COMMUTABLE SERUM

The Power Behind the Throne

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Introduction

The concept of commutability in reference materials (RMs) and control materials (CMs) is pivotal for ensuring the accuracy and reliability of clinical chemistry laboratory analyses.

Commutability refers to the ability of a reference material to demonstrate inter-method behavior that is comparable to that of native patient samples. This white paper explores the significance of commutable quality materials, focusing on guidelines like CLSI C37-A, and their benefits to clinical chemistry laboratories.

Understanding Commutability

Commutability was initially defined in the context of enzyme activity but has since been broadened to include all analytes. A material is considered commutable if, when measured by different analytical methods, it produces results that are consistent with those obtained from native clinical samples.

This property ensures that the calibration and quality control materials used in laboratories accurately reflect the behavior of patient samples across various analytical platforms.

To produce results that are “correct” or “true” for serum or plasma or urine samples from patients being tested, a modern clinical chemistry laboratory needs at least three things:

Reference Procedures

There would need to be agreed upon methods to assign true or, “reference“ value[s] to the concentration of an[y] analyte[s] being tested. Such values could also be assigned by harmonization if no agreed upon reference procedure exists.

Standardized Equipment and Reagents

The laboratories would need instruments and reagents from manufacturers that were standardizable to these values employing agreed upon reference or harmonized procedures to produce them.

Commutable Pools

The laboratory would need pools of serum (or plasma or urine) that they could use to compare their values through EQAs to other laboratories and to different times in the same laboratory.

All these basics are achievable, however, only recently. Because of the short time these elements have been available, most laboratories must still search for reference based equipment and materials for their everyday uses.

Reference Procedures:

By the end of the 1990s, there were only a few reference procedures that were agreed upon and these were available only through a diverse group of specialized laboratories and organizations. The Centers for Disease Control and Prevention, for example, could provide Abell Kendall results for cholesterol, which was agreed upon as a reference procedure. Further, there were a group of laboratories in the United States and abroad, known as the Cholesterol Reference Method Laboratory Network (CRMLN), that could provide reference values for blood lipids with precision and accuracy.

These pools, known as the Cardiovascular Disease Biomarker Standardization Programs, formally referred to as Liquid Standardization Programs (LSP), still exist and can be applied for through the CDC at the Clinical Standardization Programs (CPS).

Additional CSP standardization programs include:

- Hormone Standardization Programs for Testosterone and Estradiol
- Vitamin D Standardization-Certification Program
- Thyroid Hormone Standardization
- Parathyroid Hormone Standardization

The Joint Committee for Traceability in Laboratory Medicine (JCTLM) was established in 2002 through a declaration of cooperation between the International Bureau of Weights and Measures (BIPM), The International Federation of Clinical Chemistry and Laboratory Medicine (IFCC), and the International Laboratory Accreditation Cooperation (ILAC) in response to the implementation of the European Community Directive 98.79/EC for in vitro medical devices. Since its founding, the role of the JCTLM has expanded to become a global resource for implementing metrological traceability in laboratory medicine and provides a listing of all metrology laboratories.

Currently there are 99 member states and associate states and economies in this listing. In addition to these listings there are several independent laboratories that provide reference procedures. In the early 2000s the number of reference procedures listed by the JCTLM was quite small, however, today it lists 290 reference materials, 238 reference methods and 285 reference services.

Industry Participation

The participation of the laboratory industry in developing instruments and reagents that are based on materials for calibrators and controls with reference procedures is a work in progress.

When the CDC approached our laboratory in the late 1990s to produce a “commutable” pool for lipids, they had identified a dozen well known industrial sources that produced instruments and reagents that were used to measure lipids in laboratories. We were tasked with producing two pools, one high and one low in cholesterol.

Two large pools of blood samples were created, each containing 41 and 43 individual donor units, respectively. To ensure accuracy, companies were provided with samples from both the pools and the individual donors used for each pool. These samples were analyzed to measure cholesterol levels.

The cholesterol levels calculated from the individual donor samples closely matched the measured levels of the pooled samples. This high degree of correlation, with less than a 2.2% overall deviation, and less than a 1.5% deviation when excluding one outlier, strongly suggests that the pooling process did not introduce any significant matrix effects.

This finding confirmed the validity of the pooling method, which is endorsed by the Clinical Laboratory Standards Institute or (CLSI), as a reliable approach to creating commutable pools. These pools can serve as valuable reference materials for accurate cholesterol measurements in clinical laboratories.

This procedure was revisited recently by the original authors and brought up to date in this revised procedure: "An updated protocol based on CLSI document C37 for preparation of off-the-clot serum from individual units for use alone or to prepare commutable pooled serum reference materials". What is particularly interesting is that the supplement to the article, which is published with the article, lists dozens of reference based pools that in many cases are tested for commutability. Nearly half of all of these pools, for example the College of American Pathologist's accuracy based (ABX) pools, the Health Science Authority (HSA) pools, the CDC's LSP pools (mentioned above), a number of the NIST's standard reference materials (SRMs) many of which are also used by such organizations as the RELA EQA program, have been tested for commutability.

Benefits of Commutability in Clinical Chemistry

Accuracy in Calibration and Quality Control

Commutable reference materials (CRMs) ensure that calibration curves and quality control checks are representative of real patient samples, thereby reducing bias in measurement procedures. This accuracy is crucial for patient care, where even small errors can lead to significant clinical misjudgments.

Inter-Laboratory Comparability

When laboratories use commutable materials, the results obtained are more comparable across different labs, enhancing the standardization of clinical chemistry results. This is particularly important for patient follow-up across different healthcare facilities.

Enhanced Proficiency Testing (PT) and External Quality Assessment (EQA)

Commutability in PT/EQA materials ensures that the assessment of laboratory performance is fair and reflective of real-world conditions. Non-commutable materials can lead to false conclusions about a laboratory's performance.

Regulatory Compliance and Standardization

Regulatory bodies and standardization efforts like those by CLSI and IFCC emphasize commutability for traceability to higher-order reference methods or materials. This compliance ensures that clinical chemistry results are globally recognized and trusted.

Cost-Effectiveness

While the initial setup might require investment, the long-term benefits include reduced need for method-specific calibrators and controls, potentially lowering overall costs through standardization.

Challenges and Considerations

Material Stability and Preparation

Achieving commutability often involves complex preparation processes to mimic the matrix of human serum or plasma, which can be challenging for unstable analytes or those requiring preservatives.

Validation

The validation of commutability requires a rigorous process involving multiple analytical methods and a significant number of clinical samples, which can be resource-intensive.

Dynamic Nature of Clinical Chemistry

The field evolves, with new analytes and methods emerging, necessitating continuous updates to commutability assessments.

Conclusion

This groundbreaking project, a collaborative effort between the CDC, NIST, CAP, CLSI and Solomon Park in 1999, has revolutionized lipid measurements in clinical chemistry. By developing the C37-A procedure, they established a method for producing commutable pools for many analytes—a crucial step towards standardized, reliable, and comparable laboratory results.

Commutable pools, with their assigned reference values, serve as a cornerstone for clinical chemistry. They enable manufacturers to design equipment and reagents that deliver accurate results, aligning with established reference procedures. This standardization ensures that laboratories worldwide can produce consistent and reliable measurements, ultimately improving patient care.

As clinical chemistry continues to advance, the significance of commutability will only increase. By prioritizing the development and utilization of high-quality commutable reference and control materials, we can further enhance the accuracy and reliability of laboratory testing, leading to better patient outcomes.

This white paper advocates for the adoption of commutable materials as a standard practice in clinical chemistry, promoting a future where laboratory results are universally reliable and clinically actionable.

At Solomon Park, we are committed to providing high-quality commutable test kits through our SPRL-RefKits™ service. Our CDC LRC and ISP Kits and AccuBase-CQM™ custom quality control materials are designed to meet your specific laboratory needs.

To learn more about how our products can enhance your laboratory's performance, please contact Solomon Park Research Labs for a consultation.

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