

<b>TITLE: Process for Demonstrating the Extent-of-equivalence of Reference Measurement Methods/Procedures (RMM/Ps) For The Same Nominal Measurand</b>			
Author : D. L. Duewer	Date: 2006/01/24 Version : 1.1	Authorized : JCTLM Executive	JCTLM WG1 P-04B

**PROCESS FOR DEMONSTRATING  
THE EXTENT-OF-EQUIVALENCE  
OF MULTIPLE REFERENCE  
MEASUREMENT  
METHODS/PROCEDURES (RMM/Ps)  
FOR THE SAME NOMINAL  
MEASURAND**

**JCTLM WG1-P-04B**

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**PROCESS FOR DEMONSTRATING THE EXTENT-OF-EQUIVALENCE OF REFERENCE MEASUREMENT METHODS/PROCEDURES (RMM/Ps) FOR THE SAME NOMINAL MEASURAND**

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**2. Purpose**

This procedure describes the process to be followed by the appropriate JCTLM Working Group 1 Review Teams when there are two or more Reference Measurement Method/Procedures (RMM/Ps) that are nominally fit for the identical purpose(s). The process is intended to ensure that extent-of-equivalence information is available for these RMM/Ps. When more than one RMM/P is listed by the JCTLM, potential users need this information to make an informed selection of the RMM/P best suited to their needs.

**3. Scope**

This procedure is to be applied to JCTLM-listed RMM/Ps that are nominally fit for the same purpose and that do not share the same principles of measurement. RMM/Ps that are minor variations of the same measurement principles do not require extent-of-equivalence demonstration beyond that provided by method validation studies.

**4. Acronyms**

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

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## 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 Executive has the following responsibilities under this procedure.
  - 6.1.1. To accept or reject nominated Final Reports of RMM/P extent-of-equivalence demonstrations.
- 6.2. The JCTLM Secretariat has the following responsibilities under this procedure.
  - 6.2.1. When requested by an authorized WG1RTL, to request RMM/P nominators provide sufficient technical support to ensure that representative measurement results can be obtained.
  - 6.2.2. When requested by an authorized WG1RTL, to request CRM producer/suppliers provide CRMs for use in RMM/P extent-of-equivalence studies.
  - 6.2.3. To place WG1RT recommendations before the JCTLM Executive and communicate the Executive's decisions to the WG1 Chair.
  - 6.2.4. To appropriately post approved RMM/P extent-of-equivalence reports on the JCTLM/BIPM website.
- 6.3. The WG1 Chair(s) has the following responsibilities under this procedure.
  - 6.3.1. To initiate extent-of-equivalence evaluation when two or more RMM/Ps are identified as being fit for the same purpose.
  - 6.3.2. To review WG1RT recommendations
  - 6.3.3. To communicate WG1 recommendations to the JCTLM Secretariat and JCTLM Executive decisions to the WG1RTs.
- 6.4. The WG1RTLs have the following responsibilities under this procedure.
  - 6.4.1. To ensure that WG1RT extent-of-equivalence studies are performed, reports are drafted and recommendations communicated to the WG1 Chair(s) in a timely manner.
  - 6.4.2. If necessary, to communicate with the JCTLM Secretariat regarding procurement of CRMs needed for extent-of-equivalence testing.
- 6.5. The WG1RTs have the following responsibilities under this procedure.
  - 6.5.1. To evaluate the need for and scientific utility of particular RMM/P demonstration studies, as well as identifying whether resources are available to reliably demonstrate extent-of-equivalence among the set of RMM/Ps.
  - 6.5.2. For those studies deemed useful, necessary and fundable, to define an appropriate measurement protocol and a suite of samples (possibly including

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CRMs, calibrants, control materials, multi-donor samples, and native single-donor samples) for evaluating RMM/P measurement performance for a particular measurand(s) in a given matrix or matrices.

- 6.5.3. To identify one or more qualified measurement laboratory(ies) willing to perform any necessary measurements. In general, all involved RMM/P nominators are expected to participate.
- 6.5.4. In collaboration with the measurement laboratory(ies), to define an appropriate measurement protocol.
- 6.5.5. To decide if the suite of samples evaluated adequately represented the population of samples claimed as appropriate for analysis with the RMM/Ps.
- 6.5.6. In collaboration with the measurement laboratory and others who may be actively involved in the evaluation, to prepare a Final Report of the extent-of-equivalence determination.
- 6.5.7. When appropriate, to publish the results of extent-of-equivalence studies in peer-reviewed and trade journals.
- 6.6. The measurement laboratories that agree to perform necessary measurements have the following responsibilities under this procedure.
  - 6.6.1. To perform the necessary measurements.
  - 6.6.2. To prepare a report of analysis that suitably documents the results of the measurements and the measurement systems used.
  - 6.6.3. In collaboration with the WG1RT, to prepare a Final Report documenting the extent-of-equivalence of the evaluated RMM/Ps.

## 7. Procedure

- 7.1. The process for demonstrating the extent-of-equivalence of RMM/Ps will be initiated by the WG1 Chair(s) whenever two or more RMM/Ps that are nominally fit for the same purpose are identified in the JCTLM database. The WG1 Chair(s) will assign responsibility for supervising the evaluation to an appropriate WG1RT. When possible, the extent-of-equivalence demonstration process should be completed within 12 months of the initiation of the process.
- 7.2. Since RMM/Ps nominators are expected to provide extent-of-equivalence information gathered during method validation as part of the nomination process, it is anticipated that relatively few JCTLM-initiated extent-of-equivalence studies will be required. The nominator-supplied validation data are to be included in the JCTLM RMM/Ps Listing and should adequately inform potential users even when direct comparisons are not available.
- 7.3. Even when the available extent-of-equivalence information are contradictory, it must be recognized that direct RMM/P extent-of-equivalence demonstration is intrinsically resource-intensive. Reliable demonstrations will require execution of each RMM/P involved by recognized experts as well as the analysis of numerous typical samples and CRMs. New studies will therefore be initiated only when: 1) the

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extent-of-equivalence demonstration is requested by a JCTLM stakeholder, 2) the WG1RT determines that the demonstration is necessary, and 3) the resources for performing a meaningful demonstration are available. That is, extent-of-equivalence demonstration will be initiated by JCTLM WG1 only when it is deemed scientifically useful, necessary and funded. Unless these conditions are met for a particular set of RMM/Ps, any direct extent-of-equivalence demonstration will be deferred until such time as the conditions are met.

- 7.4. The extent-of-equivalence of two or more RMM/Ps is best demonstrated by analyzing the same, representative suite of samples with each of the RMM/Ps. Where appropriate and available, the suite may include calibration and natural-matrix CRMs, multi-donor blended and spiked materials, as well as single-donor samples.

A extent-of-equivalence evaluation will be meaningful only if “identical” samples are presented to all RMM/Ps. Sufficient quantities of all materials must be available to provide suitable split-samples for all RMM/Ps involved. If the evaluation involves multiple measurement laboratories, the entire sample suite should be assembled and disseminated to the participating analysts at the same time using as similar shipping procedures as possible.

All measurements should be obtained under repeatability conditions by analysts skilled in the RMM/P, using fit-for-purpose materials and instrumentation.

The following apply separately to each measurand/matrix evaluated:

- 7.4.1. Measurement performance characteristics as functions of measurand level. The relative trueness and repeatability claims of an RMM/P can be verified through the analysis of a series of samples having measurand levels that span the expected analytical range. Since repeatability verification will involve the analysis of independently prepared aliquots, CRMs and/or multi-donor sample pools may be the sample materials of choice for this basic verification of measurement performance.
- 7.4.2. Commutability. The relative influence of variability in the physical and chemical composition expected in “routine” samples should be evaluated through analysis of a series of samples representative of the entire intended sample population(s) for the RMM/Ps. Where available, single-donor samples typical of the expected range of abnormal conditions should be included. Where such samples cannot be obtained in sufficient quantity for analysis by all of the RMM/Ps being evaluated, use of exogenously modified multi-donor pools may be necessary.
- 7.5. One or more measurement laboratory(ies) capable of adequately performing all of the measurements must be identified. The nominators of the RMM/Ps involved are expected to participate, but it may be desirable to include other laboratories that have demonstrated measurement competence with one or more of the RMM/Ps for the given measurand(s) in the given sample matrix.

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- 7.6. In consultation with the identified laboratory(ies), an appropriate measurement protocol must be developed that has good potential for demonstrating the relative extent-of-equivalence of the RMM/Ps over a representative range of sample materials. The protocol should also provide for verifying the claimed measurement performance characteristics of the RMM/Ps. Example protocols are provided in the Attachments to this Procedure.
- 7.7. If necessary, the responsible WG1RT requests the JCTLM Secretariat to request the RMM/P nominators to provide sufficient technical support for the comparison to ensure representative measurement results for all RMM/Ps involved.
- 7.8. If necessary, the responsible WG1RT asks the JCTLM Secretariat to request that interested parties help provide an appropriate suite of CRMs, control materials, and multiple- and single-source samples for the evaluation.
- 7.9. The identified measurement laboratory(ies) perform(s) the measurements and prepares a report of analysis detailing their analysis of all samples in the evaluation suite.
- 7.10. The measurement laboratory will send the report of analysis to the WG1RTL responsible for the demonstration. In the event of unanticipated measurement difficulties, the WG1RT and the measurement laboratory(ies) should together attempt to resolve the difficulties or deficiencies. If the WG1RT judges that the data remain insufficient for valid comparison, the measurement protocol should be re-evaluated and/or a new evaluation effort must be initiated.
- 7.11. Once adequate extent-of-equivalence data are available, the responsible WG1RT will determine the extent-of-equivalence of the RMM/Ps. Extent-of-equivalence can be evaluated and displayed using “Brand-Altman”-style plots of the differences in values as a function of measurand level, relative to the claimed RMM/P measurement performance characteristics.
- 7.12. A draft report of the extent-of-equivalence of the evaluated RMM/Ps 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.
- 7.13. Once the report is approved by all co-authors, the WG1RTL will submit the draft Final Report to the WG1 Chair(s) for review. The WG1 Chair(s) will communicate any concerns and suggestions about the draft Report to the WG1RTL. The WG1RTL will coordinate any needed revision and further review. Once approved by all co-authors and the WG1 Chair, the WG1 Chair(s) will recommend approval of the Final Report to the JCTLM Executive. The JCTLM Secretariat will ensure timely communication between the WG1 and JCTLM Executive. In the event of an adverse decision by the JCTLM Executive, the WG1 Chair(s) will coordinate timely communication of the Executive’s concerns and suggestions to the WG1RTL.
- 7.14. If the results of an approved extent-of-equivalence study indicate discordance among the evaluated RMM/Ps relative to fit-for-purpose criteria, the WG1 Chair(s) will refer all RMM/Ps in the compared set to their nominators for further investigation to resolve the discrepant results. A comment noting that the extent-of-equivalence of

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the RMM/Ps is under further review will be added to all of the listing of all of the RMM/Ps until resolution is achieved or one or more of the RMM/Ps is withdrawn by its nominator.

## 8. Related documents

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

## 9. Attachments

Attachment 1	Extent-of-equivalence of IDMS and Abel-Kendall Measurement of Total Cholesterol in Human Serum
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### Revision History

Version number	Date of Issue/Review	Summary of change
1.0	11/15/2005	Separated from JCTLM WG1-P-0 Version 2.0
1.1	24/01/2006	Correction to minor textual errors

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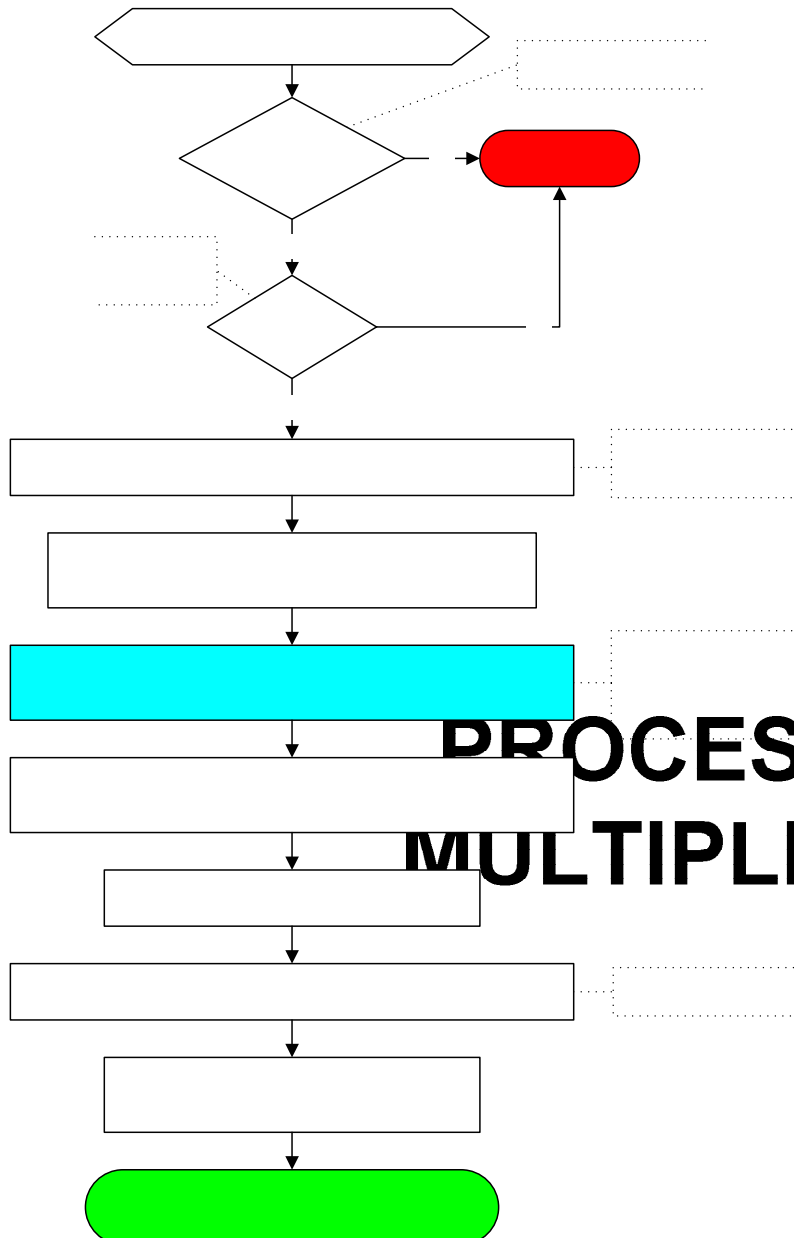
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10. Flowchart



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For Each Set of Multiple

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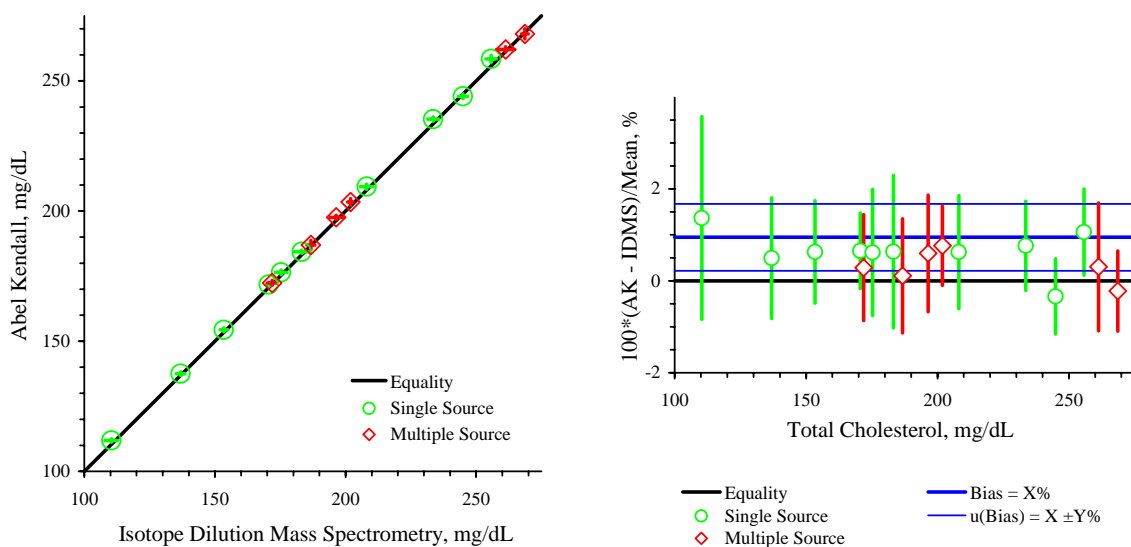
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**Attachment 1 IDMS versus Abel-Kendall Cholesterol**

**Assessment of Extent of Equivalence of IDMS and Abel-Kendall Cholesterol Measurements in Liquid Frozen Serum**



Private communication from David L. Duewer, Michael J. Welch, and Mary M. Kimberly. NIST provided the IDMS measurements, CDC provided the Abel-Kendall measurements. The “error bars” represent approximate 95% confidence intervals on the expected values.