

METROLOGY APPLIED TO ACHIEVING THE HIGHEST QUALITY OF MEASUREMENT IN LABORATORY MEDICINE

Effective diagnosis and treatment of disease requires the medical laboratory to produce reliable, repeatable, reproducible, compatible and comparable measurement results. Laboratories necessarily use different measurement procedures and calibration standards for many reasons, but such differences should not produce different measurement results. International organizations devoted to improving the quality of laboratory medicine and the accuracy of test results are collaborating with the international metrology (measurement science) community to achieve comparability of laboratory test results throughout the world, and the Joint Committee for Traceability in Laboratory Medicine (JCTLM) was formed to take a lead in this activity.

FREQUENTLY ASKED QUESTIONS – INTENDED FOR LABORATORY PROFESSIONALS AND COMPANIES IN LABORATORY MEDICINE

| QUESTION | ANSWER/COMMENT |
|---|---|
| What is the Joint Committee for Traceability in Laboratory Medicine (JCTLM)? | The JCTLM is an international committee founded by the BIPM, IFCC and ILAC to facilitate improvement in the equivalence (compatibility) of measurement results used in medicine. |
| What is meant by “equivalence” of measurement results? | Equivalence of measurement results, or their comparability, in the common sense of the word, implies close agreement in the values measured for the same substances, when being analyzed by different kits. Metrological comparability is traceability to the same reference. |

| QUESTION | ANSWER/COMMENT |
|---|---|
| <p>What is metrological traceability?</p> | <p>Metrological traceability in the general sense is the means by which measurement values in routinely analyzed samples are quantitatively related to the certified value of a reference material. For a chemically well-defined analyte, this is usually the purest and best characterized certified reference material for the measurand. Metrological traceability is defined as the property of a measurement result whereby the result can be related to a reference through a documented unbroken chain of calibrations.</p> |
| <p>How is comparability achieved?</p> | <p>Comparability is achieved by measurements being traceable to the highest-order reference materials and/or methods available.</p> |
| <p>How does metrological traceability improve the reliability and consistency of laboratory measurement results?</p> | <p>Metrological traceability enables values to be assigned to calibrators that will be routinely used for laboratory methods to be related to common, highly characterized higher-order materials. Different methods can then produce measurement results of the same accuracy in different laboratories, with different instruments and with different test kits or reagents.</p> |
| <p>What is meant by 'higher-order' reference material?</p> | <p>A higher-order reference material is a certified reference material, meeting internationally accepted quality requirements, to which other measurement results can be referenced, and its measurement uncertainty is completely established. Metrologically a higher-order material is a reference material higher in the traceability chain.</p> |

| QUESTION | ANSWER/COMMENT |
|---|---|
| <p>How does a higher-order reference material differ from a calibrator used in routine measurements?</p> | <p>Certified, highest order reference materials are used by manufacturers to assign values to in-house calibrators. These reference materials are subsequently used by the manufacturer to assign values to analytes in the calibrators and controls sold by them for use in routine laboratories. JCTLM through its list of higher-order materials provides a mechanism for manufacturers to make their products traceable to a common or equivalent reference material.</p> |
| <p>What is meant by metrological hierarchy?</p> | <p>The metrological hierarchy is the chain of calibration procedures that transfer values from the highest-order reference material to the next lower level calibrator until values are assigned finally to calibrators for routine use by a manufacturer. Value assignment at the highest level in the metrological hierarchy commonly employs higher-order reference methods.</p> |
| <p>What is meant by 'higher-order' reference methods?</p> | <p>Higher-order reference methods are well documented, high accuracy methods used for assigning values to calibration materials. At the highest level the methods are frequently expensive to develop, too complicated for routine use and not suitable for high throughput analysis. JCTLM provides the database in which reference measurement methods and procedures can be found.</p> |
| <p>Who develops and provides higher-order calibration materials?</p> | <p>Higher-order (highest order) materials are most commonly produced and distributed by national metrology institutes (NMIs), e.g. NIST (USA), IRMM (EU), LGC (GB), WHO, NIBSC (GB), NIM(CN), NMIJ(JP), ReCCS (JP), CENAM (MX), etc. Some commercial sources also provide reference materials listed by JCTLM.</p> |

| QUESTION | ANSWER/COMMENT |
|--|---|
| <p>What services does the JCTLM provide to laboratory medicine?</p> | <p>JCTLM provides free lists of reference materials and methods that are necessary for achieving comparability of measurement results. Lists are accessible free of charge and provide the necessary information for manufacturers of medical diagnostic test kits to be compliant with European and international regulations and written standards that require metrological traceability to be established for test kit calibrators and/or metrologically traceable measurement results.</p> |
| <p>What is the JCTLM database of reference materials, measurement methods, and measurement services?</p> | <p>The JCTLM database comprises lists of higher-order reference materials, measurement methods and services that have been reviewed against appropriate metrological criteria and judged to be compliant with applicable ISO standards. The easily searchable database can be accessed at http://www.bipm.org/jctlm/ is for use by persons and companies involved in laboratory medicine.</p> |
| <p>What can an organization or company do if it does not have the facilities or staff to perform reference measurement procedure?</p> | <p>Consult the JCTLM database for reference measurement service laboratories that have been accredited to perform such services and whose credentials and ability to perform reference measurement services are reviewed by the review teams of JCTLM.</p> |

| QUESTION | ANSWER/COMMENT |
|--|---|
| <p>How are reference measurement laboratories identified and how do they facilitate implementation of a reference measurement system?</p> | <p>Prospective users of reference measurement laboratories can contact an accredited laboratory of their choice using the information found in the JCTLM database. Using a Reference Measurement Service provider permits companies to be compliant with the traceability requirements of the EU without having to invest in the specialized instrumentation and procedures of reference measurement methods.</p> |
| <p>How does the JCTLM database aid in the achievement of comparability and traceability and quality of patient test results?</p> | <p>The JCTLM database identifies appropriate materials, methods and services for achieving traceability. Traceability to a common reference material via a successive series of calibrations provides a basis for companies to develop their products to be as accurate as technically achievable.</p> |
| <p>What value does JCTLM add to laboratory medicine? Manufacturers? Routine laboratories?</p> | <p>Activities and resources made available by JCTLM in support of comparability of measurement results and traceability provide tools, education and support for the practice of laboratory medicine worldwide. JCTLM volunteer experts from many countries review submissions for listing in the JCTLM databases and promote comparability and traceability in their home countries.</p> |

SPECIFIC QUESTIONS – INTENDED FOR PROVIDERS OF REFERENCE MATERIALS AND DEVELOPERS OF REFERENCE MEASUREMENT METHODS FOR THE LABORATORY MEDICINE INDUSTRY

| QUESTION | ANSWER/COMMENT |
|--|---|
| What are the benefits to national metrology institutes (as producers of certified reference material used in medical laboratory testing) of nominating their materials for listing their reference materials in the JCTLM database? | Availability of certified materials produced by the metrology institute becomes more widely known to the user community. |
| What are the benefits to manufacturers of laboratory test kits from using reference materials listed in the JCTLM database? | Customer knowledge that traceability of the calibrators is to the highest available reference materials assures the customers of the manufacturer’s commitment to quality products. |
| What are the costs to producers of certified reference material of meeting the requirements for listing in the JCTLM database? | Certified reference materials that can be listed must be produced in compliance with the ISO standards 15194, 18153 and 17511 which have been adopted by JCTLM as the basis for its review to qualify for listing. Costs are incurred in two ways: 1) cost of obtaining knowledge of the ISO standards and 2) costs of changes in processes and documents to achieve compliance with the ISO standards. Unless a producer is very familiar with the relevant ISO standards, ALL standards (documents) referenced in ISO 15194(2009), etc. will be needed to understand the requirements for listing. Production and documentation costs depend on how nearly compliant a producers processes and documentation already meet the requirements; this is only known by the producer. |

| QUESTION | ANSWER/COMMENT |
|---|---|
| When are submissions to JCTLM for review and listing due? | Initial submissions are normally due by May, final submissions with responses to queries from review groups are due in September. Questions and advice for submitting can be obtained by contacting the JCTLM Secretariat at the BIPM, ictlm@bipm.org |
| What is the timeline for review? | The submissions are forwarded to the appropriate review teams in June following each annual call for nominations, with a deadline for recommendations from review teams on 31 October. |
| How long must a material be available for users to have the material listed in the JCTLM database? | Producer has to ensure that the material when accepted for listing in the JCTLM database be available for eighteen months. |
