

Metrological Traceability and Its Implementation; A Report

This document provides guidance to manufacturers for establishing and reporting metrological traceability.

A Clinical and Laboratory Standards Institute report for global application.



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ISO/TC 212 standards, and ISO/TC 76 standards*



Clinical and Laboratory Standards Institute

Providing NCCLS standards and guidelines, ISO/TC 212 standards, and ISO/TC 76 standards

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Abstract

Clinical and Laboratory Standards Institute document X5-R—*Metrological Traceability and Its Implementation; A Report* provides guidance on establishing traceability of the chemical calibration step in clinical laboratory measurements, based on the traceability requirements for *in vitro* diagnostic (IVD) medical devices as given in ISO 17511¹ and ISO 15183,² and in accordance with the requirements for traceability as stated in the IVD Directive [i.e., Directive of the European Parliament on *In Vitro* Diagnostic Medical Devices (Directive 98/79/EC)³]. Though this report is aimed principally at manufacturers of IVD medical devices, the concepts and approaches recommended may be extended to apply to routine analysis conducted in the clinical laboratory either with commercially available or “home-brew” IVDs.

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Report

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Foreword

Clinical and Laboratory Standards Institute document X5-R—*Metrological Traceability and Its Implementation; A Report* is intended to explain traceability, how it is established, and how it benefits the *in vitro* diagnostics (IVD) industry and the practice of clinical laboratory medicine.

Metrological traceability is one way to ensure comparability in laboratory test results between laboratories, regions, and countries. Much confusion exists on how to implement the traceability scheme on a practical level. For some measurands, there is a clearly established traceability pathway; for others, demonstrating traceability is more complex.

X5-R explains the basics of traceability and defines a reference measurement system that includes reference materials, reference measurement procedures, and reference laboratories and laboratory networks.

X5-R outlines what is required by manufacturers to demonstrate traceability, provides guidance on explaining the results of studies to the customers, and describes what laboratories must do to validate results based on traceability concepts. X5-R has been developed as a companion to ISO 17511¹ and ISO 18153² standards on metrological traceability, and draws on discussions and outcomes of the Joint Committee on Traceability in Laboratory Medicine (JCTLM), which has developed criteria for acceptable reference materials and procedures and a provisional list of acceptable reference materials and procedures.

This report is intended for industry and clinical laboratorians.

The development of X5-R—*Metrological Traceability and Its Implementation; A Report* is a joint responsibility of IFCC and CLSI. X5-R has been developed by a working group composed of representatives from National Institute of Standards and Technology (NIST), International Bureau of Weights and Measures (BIPM), IFCC, and CLSI.

Key Words

Calibrator, certified reference material, commutability, metrological traceability, reference measurement procedure, uncertainty of measurement, validation, value assignment

Metrological Traceability and Its Implementation; A Report

1 Scope

X5-R provides guidance on establishing traceability of the chemical calibration step in clinical laboratory measurements, based on the traceability requirements for *in vitro* diagnostic (IVD) medical devices as given in ISO 17511¹ and ISO 18153,² and in accordance with the requirements for traceability as stated in the IVD Directive (i.e., Directive of the European Parliament on *In Vitro* Diagnostic Medical Devices Directive 98/79/EC³). Though this report is aimed principally at manufacturers of IVD medical devices, the concepts and approaches recommended may be extended to apply to routine analysis conducted in the clinical laboratory either with commercially available or “home-brew” IVDs.

This report specifically addresses traceability of the chemical calibration of a routine measurement procedure to the highest order reference that is available for a measurand. A traceable result requires that traceability be established for all quantities that have significant influence on the magnitude of the results. Traceability is discussed in more complete scope in other references, most notably, the Eurachem/CITAC^a Guide: Traceability in Chemical Measurements⁴ (available at <http://www.measurementuncertainty.org/>), the principles of which are applied for laboratory medicine in this report.

The primary area of activity to which this report can be applied is the determination of “assigned” values for calibrators and trueness controls for IVD measurement devices that are intended for use in the quantitative measurement of defined substances in human body fluids. While the focus of this report is on establishing traceability of manufacturers’ product calibrators, this is likely to be the key element in the traceability of results at the patient bedside performed on bodily fluids from patients.

This report discusses measurement uncertainty and method validation in relation to their respective roles in achieving traceability. Detailed descriptions of these processes are not provided, and may be found elsewhere (see the References section).

Throughout this report, it is assumed that laboratories or manufacturing facilities following the present guidance have in place effective quality assurance and control measures to ensure that all applicable measurement processes are stable and in control. These measures include, but are not limited to, appropriately qualified staff, continuous documented training of the technical staff, proper maintenance of equipment, correctly prepared reagents, and use of documented measurement procedures and control charts. ISO 17025⁵ provides a detailed description of the expectations of a competent laboratory responsible for chemical calibration and testing in general. ISO 15189⁶ builds on ISO 17025⁵ and provides recommendations specific to medical laboratories. Also of interest is ISO 15195⁷ which identifies specific aspects of calibration laboratories in the field of laboratory medicine.

2 Introduction

The primary goal of laboratory medicine is to provide information that is useful to assist medical decision-making and foster optimal health care. This information should be interpretable regardless of the laboratory or particular device employed to measure it. To achieve this, one must be able to obtain equivalent measurement results for the same measurand from a variety of measurement procedures and laboratories.

The ability to achieve equivalent results depends on *traceability* to common standards and is facilitated by expressing results in common units. A traceability network and common units lead to a harmonized

^a CITAC is the Cooperation of International Traceability in Analytical Chemistry.