference Materials and Reference Measurement Procedures to the JCTLM Executive.

6. Procedure

- 6.1. Completed nomination forms are forwarded from the WG1 Chair and received by WG1RTLs.
 - 6.1.1. JCTLM WG1-P-02-F-01 Certified Reference Material Nomination Form
 - 6.1.2. JCTLM WG1-P-02-F-02 Reference Measurement Procedure Nomination Form
 - 6.1.3. Each WG1RTL distributes the list to the WG1RT Members.
- 6.2. The WG1RT audits the completed nominations.

TITLE – Process for Review and Approval of Nominated Certified Reference Materials and Reference Measurement			
Author : R. R. Miller	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG1 P-03

- 6.2.1. Prior to reviewing any nominations, the appropriate standards will be reviewed by the WG1 Review Team. Checklists may be used to facilitate the review.
 - 6.2.1.1. ISO 15194 is the appropriate standard for CRMs.
 - 6.2.1.2. ISO 15193 is the appropriate standard for RMPs.
 - 6.2.1.3. Upon review of the standards, the attributes specified in them may be listed as “waived”. An attribute may be waived if it is not applicable for the class of measurands in question.
 - 6.2.1.4. If an attribute is waived by a WG1RT, technical justification for waiving it must be stated. That justification must be included with the final recommendation to the WG1 Chair who will determine if the justification is applicable. However, it is recommended that waived attributes be communicated to the Chair as early as possible. The Chair may use the membership of WG1 to assist with this determination.
 - 6.2.1.5. The remaining attributes may also be assigned a Critical and a Major importance. For a nomination to be recommended by the review team, all Critical Attributes must be present. There may be Major attributes that are not present. For major attributes that are not present, justification for their absence must be documented. The absence of such attributes will be communicated to the nominator.
 - 6.2.1.6. The absence of Critical and/or Major Attributes will be described in the written Material or Procedure review summaries used by WG1RTLs as a part of their recommendations to the Chair of WG1 for approval.
- 6.2.2. Review Team Members, either individually or as a group, review the individual nominations for compliance to appropriate ISO standards.
 - 6.2.2.1. Additional information may be required from the nominator for clarification. If so, the additional information will be added to the form and checklist, as appropriate.
- 6.2.3. Upon completion of the review, the WG1RTL will circulate the recommendation and supporting forms/checklists to the members of the team.
- 6.2.4. Consensus will be obtained by the WG1RT for each recommendation.
- 6.3. Documentation of the basis for the decision to list or not list for each CRM and RMP will be found in the Reference Material Review Summary Form WG1-P03-F-01 or Reference Measurement Procedure Review Summary Form WG1-P03-F-02.
- 6.4. Reference Material Review Summary Form WG1-P03-F-01 or Reference Measurement Procedure Review Summary Form WG1-P03-F-02 will be sent to producers of CRMs and developer/owners of RMPs after the completion of the review process.
- 6.5. The WG1RTL forwards the recommendation, forms and checklists to the WG1 Chair.
 - 6.5.1. The WG1 Chair will review the recommendation and documentation for compliance to this procedure and clarity of the information.

TITLE – Process for Review and Approval of Nominated Certified Reference Materials and Reference Measurement			
Author : R. R. Miller	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG1 P-03

- 6.5.2. If clarification is needed, the WG1 Chair will request it from the WG1RTL.
- 6.5.3. If necessary, the WG1 Chair may utilize the WG1 membership as a resource to assure consistency of the recommendations made by the different review teams.
- 6.6. If the consensus opinion is that the CRM or RMP **does not** meet the relevant criteria, the JCTLM Secretariat will inform the nominator of the identified deficiencies by providing them with a copy of the relevant Reference Material Review Summary Form – WG1--P03--F-01 or the Reference Measurement Procedure Review Summary Form - WG1--P03-F02-F-02.
- 6.7. If the consensus opinion is that the CRM or RMP **does** meet the relevant criteria, the JCTLM Secretariat adds the CRM or RMP to the list of CRMs and RMPs that will be provided to the JCTLM Executive for approval for inclusion on the relevant JCTLM lists.
- 6.8. For all CRMs evaluated, the WG1RT evaluates whether other newly evaluated or currently JCTLM listed CRMs are intended for the same purpose. All such CRMs will be placed on a list of candidates for comparability evaluation by the WG1RTL according to procedure JCTLM WG1-P-04 “Process for the Demonstration of the Comparability of Certified Values of the Same Measurand in Multiple Materials Having the Same Nominal Matrix.” Comparability is not a requirement for recommending a CRM for JCTLM listing; comparability information is provided only to aid potential users of CRMs to make an informed choice of materials when more than one material is nominally fit for a given purpose.
- 6.9. Completed Reference Material Review Summary Forms WG1-P03-F-01 and Reference Measurement Procedure Review Summary Forms WG1-P03-F-02 and the list of candidate materials for comparability testing will be maintained by the JCTLM Secretariat.

7. Related Documents

ISO 15193	In vitro diagnostic systems – Measurement of quantities in samples of biological origin – Presentation of reference measurement procedures
ISO 15194	In vitro diagnostic systems – Measurement of quantities in samples of biological origin – Description of reference materials
JCTLM WG1-P-00	Quality Policy and Definitions
JCTLM WG1-P-01	Outline of JCTLM Procedures for Evaluating Materials and Procedures to be listed as Being of Higher Metrological Order
JCTLM WG1-P-02	Process for Requesting and Accepting Nominations for Certified Reference Materials and Reference Procedures
JCTLM WG1-P-02-F-01	Certified Reference Material Nomination Form
JCTLM WG1-P-02-F-02	Reference Measurement Procedure Nomination Form

TITLE – Process for Review and Approval of Nominated Certified Reference Materials and Reference Measurement			
Author : R. R. Miller	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG1 P-03

JCTLM WG1-P-04 Process for the Demonstration of the Comparability of Certified Values of the Same Measurand in Multiple Materials Having the Same Nominal Matrix

JCTLM WG1-P03-F-01 Reference Material Review Summary Form

JCTLM WG1-P03-F-02. Reference Measurement Procedure Review Summary Form

8. Attachments

Attachment 1 Flow chart, Review and Approval of Nominated Certified Reference Materials and Reference Measurement Procedures.

Attachment 2 JCTLM WG1-P03-F-01 Reference Material Review Summary Form

Attachment 3 JCTLM WG1-P03-F-02. Reference Measurement Procedure Review Summary Form

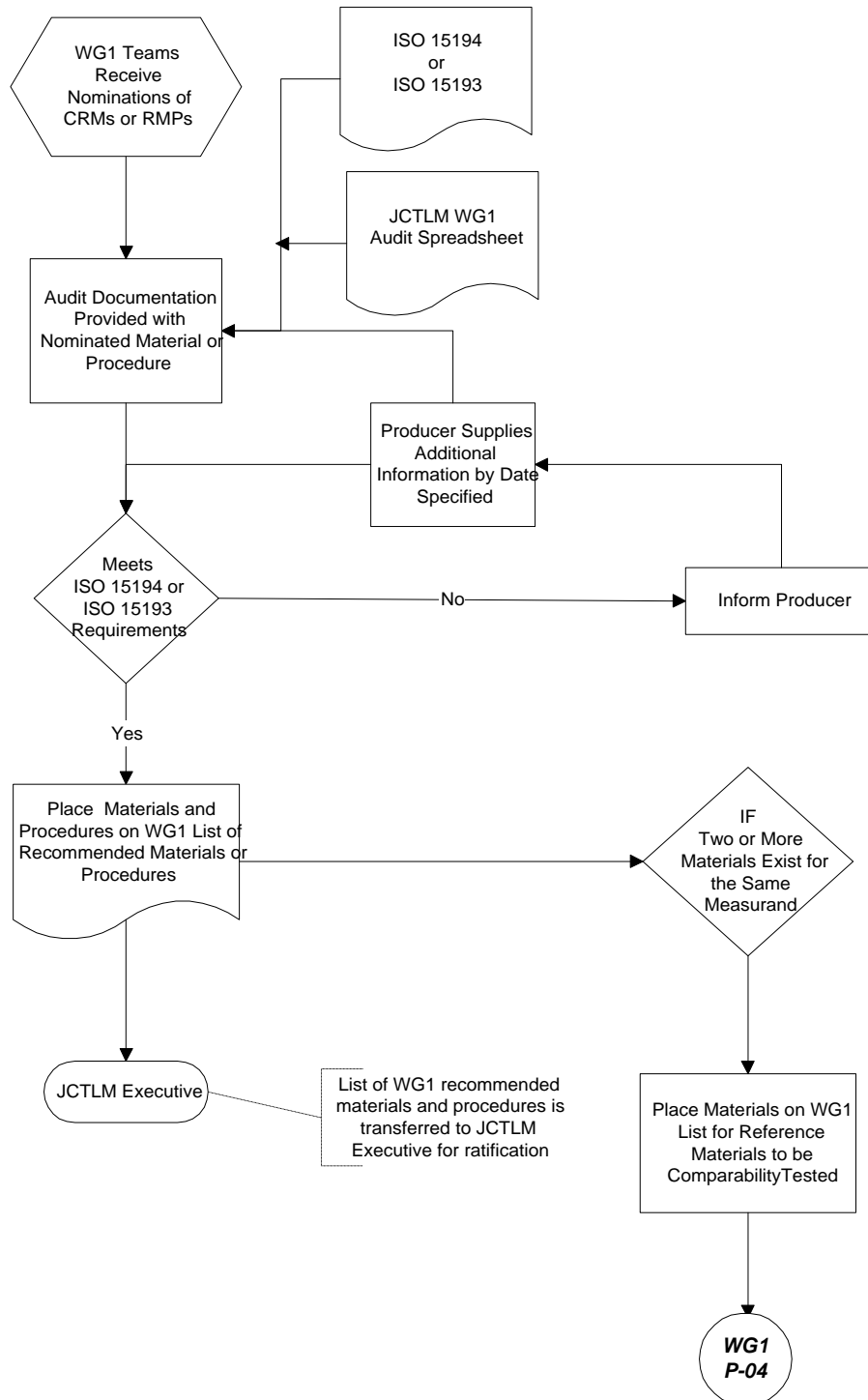
Revision History

Version number	Date of Issue/Review	Summary of change
1.0	23/02/2004	Initial issue of WG1 Quality System Procedures

TITLE – Process for Review and Approval of Nominated Certified Reference Materials and Reference Measurement			
Author : R. R. Miller	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG1 P-03

Attachment 1 Flowchart

REVIEW AND APPROVAL OF NOMINATED REFERENCE MATERIALS AND REFERENCE MEASUREMENT PROCEDURES OF A HIGHER METROLOGICAL ORDER *WG1-P-03*



TITLE – Process for Review and Approval of Nominated Certified Reference Materials and Reference Measurement			
Author : R. R. Miller	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG1 P-03

Attachment 2 JCTLM WG1-P03-F-01 Reference Material Review
Summary Form

**Essential Requirements Checklist
ISO 15194 Description of Reference Materials**

Analyte: (Column D) _____

JCTLM Identifier: (Column B) _____

Contact Person (Column AK/AL) _____

Certifying Organization (Column K) _____

Element	15194 Standard Section	Spreadsheet Column	Comments
There is a clear definition of the units used for the measurand in question.		V	
There is a sustainable source for the material		AN	
Title page/Title of report		C, D	
Warning and safety precautions	5.2	AG	Check for presence or absence only
Scope	5.4	G	
Definitions			
Justification for choice of reference material	5.6	AD	
Specific characteristics	5.8	G,H,	
Assigned value		Q, R, S	
Uncertainty of Measurement or confidence interval		T, U, V	
Validation	5.9	AH	
Intended function	5.10	AE	
Instructions for use	5.11	AE	
Are there Patent restrictions?		Add to AG	For information only
Supplier	5.12	K, N	
Dates of updates or certificate approval available?	5.15	AF	

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Author : R. R. Miller	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG1 P-03

**Attachment 3 JCTLM WG1-P03-F-02 Reference Measurement Procedure
Review Summary Form**

**Essential Requirements Checklist
ISO 15193 Reference Measurement Procedure**

Requirement	15193 Standard Section	Spreadsheet Column
The testing protocol <u>does not</u> require multiple-site testing to obtain an analytical result.		
Method Validation (inter-laboratory studies)	4.16	V,W
Is the measurand clearly defined?		
Description of Methodological Principle	4.6	K
Sample type	4.10	C
Analytical Reliability	4.14	See below
Analytical Range	4.14.5; 15	N,O,P
Uncertainty	4.14.4	Q,R,S
For a secondary procedure is the calibration material available?	4.11.2f	Add to columns L,M
Traceable to SI? (Yes/ no)	4.11.2e	E
Certified? / Credentialed? (Yes/no)		Add to column Y
Other means of validation used	(FIO)	Add to column X
References available?	4.1	T,U,V,W
There are no known patent issues		
Method Instructions contains		List missing items in AC
Sample handling and preparation	4.10	
Reagent preparation	4.8	AC
Required equipment	4.9	AC
Preparation and operation of measuring system	4.11; 4.12	AC
Calculations/data processing	4.13	AC
Is the method credentialed/developed by another recognized organization? (yes/no)	(FIO)	J
Are there patent issues with either the method or any of the reagents involved?	(FIO)	

Required Items from Table 1 of ISO 15193 that are not included above:

- ◆ Title Page, Foreword, Title, and Scope - Considered formatting; may not be in current method references.
- ◆ Normative references – Will be covered in other parts above (columns T,U,V,W)
- ◆ Warning and Safety Precautions and Special Cases – Will contain laboratory specific information and should be in the laboratory specific procedure.
- ◆ Reporting/report form and dates of authorization/revision – Will be in laboratory specific procedure, not necessarily references provided.

TITLE: Process for the Demonstration of the Comparability of Certified Values of the Same Measurand in Multiple Materials			
Author : D. L. Duewer	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG1 P-04

***PROCESS FOR THE
DEMONSTRATION OF THE
COMPARABILITY OF CERTIFIED
VALUES OF THE SAME MEASURAND
IN MULTIPLE MATERIALS HAVING
THE SAME NOMINAL MATRIX***

DAVID L. DUEWER

PROCEDURE

JCTLM WG1-P-04

AUTHOR	AUTHORIZED
NAME DAVID L. DUEWER	NAME
FUNCTION MEMBER, PROCEDURES TEAM	FUNCTION
SIGNATURE	SIGNATURE

TITLE: Process for the Demonstration of the Comparability of Certified Values of the Same Measurand in Multiple Materials			
Author : D. L. Duewer	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG1 P-04

PROCESS FOR THE DEMONSTRATION OF THE COMPARABILITY OF CERTIFIED VALUES OF THE SAME MEASURAND IN MULTIPLE MATERIALS HAVING THE SAME NOMINAL MATRIX

1. Contents

PARAGRAPH	TITLE	PAGE
1.	CONTENTS	2
2.	PURPOSE	2
3.	SCOPE	2
4.	ACRONYMS	3
5.	DEFINITIONS	3
6.	RESPONSIBILITIES AND AUTHORIZATIONS	3
7.	PROCEDURE	4
8.	RELATED DOCUMENTS	6
9.	ATTACHMENTS	7
10.	REVISION HISTORY	7
ATTACHMENT 1	POTASSIUM EXAMPLE	8
ATTACHMENT 2	CHOLESTEROL EXAMPLE	11
ATTACHMENT 3	FLOWCHART	14

2. Purpose

This procedure describes the process to be followed by the appropriate JCTLM Working Groups when there are two or more List I CRMs that are nominally fit for the identical purpose(s). The process is intended to ensure that comparability information is available for these materials. When more than one material is listed by the JCTLM, potential CRM users need comparability information to make an informed selection of the material(s) best suited to their needs.

3. Scope

This procedure is to be applied to all List I CRMs that are listed by the JCTLM when two or more of the materials are nominally fit for the same purpose; i.e., the materials have nominally identical matrix and they carry certified values for one or more of the same measurands. Replacement lots of certified reference materials CRMs are deemed to be new materials and are thus subject to the comparability testing procedures described for new materials.

TITLE: Process for the Demonstration of the Comparability of Certified Values of the Same Measurand in Multiple Materials			
Author : D. L. Duewer	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG1 P-04

4. Acronyms

Acronyms used in these procedures are defined in the document JCTLM WG1-P-00, Quality Policy and Definitions.

5. Definitions

Definitions for the terms used in these procedures are given in the document JCTLM WG1-P-00, Quality Policy and Definitions.

6. Responsibilities and Authorizations

- 6.1. The JCTLM Secretariat has the following responsibilities under this procedure.
 - 6.1.1. To request CRM producers to supply their nominated materials to identified measurement laboratories for comparability studies as requested by authorized WG1RTs.
 - 6.1.2. To appropriately web-post the Final Reports on material comparability as provided by the WG1.
- 6.2. The WG1RTLs have the following responsibilities under this procedure.
 - 6.2.1. To refer CRMs accepted by WG1 as fit for the same purpose to the WG1 Chair to arrange comparability evaluation.
 - 6.2.2. To evaluate the Final Reports submitted by the WG1RTs.
 - 6.2.3. To forward accepted Final Reports to the JCTLM Secretariat and to the producers of the CRMs evaluated.
- 6.3. The WG1RTs have the following responsibilities under this procedure.
 - 6.3.1. To define appropriate measurement performance criteria for the particular measurand(s) in the given matrix.
 - 6.3.2. To identify a qualified measurement laboratory willing to perform any necessary measurements.
 - 6.3.3. In collaboration with the measurement laboratory, to define an appropriate measurement protocol.
 - 6.3.4. To determine the comparability of the evaluated CRMs.
 - 6.3.5. In collaboration with the measurement laboratory and others who may be actively involved in the evaluation, to prepare a Final Report of the comparability determination.
 - 6.3.6. When appropriate, to publish the results of comparability studies in peer-reviewed and trade journals.
- 6.4. The measurement laboratories that agree to perform necessary measurements have the following responsibilities under this procedure.

TITLE: Process for the Demonstration of the Comparability of Certified Values of the Same Measurand in Multiple Materials			
Author : D. L. Duewer	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG1 P-04

- 6.4.1. In collaboration with the WG1RT, to define an appropriate measurement protocol that will with good likelihood meet the defined measurement performance criteria defined by the WG1RT.
- 6.4.2. To perform the necessary measurements.
- 6.4.3. To prepare a report of analysis that suitably documents the performed measurements and the measurement systems used.
- 6.4.4. In collaboration with the WG1RT, to prepare a Final Report documenting the comparability of the evaluated CRMs.

7. Procedure

- 7.1. The process for demonstrating the comparability of materials will be initiated by WG1 Chair whenever two or more materials that are nominally fit for the same purpose are listed in the JCTLM database. WG1 Chair will assign responsibility for supervising the procedure to an appropriate WG1RT. When possible, the comparability demonstration process should be completed within 12 months of the initiation of the process.
- 7.2. Identify Measurement Performance Requirements. Comparability evaluation requires adequate relative, not absolute, measurements of measurand level in the different materials. The major considerations for selecting an appropriate measurement system for these relative measurements are sensitivity, specificity, linearity, and repeatability. It is the responsibility of the designated WG1RT to establish fit-for-purpose criteria for these performance metrics for each set of multiple materials, given the stated purpose of the materials and the certified values and uncertainties of the measurands.

The following apply separately to each measurand evaluated:

- 7.2.1. Sensitivity: the measurement system must provide an adequately sensitive signal at the lowest level certified in any of the materials.
- 7.2.2. Selectivity: the measurement system must provide an adequately selective signal given the materials' general matrix and any explicitly stated material components.
- 7.2.3. Linearity: the measurement system must provide an adequately linear signal to allow direct proportional comparison between the signals of the lowest and highest levels certified in any of the materials.
- 7.2.4. Repeatability: the measurement system must provide adequate repeatability precision over the time course of all measurements required for the comparison, relative to the certified uncertainties of the materials.
- 7.3. Are Adequate Data Available? CRM producers are encouraged to acquire the needed among-CRM comparability data as a component of their certification process. For established CRMs, other interested parties may have performed and published the needed information. The responsible WG1RT will investigate the availability of comparability information and, if it exists, evaluate the data against the criteria established above. If the existing data are adequate, proceed to Section 6.4; if no

TITLE: Process for the Demonstration of the Comparability of Certified Values of the Same Measurand in Multiple Materials			
Author : D. L. Duewer	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG1 P-04

information is available or the available information is not adequate, proceed with Section 6.3.

7.4. Adequate Data are Not Available. If adequate comparability data are not available, the responsible WG1RT should initiate a program to acquire adequate data.

7.4.1. A laboratory capable of adequately performing the measurements must be identified. The CRM producers involved are the likely candidates, but any laboratory that has demonstrated measurement competence for the given measurand(s) in the given sample matrix should be considered.

7.4.2. In consultation with the identified laboratory, an appropriate measurement protocol must be developed that has good potential for satisfying the performance criteria of Section 7.1. The protocol should provide for at least two independent replicate determinations of the measurand(s) for each unit of each material analyzed. The protocol should not require consumption of more than two units of each of the relevant CRMs. Example protocols are provided in the Attachments to this Procedure.

7.4.3. The responsible WG1RT requests the JCTLM Secretariat to request shipment of the relevant CRMs to the identified laboratory.

7.4.4. The identified measurement laboratory performs the measurements and prepares a report of analysis that documents: the analytical measurement process employed, the measurement linearity over the measurand levels of interest, measurement repeatability over the measurand levels of interest, and the measurement results for each material.

7.4.5. The measurement laboratory should send the report of analysis to the WG1RTL who solicited the study. In the advent of unanticipated measurement difficulties or results that do not meet the performance criteria of Section 6.1, the WG1RT and the measurement laboratory should together attempt to resolve the difficulties or deficiencies. If the WG1RT judges that the data remain insufficient for valid comparison, the measurement performance criteria should be re-evaluated and/or a new measurement effort must be initiated.

7.5. Adequate Data are Available. Once adequate comparability data are available, the responsible WG1RT will determine the comparability of the materials.

7.5.1. Given sufficiently unbiased measurements such as those summarized in Table 1 and Figures 1a and 1b of Attachment 1, comparability can be evaluated from the extent of overlap between the 95% confidence intervals of the measured value, $X_i \pm U_{95}(X_i)$, and the certified value, $C_i \pm U_{95}(C_i)$, of each material. The least squares regression of the measured X_i as a linear function of the certified values, $X_i = a + bC_i$, enables evaluation of bias: within their asymptotic uncertainties, the intercept is zero and the slope is one.

While Figure 1a displays both the measured and certified value intervals, it is difficult to visually compare them due to the range of measurand levels in the CRMs. Figure 1b provides a much more interpretable display by expressing the intervals relative to the certified values: $X_i/C_i \pm U_{95}(X_i)/C_i$ and $1 \pm U_{95}(C_i)/C_i$. For all materials, there is a nearly complete overlap between

TITLE: Process for the Demonstration of the Comparability of Certified Values of the Same Measurand in Multiple Materials			
Author : D. L. Duewer	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG1 P-04

the measured and certified intervals: these CRMs are fully and about equally comparable for potassium.

- 7.5.2. Relative comparability can be evaluated using biased measurement systems. The measured and certified values summarized in Table 2 and Figures 2a and 2b of Attachment 2 are linearly related; however, while the intercept is zero to within model error, the slope is not unity, i.e., the measurement system is proportionally biased. The measurement and certified value intervals must be suitably adjusted before they can be compared.

Figure 2b displays the relative measurement interval, $X_i/C_i \pm U_{95}(X_i)/C_i$ and the slope-scaled certified intervals, $b \pm U_{95}(C_i)/C_i$. While the intervals for all materials do overlap, the overlap for two of the materials is marginal. Thus, while these CRMs are comparable for cholesterol, a few of the materials are less comparable than are the majority. The variability in the size and overlap of the measurement and certified value intervals in Figure 2b suggest that the certified uncertainties (including the material homogeneity component) of several materials should be re-evaluated.

- 7.5.3. Similar, analyses can be used as long as a functional relationship between measured and certified values can be established. A detailed report of such analyses is in preparation.
- 7.6. A draft report of the comparability of the evaluated CRMs will be prepared by the responsible WG1RT. When resources allow, preparation of the report for publication in an appropriate peer-reviewed forum will help assure potential users of the study's probity as well as publicizing the JCTLM's efforts. All parties actively involved in the study should co-author the report.
- 7.7. Once the report is approved by all co-authors, the WG1RTL will submit the draft to the WG1 for approval. After review and approval, the WG1 Chair will provide the JCTLM Secretariat with the Final report in a format suitable for webpage publication. The JCTLM Secretariat will ensure that all of the CRM producers involved are sent copies of the report.
- 7.8. If the CRMs are found not to be comparable, the WG1 Chair will refer all CRMs within the comparison set to their producers for further investigation to resolve the discrepant results. All listed CRMs will be annotated to indicate that comparability is under further investigation.

8. Related documents

JCTLM WG1-P-00	Quality Policy and Definitions
JCTLM WG1-P-01	Outline of JCTLM Procedures for Evaluating Materials and Procedures to be Listed as Being of Higher Metrological Order
JCTLM WG1-P-03	Process for Review and Approval of Nominated Certified Reference Materials and Reference Measurement Procedures

TITLE: Process for the Demonstration of the Comparability of Certified Values of the Same Measurand in Multiple Materials			
Author : D. L. Duewer	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG1 P-04

9. Attachments

- Attachment 1 Example, Comparison of Certified and Measured Values of Potassium in Human Serum CRMs
- Attachment 2 Example, Comparison of Certified and Measured Values of Cholesterol in Human Serum CRMs
- Attachment 3 Flow chart, Process for the Demonstration of the Comparability of Certified Values of the Same Measurand in Multiple Materials Having the Same Nominal Matrix

10. Revision History

Version number	Date of Issue/Review	Summary of change
1.0	09/15/2004	Initial issue of WG1 Quality System Procedures

TITLE: Process for the Demonstration of the Comparability of Certified Values of the Same Measurand in Multiple Materials			
Author : D. L. Duewer	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG1 P-04

Attachment 1 Potassium Example

Table 1: Protocol, Measurements, and Summary Statistics for the Comparison of Certified and Measured Values of Potassium in Human Serum CRMs
All values are in nmol/L.

CRM ^a	Certified ^b		Measured ^c				Summary Statistics				
	Value	U ₉₅	Campaign 1		Campaign 2		Mean	SD	R ^d	u _c ^e	U ₉₅ ^f
			Value	U ₉₅	Value	U ₉₅					
JCCRM 111-5, L	3.250	0.020	3.241	0.027	3.241	0.025	3.241	0.000	0.013	0.013	0.026
JCCRM 111-5, M	4.400	0.020	4.419	0.027	4.400	0.034	4.410	0.013	0.015	0.020	0.041
JCCRM 111-5, H	5.690	0.020	5.698	0.047	5.706	0.044	5.702	0.006	0.023	0.023	0.047
SRM 909b, Lv 1	3.424	0.025	3.437	0.028	3.425	0.027	3.431	0.008	0.014	0.016	0.032
SRM 909b, Lv 2	6.278	0.052	6.286	0.052	6.248	0.048	6.267	0.027	0.025	0.037	0.073
SRM 956a, Lv 1	6.008	0.020	5.983	0.049	6.008	0.046	5.996	0.018	0.024	0.030	0.059
SRM 956a, Lv 2	3.985	0.020	3.993	0.033	3.993	0.031	3.993	0.000	0.016	0.016	0.032
SRM 956a, Lv 3	2.025	0.008	2.022	0.017	2.016	0.016	2.019	0.004	0.008	0.009	0.019

- a CRMs suitable for the calibration or verification of potassium in human serum proposed for listing by the JCTLM as of May, 2003. Materials with prefix 'JCCRM' are available from the National Institute of Materials and Chemical Research, Japan; those with prefix 'SRM' are available from the National Institute of Standards and Technology (NIST), USA.
- b Certified values and 95% confidence level uncertainties as listed on the CRM Certificates.
- c Measured values and fully evaluated 95% confidence level uncertainties. The determinations were performed at NIST using isotope dilution mass spectroscopy. The potassium level of each level of every CRM was fully evaluated in two separately analyzed vials of the material. The two sets of vials were analyzed in separate measurement campaigns.
- d Expected repeatability standard deviation of a single determination in this matrix in this laboratory using the given method, estimated as one-half of the pooled Campaign 1 and 2 U₉₅ values:

$$R = 0.5 \sqrt{\frac{U_{95,1}^2 + U_{95,2}^2}{2}}$$

- e Combined uncertainty, $u_c = \sqrt{SD^2 + R^2}$.
- f Approximate 95% confidence expanded uncertainty, $2u_c$.

TITLE: Process for the Demonstration of the Comparability of Certified Values of the Same Measurand in Multiple Materials

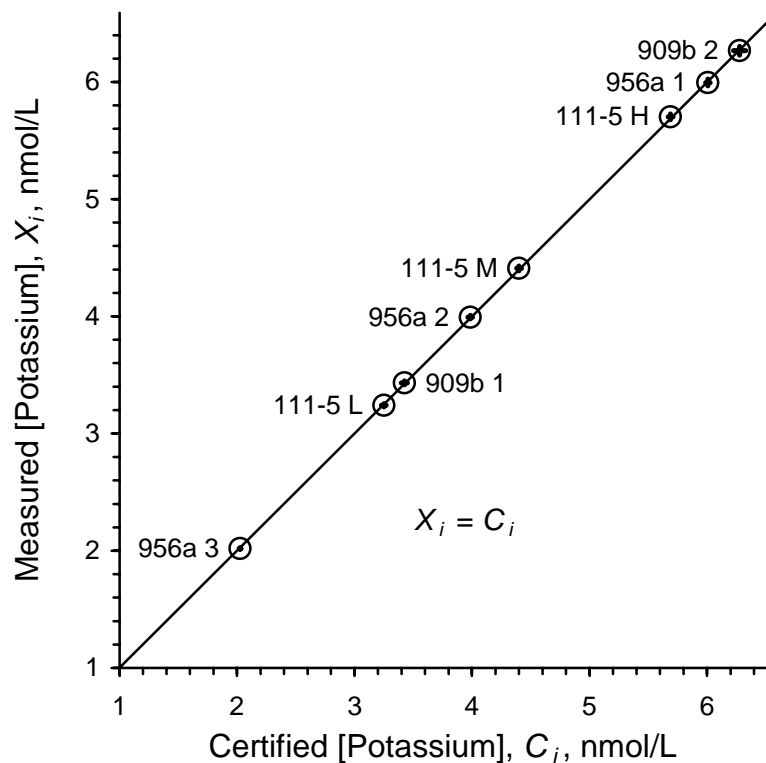
Author : D. L. Duewer

Date : 09/15/2004
Version : 1.0

Authorized :

JCTLM WG1
P-04

Figure 1a: Scattergram Display of the Comparability of Potassium in Human Serum CRMs



The horizontal axis reports the certified values, C_i ; the vertical reports the average measured values, X_i . Each level of each CRM is displayed as approximate 95% uncertainty intervals along both axes. The intersection of these intervals is bounded by an open circle to aid visual inspection. The line denotes the identify function: $X_i = C_i$. This model was chosen after finding that the intercept of the linear model was not significantly different from zero and the slope was not significantly different from unity: $X_i = (0.003 \pm 0.013) + (0.9993 \pm 0.0028) \times C_i$.

TITLE: Process for the Demonstration of the Comparability of Certified Values of the Same Measurand in Multiple Materials

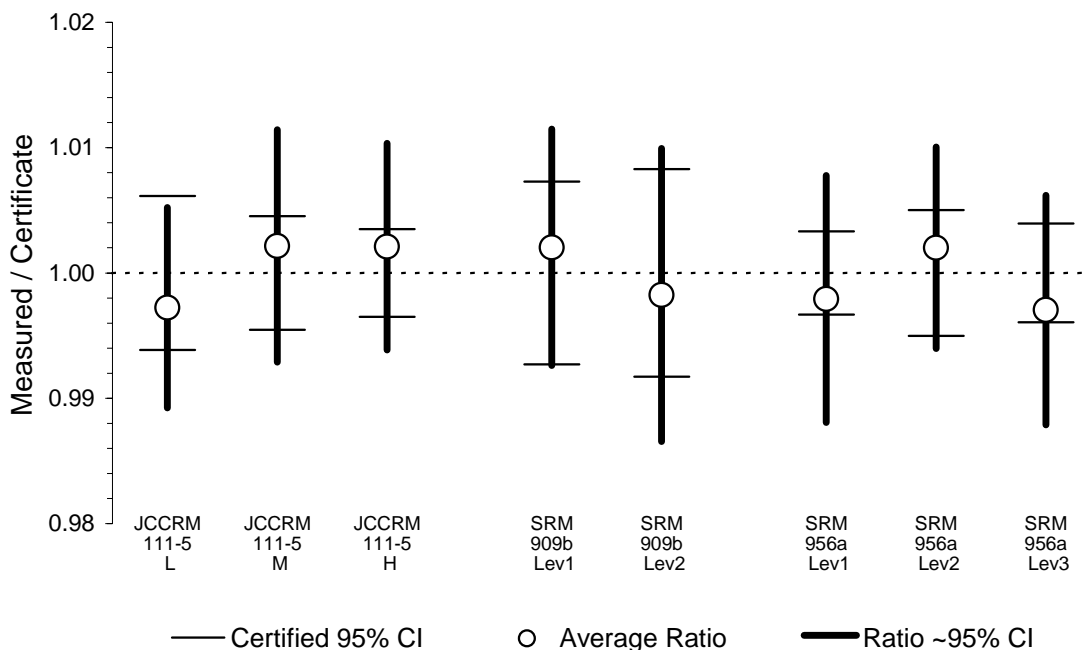
Author : D. L. Duewer

Date : 09/15/2004
Version : 1.0

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JCTLM WG1
P-04

Figure 1b: Ratio Display of the Comparability of Potassium in Human Serum CRMs



The horizontal axis reports the CRMs evaluated. The vertical axis reports the ratio between the average measured and certified values of each CRM, X_i/C_i . The open circles denote these average ratios; the dark vertical lines represent the approximate 95% uncertainty interval on these averages. The light horizontal lines represent the certified 95% confidence intervals. The dotted line represents the expected ratio for the suite of all materials given the observed identity between the measured and certified values.

TITLE: Process for the Demonstration of the Comparability of Certified Values of the Same Measurand in Multiple Materials			
Author : D. L. Duewer	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG1 P-04

Attachment 2 Cholesterol Example

Table 2: Protocol, Measurements, and Summary Statistics for the Comparison of Certified and Measured Values of Cholesterol in Human Serum CRMs
All values are in mg/dL.

CRM ^a	Certified ^b		Measured ^c		Summary Statistics				
	Value	U ₉₅	Set 1	Set 2	Mean	SD	R ^d	u _c ^e	U ₉₅ ^f
JCCRM 211-1, H	205.20	0.80	203.80	204.20	204.00	0.29	0.72	0.78	1.55
JCCRM 211-1, M	262.40	1.00	259.02	260.35	259.68	0.94	0.92	1.32	2.63
SRM 909b, Lv 1	146.40	1.11	146.21	146.40	146.31	0.13	0.52	0.54	1.08
SRM 909b, Lv 2	235.30	1.85	233.45	233.80	233.63	0.24	0.83	0.87	1.73
SRM 968c, Lv 1	133.50	1.30	132.08	132.40	132.24	0.22	0.47	0.52	1.04
SRM 968c, Lv 2	166.90	1.70	166.11	166.20	166.15	0.06	0.59	0.60	1.19
SRM 1589a	157.76	0.37	154.97	155.50	155.24	0.37	0.55	0.67	1.34
SRM 1951a, Lv 1	182.15	0.45	181.63	182.10	181.86	0.34	0.64	0.73	1.45
SRM 1951a, Lv 2	276.67	0.55	277.14	276.95	277.05	0.14	0.98	0.99	1.98
SRM 1952a, Lv 1	147.50	0.96	147.04	147.20	147.12	0.11	0.52	0.53	1.07
SRM 1952a, Lv 2	233.40	0.96	231.68	229.25	230.47	1.72	0.82	1.90	3.81
SRM 1952a, Lv 3	333.00	1.65	327.28	330.45	328.87	2.24	1.19	2.53	5.07

- a CRMs suitable for the calibration or verification of cholesterol in human serum proposed for listing by the JCTLM as of May, 2003. Materials with prefix 'JCCRM' are available from the National Institute of Materials and Chemical Research, Japan; those with prefix 'SRM' are available from the National Institute of Standards and Technology (NIST), USA.
- b Certified values and 95% confidence level uncertainties as listed on the CRM Certificates.
- c Measurements performed at NIST using isotope dilution/gas chromatography/mass spectroscopy. The cholesterol level of each level of every CRM was determined in two separately analyzed aliquots. Each set of aliquots was analyzed during a single 24 hour period.
- d Expected repeatability standard deviation of a single determination in this matrix in this laboratory using the given method, 0.35% of the measured value.
- e Combined uncertainty, $u_c = \sqrt{SD^2 + R^2}$.
- f Approximate 95% confidence expanded uncertainty, $2u_c$.

TITLE: Process for the Demonstration of the Comparability of Certified Values of the Same Measurand in Multiple Materials

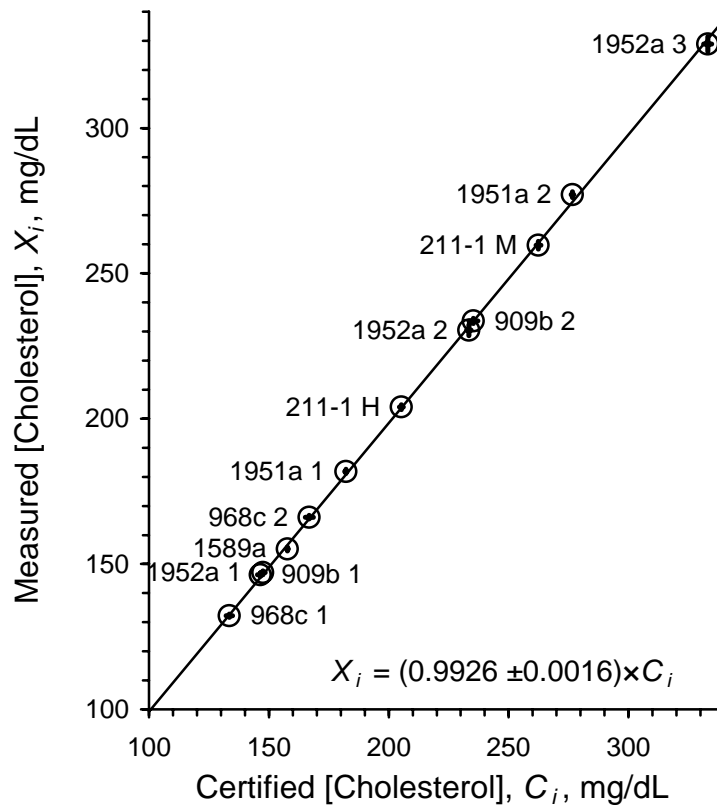
Author : D. L. Duewer

Date : 09/15/2004
Version : 1.0

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JCTLM WG1
P-04

Figure 2a: Scattergram Display of the Comparability of Cholesterol in Human Serum CRMs



The horizontal axis reports the certified values, C_i ; the vertical reports the average measured values, X_i . Each level of each CRM is displayed as approximate 95% uncertainty intervals along both axes. The intersection of these intervals is bounded by an open circle to aid visual inspection. The line denotes the best linear model for the relationship between the measured values and the certified values: $X_i = (0.9926 \pm 0.0016) \times C_i$. This proportional model was chosen after finding that the intercept of the linear model was not significantly different from zero: $X_i = (0.92 \pm 1.27) + (0.9885 \pm 0.0059) \times C_i$.

TITLE: Process for the Demonstration of the Comparability of Certified Values of the Same Measurand in Multiple Materials

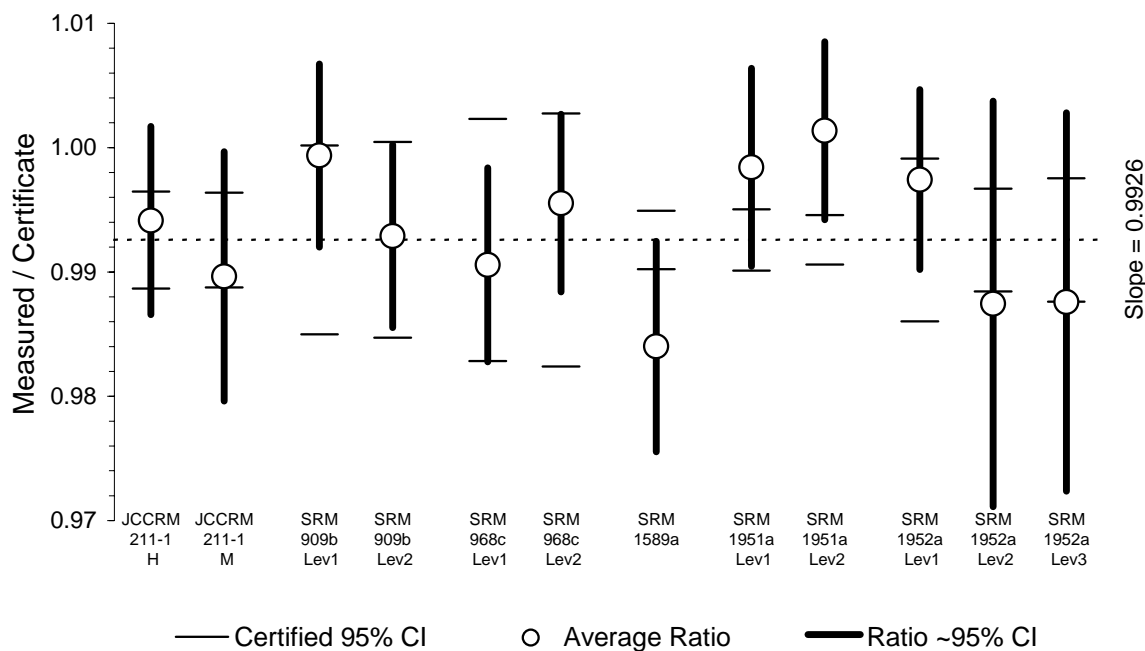
Author : D. L. Duewer

Date : 09/15/2004
Version : 1.0

Authorized :

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P-04

Figure 2b: Ratio Display of the Comparability of Cholesterol in Human Serum CRMs



The horizontal axis reports the CRMs evaluated. The vertical axis reports the ratio between the average measured and certified values of each CRM, X_i/C_i . The open circles denote these average ratios ; the dark vertical lines represent the approximate 95% uncertainty interval on these averages. The light horizontal lines represent the certified 95% confidence intervals, scaled by the proportional model for the relationship between the measured values and the certified values: $X_i = (0.9926 \pm 0.0016) \times C_i$. The dotted line represents the expected ratio for the suite of all materials given the observed proportionality between the measured and certified values.

TITLE: Process for the Demonstration of the Comparability of Certified Values of the Same Measurand in Multiple Materials

Author : D. L. Duewer

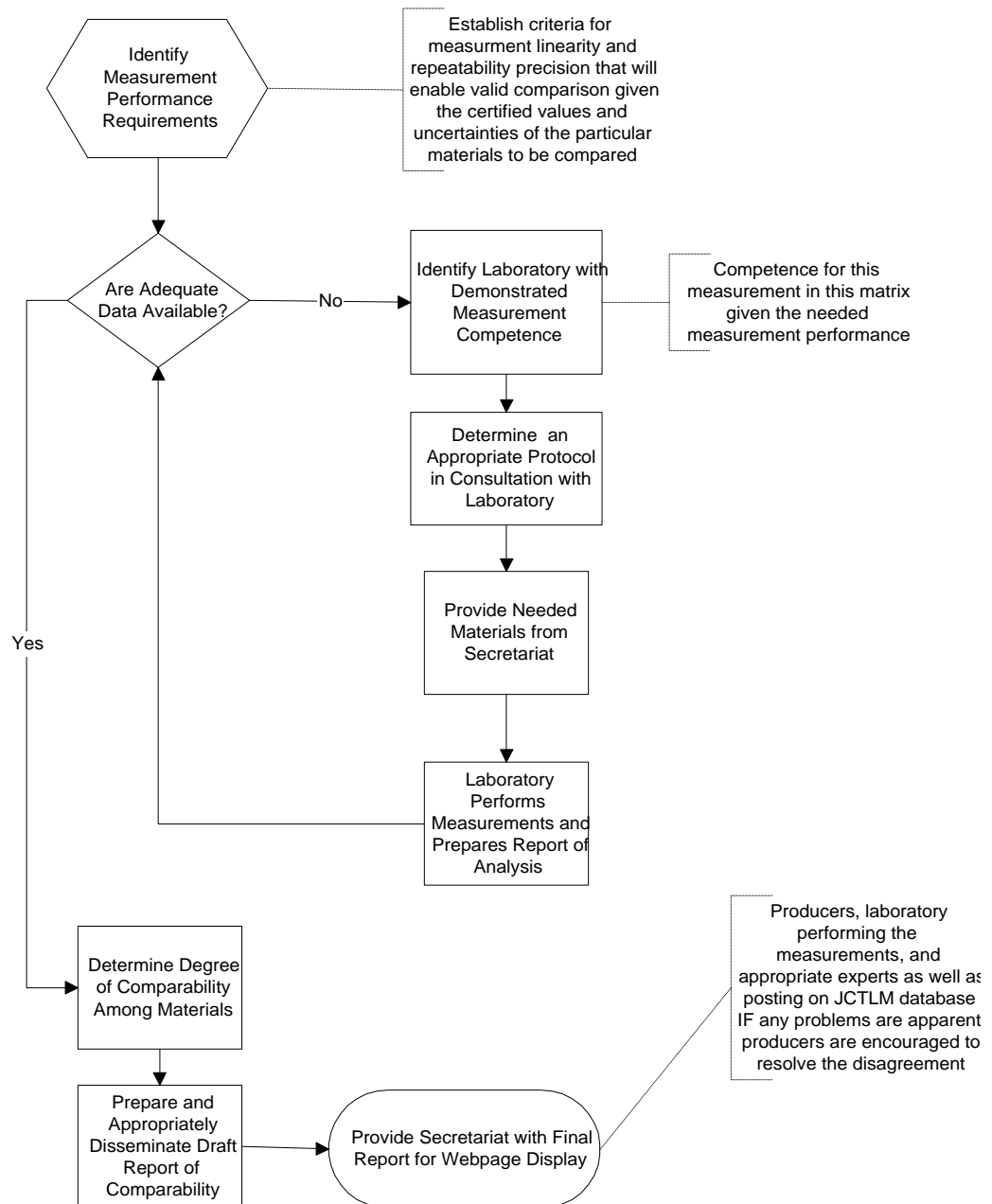
Date : 09/15/2004
Version : 1.0

Authorized :

JCTLM WG1
P-04

Attachment 3 Flowchart

PROCESS FOR THE DEMONSTRATION OF THE COMPARABILITY OF CERTIFIED VALUES OF THE SAME MEASURAND IN MULTIPLE MATERIALS HAVING THE SAME NOMINAL MATRIX WG1-P-04



TITLE: Removal of entries from the JCTLM list			
Author: R I Wielgosz	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG1 P-05

***PROCESS FOR THE REMOVAL OF
ENTRIES FROM THE JCTLM LISTS
OF AVAILABLE HIGHER ORDER
REFERENCE MATERIALS AND
REFERENCE MEASUREMENT
PROCEDURES***

ROBERT I. WIELGOSZ

PROCEDURE

JCTLM WG1-P-05

AUTHOR	AUTHORIZED
NAME ROBERT I. WIELGOSZ	NAME
FUNCTION MEMBER, JCTLM WG1	FUNCTION
SIGNATURE	SIGNATURE

TITLE: Removal of entries from the JCTLM list			
Author: R I Wielgosz	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG1 P-05

PROCESS FOR THE REMOVAL OF ENTRIES FROM THE JCTLM LISTS OF AVAILABLE HIGHER ORDER REFERENCE MATERIALS AND REFERENCE MEASUREMENT PROCEDURES

1. Contents

PARAGRAPH	TITLE	PAGE
1.	CONTENTS	2
2.	PURPOSE	2
3.	SCOPE	2
4.	ACRONYMS	2
5.	DEFINITIONS	2
6.	RESPONSIBILITIES AND AUTHORIZATIONS	3
7.	PROCEDURES	3
8.	RELATED DOCUMENTS	4
9.	REVISION HISTORY	4
	ATTACHMENT 1 FLOWCHART	5

2. Purpose

This procedure describes the process to be followed for the removal of entries from the approved JCTLM lists of available CRMs and RMPs of a higher metrological order.

3. Scope

The procedure will be applied to all requests received for the removal of entries from the approved JCTLM lists of available CRMs and RMPs of a higher metrological order.

4. Acronyms

Acronyms used in these procedures are defined in the document JCTLM WG1-P-00, Quality Policy and Definitions.

5. Definitions

Definitions for the terms used in these procedures are given in the document JCTLM WG1-P-00, Quality Policy and Definitions.

TITLE: Removal of entries from the JCTLM list			
Author: R I Wielgosz	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG1 P-05

6. Responsibilities and Authorizations

- 6.1. The JCTLM Executive has the authority to approve the removal of entries from the JCTLM list following a request that is confirmed by the producer of a CRM or the developer/owner of a RMP.
- 6.2. The JCTLM Executive has the authority to approve the removal of CRMs from the JCTLM list where the request for removal does not originate from the producer when the request has been investigated and upheld by WG1.
- 6.3. The JCTLM Executive has the authority to approve the removal of RMPs from the JCTLM list where the request for removal does not originate from the developer/owner of the RMP when the request has been investigated and upheld by WG1.
- 6.4. It is the responsibility of the WG1 Chair to inform the JCTLM Secretariat of entries to be removed from the JCTLM list.
- 6.5. It is the responsibility of the JCTLM Secretariat to implement authorized changes to the JCTLM lists of higher order CRMs and RMPs.

7. Procedures

7.1. Verification of Requests

- 7.1.1. All requests for the removal of CRMs and RMPs received shall be transmitted to the JCTLM Secretariat.
- 7.1.2. The WG1 Chair will confirm the identity of the person and/or organization making the request and the information related to the request contained in the JCTLM list. This information will be communicated to the JCTLM Secretariat.

7.2. Treatment of Requests

- 7.2.1. The JCTLM Executive authorizes the JCTLM Secretariat to remove entries from the JCTLM list when the request has been made by the producer of the CRM or by the developer/owner of the RMP. Such requests will be automatically granted.
- 7.2.2. Where the request for removal of the entry does not originate from the producer of the CRM or developer/owner of the RMP, the WG1 chair will forward the request to the producer of the CRM or the developer/owner of the RMP. The WG1 Chair will request their consent for the removal of the material or method from the JCTLM list.
 - 7.2.2.1. In the case that consent is given, the WG1 Chair will inform the JCTLM Secretariat. The JCTLM Executive authorizes the JCTLM Secretariat to remove such entries from the JCTLM list. The WG1 Chair will inform the body that made the original request of the actions taken.

TITLE: Removal of entries from the JCTLM list			
Author: R I Wielgosz	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG1 P-05

7.2.2.2. In the case that consent is not given, the WG1 Chair will ask WG1 to make a recommendation to either maintain or remove the entry. The Chair will inform the body that made the original request and the producer or developer/owner of the actions taken. The WG1 Chair will inform the JCTLM Secretariat. The JCTLM Secretariat is authorized to take the action decided by the JCTLM Executive.

7.3. Implementation of Changes to the JCTLM List.

7.3.1. The JCTLM Secretariat will implement authorized changes to the JCTLM list in its monthly update of the JCTLM list.

7.3.2. Entries that are removed from the JCTLM list will be entered into a separate document.

7.3.3. The document will contain a comment field in which the responsible person or organization can state the reasons for removal of the CRM or RMP. Statements sent by the producer or developer/owner to the WG1 Chair will be forwarded to the JCTLM Secretariat for entry into the comment field.

8. Related Documents

JCTLM WG1-P-00	Quality Policy and Definitions
JCTLM WG1-P-01	Outline of JCTLM Procedures for Evaluating Materials and Procedures to be Listed as Being of Higher Metrological Order

9. Revision History

Version number	Date of Issue/Review	Summary of change
1.0	01/08/2004	Initial issue of WG1 Quality System Procedures

TITLE: Removal of entries from the JCTLM list			
Author: R I Wielgosz	Date : 09/15/2004 Version : 1.0	Authorized :	JCTLM WG1 P-05

Attachment 1 Flowchart

PROCESS FOR THE REMOVAL OF ENTRIES FROM JCTLM LISTS OF AVAILABLE HIGHER ORDER REFERENCE MATERIALS AND REFERENCE MEASUREMENT PROCEDURES WG1-P-05

