Clinical Chemistry Approach to Evaluation of Commutability

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SCIENTIFIC WORKING GROUP ON THE STANDARDISATION OF GENOME AMPLIFICATION TECHNIQUES (SoGAT)
Commutability is a material property describing its relationship to regular patient results

CLSI/ISO Definition:
ability of a material to yield the same numerical relationships between results of measurements by a given set of measurement procedures, purporting to measure the same quantity, as those between the expectations of the relationships obtained when the same procedures are applied to other relevant types of material (CLSI Harmonization Database).

“The mathematical relationship between two methods should be the same when measuring patient samples and pooled/modified materials”
Commutability is a requirement for reference materials

ISO definition of reference material/trueness control: material, sufficiently homogeneous and stable with reference to specified properties, which has been established to be fit for its intended use in measurement or in examination of nominal properties.

Commutability defines whether a reference material is fit for use as calibrator and trueness control.

Use of non-commutable reference materials increases variability among analytical methods and can lead to incorrect diagnosis and treatment of patients.
Assay calibration using non-commutable reference materials leads to inaccurate patient results

Recalibration of assays with non-commutable reference materials caused results for patient samples to change from pathological levels to non-pathological levels.

Non-commutable PT/EQA materials can lead to incorrect conclusions about assay accuracy.

Assays failed in PT/EQA challenges but showed good agreement when using patient samples.

Eckfeldt Arch Pathol Lab Med 1993;117:381-386
Non-commutable materials can lead to incorrect information about measurement variability in patient care.

Agreement among different assays is better with fresh-frozen (unaltered) sera than with altered sera used in regular PT/EQA surveys.

Horowitz CAP Y-A PSR 2009
Commutable reference materials assure correct calibration, accuracy assessments and ultimately accurate patient results.

Materials
- Pure Compound Calibrator/Primary Reference Material
- Serum-based Calibrator/Reference Material Trueness control

Methods
- Gravimetry
- Reference Method
- Routine Test
- Value assignment

Patient Sample
- Patient Result
- Trueness Verification Sample
- Trueness Verification Result
Assessment of Commutability

Protocols

- CLSI Guideline C53: Characterization and qualification of commutable reference materials for laboratory medicine


- CLSI Guideline EP 14: Evaluation of matrix effects (under revision)
All commutability protocols have the same basic requirements

- At least 2 analytical methods (i.e., reference method and routine method)
- 20-40 authentic patient samples with analyte concentrations spanning the reportable range of the analytical methods
- Reference/testing materials
Procedure for assessing commutability

Step 1: Establish relationship between two methods using patient samples
Procedure for assessing commutability

Step 2: Superimpose reference and control material values on the established relationship to assess equivalence

CLSI C53
Commutability assessments do not require reference methods

- Measurements performed by both methods do not need to be accurate
- The relationship between both methods does not need to be linear
Insufficient minimization of random error can lead to incorrect commutability findings

- Minimize random error through replicate measurements (n=5-6)
- Exclude highly imprecise assays
Include dilutions of reference materials in commutability studies

**NIST SRM 971**
Hormones in Human Serum
Two serum pools (unfortified):
Normal adult males (M),
Normal, premenopausal adult females (F)

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N/D: No Data    Y: Material Commutable    N: Material Non-Commutable
Commutability is assay specific and needs to be assessed for each assays individually.

Commutability table with results from pair-wise comparisons among analytical methods (1: commutable, 0: non-commutable):

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Christenson Clin Chem 2006; 52:1685–1692

- In the absence of reference methods, pair-wise comparisons among all assays need to be performed.
- Commutability is judged on the number of commutable comparisons.
Correspondence analysis is an alternate statistical approach for multi-method, multi-material comparisons.

Active elements: Patient samples and methods

Inactive elements: Materials

Commutable materials fall inside the 95% tolerance ellipse established with patient samples.
Summary

- Commutability is a material property describing its ability to assure accurate patient results when used as calibrator.

- Non-commutability of PT/EQA materials and reference materials have been described for many clinical analytes, especially complex analytes such as enzymes and other complex proteins.

- Commutability is determined by comparing relationships between methods obtained with patient samples to those obtained with materials under investigation.

- Protocols for assessing commutability have been established and are being continuously refined.
Thank you!

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For more information please contact Centers for Disease Control and Prevention
1600 Clifton Road NE, Atlanta, GA 30333
Telephone, 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
E-mail: cdcinfo@cdc.gov   Web: www.cdc.gov

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