

Demonstrating the extent-of-equivalence between multiple reference measurement methods/procedures (RMM/Ps) for the same measurand

1. Purpose

This document describes the JCTLM process which can be followed by the developers of Reference Measurement Method/Procedures (RMM/Ps) for demonstrating and evaluating the extent-of-equivalence of 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 at least one RMM/P is listed by the JCTLM, the nominator is responsible for the submission of an extent-of-equivalence report that will be made available to the end users on the JCTLM website. The extent-of-equivalence evaluation will allow demonstration of whether the RMM/Ps are fit-for-purpose when used in a calibration hierarchy for end-user measurement procedures. 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.

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3. Scope

This procedure applies to all nominations of RMM/Ps that are submitted for evaluation by JCTLM DB WG for inclusion in the JCTLM database where there are JCTLM listed RMM/Ps that are claimed to be fit for the same purpose.


4. Acronyms and definitions

All acronyms and definitions employed in the procedures of the JCTLM DB WG Quality Manual are given in the procedure document JCTLM EXE-G01, Glossary of terms and definitions.

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5. Responsibilities and authorizations


- 5.1. The JCTLM Executive Committee (EC) has the following responsibilities under this procedure.
 - 5.1.1. To accept or reject DB WG's recommendations for listing in the JCTLM Database extent-of-equivalence reports of RMM/Ps evaluated for the same measurand.
 - 5.1.2. To accept or reject DB WG's recommendation for follow up investigation of unacceptable extent-of-equivalence data for a nominated RMM/P when compared to one or more listed RMM/Ps for the same measurand.
- 5.2. The JCTLM Secretariat has the following responsibilities under this procedure.
 - 5.2.1. To forward DB WG's recommendations to the JCTLM EC and communicate the EC's decisions to the RMM/P nominators.
 - 5.2.2. To appropriately post approved RMM/Ps extent-of-equivalence reports on the JCTLM database website.
- 5.3. The DB WG Vice-Chairs have the following responsibilities under this procedure.
 - 5.3.1. To review Review Team's (RT)'s recommendations.
 - 5.3.2. To communicate DB WG's recommendations to the JCTLM Secretariat for EC approval.
- 5.4. The RT leaders have the following responsibilities under this procedure.
 - 5.4.1. To ensure that representative comparison data for RMM/P extent-of-equivalence demonstration are available for evaluation by the RT.
 - 5.4.2. If necessary, to communicate with the JCTLM Secretariat for obtaining additional supporting evidence for extent-of-equivalence studies.
- 5.5. The RTs have the following responsibilities under this procedure.
 - 5.5.1. To review the extent-of-equivalence data as part of the evaluation of a nominated RMM/P.
 - 5.5.2. To determine if the extent-of-equivalence data demonstrates that the nominated RMM/P will produce fit-for-purpose results when used in the calibration hierarchies of end-user measurement procedures.
- 5.6. The RMM/P nominator has the following responsibilities under this procedure.
 - 5.6.1. To initiate extent-of-equivalence evaluation when at least one JCTLM listed RMM/P is identified as being fit for the same purpose for the same measurand as the nominated RMM/P.
 - 5.6.2. To identify one or more qualified measurement laboratory(ies) willing to perform a comparison measurement study. In general, all involved RMM/P owners are expected to participate.
 - 5.6.3. In collaboration with the measurement laboratory(ies), to define and justify an appropriate measurement protocol and criterion for extent-of-equivalence of results.

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- 5.6.4. To prepare a report of analysis that suitably documents the results of the measurements and the measurement systems used.
- 5.6.5. The final report documenting the extent-of-equivalence determination of the evaluated RMM/Ps will be published by JCTLM as part of the listing of the RMM/P.
- 5.7. The measurement laboratory owner of a RMM/P previously listed and fit for the same purpose has the following responsibilities under this procedure
 - 5.7.1. To perform the necessary measurements.
 - 5.7.2. In collaboration with other parties involved, to prepare a final report documenting the extent-of-equivalence determination of the evaluated RMM/Ps for review by JCTLM.
 - 5.7.3. If no listed RMM/P is being actively used, then the nominator is responsible to identify a suitable measurement procedure for comparison as described in clause 6.1.2.

6. Procedure

- 6.1. The process for demonstrating the extent-of-equivalence of RMM/Ps will be initiated by the RMM/P nominator who submits a RMM/P for inclusion in the JCTLM database whenever one or more RMM/P(s) that are nominally fit for the same purpose are listed in the JCTLM database. The extent-of-equivalence demonstration process should be completed by the time the laboratory submits a RMM/P nomination for evaluation by DB WG RT.
 - 6.1.1. To comply with the validation requirements of ISO 15193:2009, RMM/P nominators are required to provide extent-of-equivalence information as part of the nomination process. (See DBWG-P-03A). This equivalence data will be included in the JCTLM RMM/Ps Listing in order to adequately inform potential users.
 - 6.1.2. In the case where no higher-order RMM/Ps are listed by JCTLM to allow for such extent-of-equivalence studies to be performed, the RMM/P nominator is required to conduct a comparison study of its nominated RMM/P with at least one existing well validated candidate RMM/P or globally available end-user measurement procedure used by a routine measurement laboratory.
 - 6.1.2.1. Alternatively, the RMM/P nominator must participate in an appropriate EQA program that uses commutable materials for the measurand in question. The nominator is responsible to provide an explanation to support that the EQA samples are commutable with clinical samples. This EQA information will be considered a sufficient extent-of-equivalence report, assuming the RMM/P is accepted for listing in the database. When another RMM/P is nominated, the originally listed and nominated RMM/Ps will conduct an extent-of-equivalence assessment.
 - 6.1.3. The nominator-supplied comparison data obtained through the above studies will be included in the JCTLM RMM/Ps listing in order to adequately inform potential users.


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- 6.1.4. In the case where there is neither an existing end-user method nor published method for a particular measurand, the RMM/P nominator will provide as an attachment to its nomination a written statement indicating that all possibilities to perform comparability assessment were investigated, and recognizing that the RMM/P will be subject to further extent-of-equivalence assessment when another published method becomes available, and to potential corrective action in case of results demonstrating differences between methods. See DBWG-P-03A.
- 6.2. 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. The suite of samples should include representative and preferably single-donor clinical samples covering a reasonable portion of the measuring intervals of the RMM/Ps in the comparison. Where appropriate and available, the suite may also include calibration and natural-matrix CRMs, multi-donor blended and spiked materials.

An extent-of-equivalence evaluation will be meaningful only if “identical” samples are presented to all RMM/Ps. Sufficient quantities 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:


- 6.2.1. 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 measuring intervals. 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 verification of measurement repeatability performance.
- 6.2.2. The relative influence of variability in the physical and chemical composition expected in “routine” clinical samples should be evaluated through analysis of a series of samples representative of the entire intended sample population(s) for the RMM/Ps. Single-donor clinical 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 multi-donor pools may be necessary.
- 6.3. The RMM/P nominator identifies JCTLM listed RMM/Ps that are nominally fit for the same purpose, and contacts the developers of these listed RMM/Ps to verify if they are willing to participate in an inter-laboratory comparison for validation a newly developed RMM/P. The developers of the JCTLM listed RMM/Ps are expected to participate.
- 6.3.1. If no listed RMM/P is being actively used, then the nominator is responsible to identify a suitable measurement procedure for comparison as described in clause 6.1.2.

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- 6.4. In consultation with the identified laboratory that agreed to participate in a comparison study, the RMM/P nominator develops an appropriate measurement protocol that will demonstrate 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 figures are provided in the Attachments to this Procedure.
- 6.5. A report of the extent-of-equivalence of the evaluated RMM/Ps will be prepared by the nominator and participating laboratories, and submitted as an attachment to the nomination of the RMM/P nominator for assessment by the DB WG RT. All parties actively involved in the study should co-author the report. Extent-of-equivalence can be evaluated and displayed using “Bland-Altman”-style plots of the differences in values as a function of measurand level, relative to the claimed comparison measurement procedure(s) performance characteristics.

7. Dealing with discordance between RMM/Ps in extent-of-equivalence studies

- 7.1. If the results of an extent-of-equivalence study indicate discordance among the evaluated RMM/Ps relative to fit-for-purpose criteria, the nominated RMM/P under review will not be accepted for listing in the JCTLM database until the discrepancy is explained. The DB WG Vice-Chair, in consultation with the DB WG Chair, will collaborate with the nominator and owners of listed RMM/Ps to investigate the discrepancy. Owners of listed RMM/Ps are expected to participate in the investigation.

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8. Related documents

JCTLM Preamble	Available at - https://www.bipm.org/en/committees/jc/jctlm/wg/jctlm-dbwg/publications
JCTLM DBWG-P-00	Quality Policy of the JCTLM Database working group REVIEW PROCEDURES for Materials and Methods
JCTLM DBWG-P-01A	Outline of JCTLM DB WG process for evaluating and listing higher order materials and methods
JCTLM DBWG-P-02A	Requesting and accepting nominations for Certified Reference Materials and Reference Measurement Methods/Procedures
JCTLM DBWG-P-03A	Review of nominated Certified Reference Materials and Reference Measurement Methods/Procedures
JCTLM DBWG-P-05	Communicating Database WG recommendations

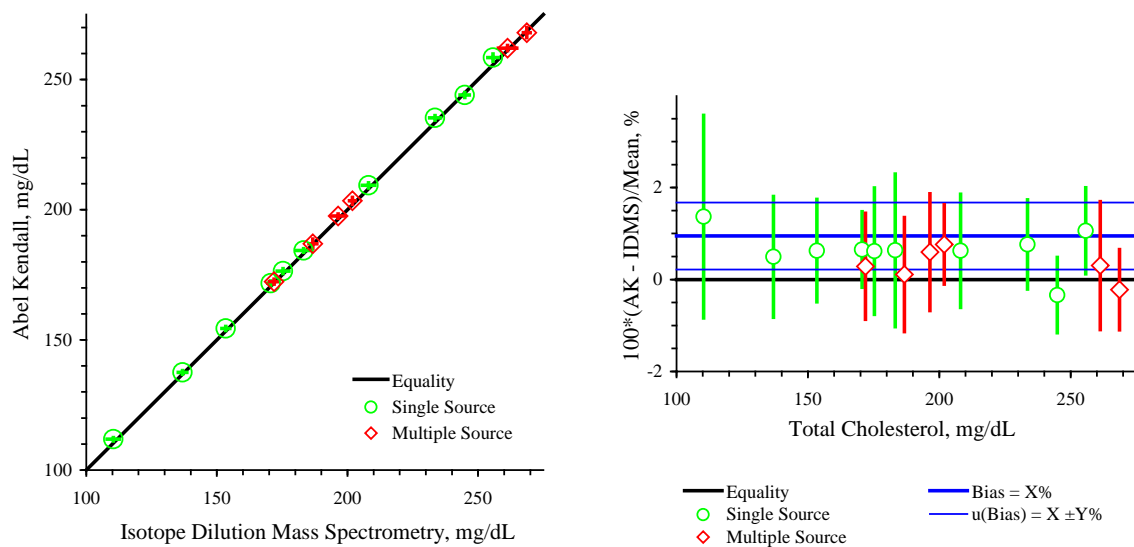
9. Revision History

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
2.0	27/01/2017	Document revised for implementing modifications requested by EC's at its 17 th meeting
2.1	27/01/2018	Revision of the text of section 6.1.1 and 6.1.2 by EC at their 19 th meeting
2.2	01/02/2019	Update of hyperlinks
2.3	01/02/2022	Editorial changes
3.0	01/02/2023	Modifications discussed at the December 2022 Executive Meeting

10. Attachment:

The following example graphs represent possible ways to show extent-of-equivalence data between two measurement procedures. Other data display approaches may also be acceptable.

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



Single Source refers to individual clinical samples. Multiple Source refers to pooled clinical samples. 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.