

POSITION STATEMENT

Harmonization of Clinical Laboratory Test Results

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Introduction

In today's healthcare environment, evidence-based clinical practice guidelines are often used to help healthcare practitioners make informed patient care decisions. These guidelines frequently rely upon laboratory test results to determine if and when treatment is necessary. The laboratory community is concerned that many healthcare professionals and patients are not aware that different measurement procedures may give different numeric values for the same test (i.e., not all measurement procedures are "harmonized"). Harmonized laboratory test results are important for making effective, necessary and correct treatment decisions to provide appropriate patient care. Unfortunately, treatment decisions based on non-uniform test results may lead to erroneous clinical or technical decisions that could negatively impact patient care (1,2).

Background

Improving the Quality of Patient Care

In 1999, the Institute of Medicine (IOM) released a report, *To Err Is Human: Building a Safer Health System*, which highlighted the number of preventable medical errors in the United States (3). Since then, there has been renewed interest within the healthcare community to improve the delivery of care and patient outcomes. Clinical laboratorians have been at the forefront of this effort, working proactively to improve the quality of laboratory test results. There is wide agreement within the medical and laboratory community that test results should be harmonized to ensure that healthcare professionals receive consistent and uniform results for making patient care decisions (4).

In the context of this position statement, harmonization includes the concepts standardization (uniformity of test results based on relation to a reference method) and harmonization (uniformity of test results when a reference method is not available).

AACC POSITION:

Laboratory test results are a critical element of patient care and must be harmonized to ensure that accurate diagnoses and appropriate treatment decisions for patients are made.

When addressing harmonization, the need to harmonize test nomenclature, specimen collection and handling, reporting units and interpretive information should also be considered. All of these issues are important, and AACC supports harmonization of all aspects of laboratory testing. This position statement specifically addresses harmonization of test result values.

Ideally, all test results should be harmonized based on calibrations that are traceable to a reference method and/or a reference material. Over the past two decades, there have been a number of prominent successes in harmonizing laboratory tests based on reference methods, such as cholesterol, glucose and hemoglobin A1C, which have contributed to significant improvements in cardiac and diabetes care. However, despite these successes, the total number of laboratory tests that have been harmonized based on reference methods remains very small.

For most laboratory tests, reference methods are not available. Reference materials have also been used to harmonize results, such as for human chorionic gonadotropin (pregnancy and cancer), transferrin (iron deficiency) and immunoglobulin (autoimmune disease) among others. However, many of the available reference materials are not suitable for use in calibration of routine test procedures primarily due to inadequate commutability with patient samples (i.e., the ability of a reference material to have interassay properties comparable to the properties demonstrated by authentic clinical samples when measured by more than one measurement procedure) (5). In some of these cases, harmonization using a consensus approach may be useful to calibrate the different measurement procedures to eliminate systematic differences in reported values (4).

Although several organizations are addressing harmonization of test procedures, centralized and cooperative global oversight is needed to ensure that the most important tests are being addressed and resources are optimally used (4). In 2010, AACC convened a conference of international and domestic stakeholders to discuss a global response to this problem. Participants recommended the creation of an oversight body to organize a worldwide approach for prioritizing and managing the harmonization of clinical laboratory test results (4). AACC worked with its domestic and international partners to create the International Consortium for Harmonization of Clinical Laboratory Results to achieve this objective. The association believes advances in this area will improve the quality of patient care.

Congress shares AACC's goal. In the accompanying language to the Consolidated and Furthering Appropriations Act of 2015, the legislative chambers urged CDC to "partner with the private sector" to harmonize clinical laboratory test results. The House Appropriations Committee also included report language in the FY 2017 Labor, HHS, Education and Related Agencies' funding bill seeking an update from CDC on its harmonization activities.

Improving Clinical Practice Guidelines

In recent years, the movement towards evidence-based medicine has emphasized the use of clinical practice guidelines to improve patient care. This shift is acknowledged by the Institute of Medicine, which stated that "trustworthy guidelines hold the promise of improving healthcare quality and outcomes" (6).

A survey of physicians found that 67 percent expect clinical guidelines to significantly impact medical decision-making (7). Unfortunately, a practice guideline recommendation based on either reference intervals or fixed decision values for a laboratory test will not be uniformly applied unless the laboratory test results are harmonized. Decisions based on non-harmonized test procedures increase the risk of erroneous clinical, financial, regulatory, or technical decisions that could negatively affect patient care (4). Improving the harmonization of test results is critical to improving the quality and value of clinical guidelines for both clinicians and patients.

Electronic Health Records

One of the important healthcare goals of the past decade has been to increase the use of electronic health records (EHRs) by providers. According to the U.S. Department of Health and Human Services more than 50 percent of physicians and 80 percent of hospitals are now using EHRs (8). Laboratory test results are a substantial and important component of EHRs. The electronic record enables clinicians to easily compare and evaluate test results over time. However, the patient's laboratory results may be from multiple testing facilities that used different measurement procedures. Comparing laboratory results from different non-harmonized measurement procedures may be confusing, which may contribute to medical errors and unnecessary ordering of repeat tests. Harmonized test results could help to significantly minimize these problems.

Considerations

The harmonization of laboratory tests globally is a significant undertaking. It requires the active involvement of numerous stakeholders, including professional organizations, clinical societies, the in vitro diagnostic (IVD) industry, metrology and public health organizations, regulatory agencies, external quality assessment providers, payers and many others. Without this collaboration, the quality of patient care may be negatively affected. The specific actions needed from these various stakeholders to attain the goal of harmonized laboratory tests are outlined below.

Laboratory Organizations

- ▶ Laboratory organizations should provide education about the variability in laboratory test results and the value of harmonizing these results to

healthcare providers, patients and policymakers.

- ▶ Laboratory organizations should provide leadership for collaboration among stakeholders to develop procedures for harmonizing test results.
- ▶ Quality indicators should be created to determine whether healthcare providers are appropriately interpreting and utilizing laboratory test results.

Clinical Societies

- ▶ Clinical societies should identify the laboratory measurement procedures used in developing a guideline along with any limitations associated with using other procedures.
- ▶ Clinical practice guidelines for interpreting laboratory results should be based on harmonized procedures.

Government

- ▶ As regulatory requirements evolve, agencies should emphasize and promote harmonized test results.
- ▶ Although nothing should be done to compromise patient safety, worldwide regulatory processes should be streamlined and harmonized to expedite recalibration of regulated IVD medical devices to achieve harmonized test results based on international consensus recommendations.

In Vitro Diagnostics Manufacturers

- ▶ Calibration of all test procedures should be traceable to a reference method and/or an appropriate reference material if available.
- ▶ When reference methods or appropriate reference materials are not available, laboratory test results should be harmonized among different measurement procedures based on a consensus approach so that uniform test results are achieved.
- ▶ The specificity characteristics of different measurement procedures for the target measurand should be sufficient to support the use of uniform interpretive criteria for test results from different procedures.

Reference Material Providers

- ▶ All providers of reference materials must take responsibility, in collaboration with IVD manufacturers, to ensure that the materials intended to be used as common calibrators for clinical laboratory measurement procedures are commutable with representative clinical patient samples.

- ▶ External quality assessment (EQA) and proficiency testing (PT) providers should use commutable materials whenever possible, especially if EQA and PT materials are intended to assess the agreement of results among different measurement procedures.

Payers

- ▶ Payers should encourage harmonization of laboratory test results to eliminate errors in treatment decisions and unnecessary repeat tests to lower the cost of patient care.

All Stakeholders

- ▶ All stakeholders should support the newly created International Consortium for Harmonization of Clinical Laboratory Results (www.harmonization.net). This consortium will prioritize and organize global activities to achieve harmonization of test results.
- ▶ All stakeholders should support developing new consensus approaches to achieve harmonization of results.
- ▶ Funding should be made available from government and private sources to accomplish harmonization of high priority laboratory tests.

References

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