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IFCC Working Group Recommendations for Assessing Commutability

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Guest: Dr. Greg Miller is a professor in the Department of Pathology and Director of Clinical Chemistry at Virginia Commonwealth University, and Chair of the IFCC Working Group on Commutability.

Bob Barrett: This is a podcast from *Clinical Chemistry,* sponsored by the Department of Laboratory Medicine at Boston Children's Hospital. I am Bob Barrett.

Commutability is an important concept in determining traceability and the relationship among different methods that are used to measure the same analyte but just how to describe and classify commutable materials is not always straightforward. The March 2018 issue of *Clinical Chemistry* published a series of three reports from the Working Group on Commutability of the International Federation of Clinical Chemistry and Laboratory Medicine, or IFCC, that describe recommendations for assessing commutability.

The Chair of the Working Group is Dr. Greg Miller. He is a Professor in the Department of Pathology and Director of Clinical Chemistry at Virginia Commonwealth University and he's our guest in today's podcast. So, Dr. Miller, commutability is a somewhat specialized topic. Can you start by explaining what commutability is and why it's important to all laboratorians?

Greg Miller: Yes. Commutability is a property of a reference material. That means the reference material has the same relationship between its measured values by two or more measurement procedures as the relationship observed for clinical samples. So stated operationally, a commutable reference material has a measurement signal in a measurement procedure that is the same as the measurement signal from clinical samples when both have the same concentration of the measurand.

When commutable reference materials are used as calibrators in the calibration hierarchy of clinical laboratory measurement procedures, the different measurement procedures can produce equivalent results for clinical samples. The equivalent results are important when making clinical decisions based on guidelines or decision values for interpreting laboratory test results. When non-commutable reference materials are used in the calibration hierarchy, the results for clinical samples are different from different

measurement procedures and can cause erroneous medical decisions based on those results.

Commutability is also important for samples used in proficiency testing or external quality assessment programs that are intended to evaluate the accuracy of results of the agreement among results from different measurement procedures.

Bob Barrett: What were the key issues addressed by the IFCC working group on commutability?

Greg Miller: Well, previously published procedures to evaluate commutability of reference materials have compared the results for a reference material to the statistical distribution of results for clinical samples measured using two different measurement procedures. The criteria for making a decision that a reference material was commutable with clinical samples were different for every pair of measurement procedures evaluated.

Also, there were no guidelines for the required measurement procedure performance to be included in a commutability assessment, and minimal guidelines for the types of clinical samples that were suitable for use in a commutability assessment. The IFCC working group was tasked to clarify the technical parameters when performing a commutability assessment and to develop new approaches that better met the needs to qualify reference materials as being suitable for use.

Bob Barrett: Doctor, can you briefly describe the recommended criteria for selecting clinical samples for use in a commutability assessment?

Greg Miller: Yes. Individual clinical samples are what measurement procedures are designed to measure and are preferred for assessing the commutability of a reference material. It is important to remember for commutability assessment that we are not evaluating the performance of a measurement procedure. Rather, we are determining if a reference material is commutable with typical clinical samples when measuring by a group of different measurement procedures. Clinical laboratory measurement procedures are not completely selective for the measurand and are influenced by interfering substances to different extents.

Clinical samples should be excluded that are known to contain interfering substances or unusual molecular forms when those influence quantities affect many of the measurement procedures in a study. The presence of an interfering substance or unusual molecular form in a clinical sample may not be known until data analysis when

identified as an "outlier" result. Sourcing more clinical samples than the minimum needed for statistical assessment is recommended to ensure that enough useable data will be available to meet the statistical power requirements for a study.

The concentrations of the clinical samples do not need to cover the full measuring interval of the measurement procedures. Rather, the clinical samples should be selected to cover a reasonable concentration interval above and below the expected concentration in the reference material or the reference materials being evaluated for commutability. The number of clinical samples to use will be based on the performance characteristics of the measurement procedures and the uncertainty required for a commutability decision.

Bob Barrett: And how are the measurement procedures qualified for inclusion in a commutability study?

Dr. Greg Miller: Well, it's important to reiterate that we are not evaluating the performance of a measurement procedure; rather we are determining if a reference material is commutable with typical clinical samples when measured by a group of different measurement procedures. The Working Group recommends to set specifications for precision and selectivity for the measurand for a measurement procedure to be included in a commutability assessment.

Those specifications are based on the uncertainty required for a commutability decision that in turn is related to how a reference material will be used.

Bob Barrett: How are criteria for acceptable commutability established?

Dr. Greg Miller: The intended use of a reference material influences the choice of a criterion for commutability assessment. The criterion for a reference material intended for use in a calibration traceability hierarchy should be a fraction of the allowable bias for an individual clinical sample result. The fraction needs to consider the position of the reference material in a traceability chain and must include risk of harm to a patient from medical decisions based on uncertainty in a result for a measurand in a clinical sample.

Proficiency testing or external quality assessment materials are usually intended to verify that an individual result is within an acceptable measurement error. The criterion for commutability should be a fraction of the bias component of the acceptance limits for evaluating an individual result.

A criterion based on the intended medical use of laboratory test results is preferred but needs to be established with

consideration of the performance capability of measurement procedures. If no available reference material can meet the criterion, the criterion may be reconsidered to permit production of a reference material that when used in a calibration traceability hierarchy substantially improves agreement in results for clinical samples among different measurement procedures, such that medical decisions are improved and the risk of harm to a patient is reduced.

Bob Barrett: Well finally Dr. Miller, were there any new statistical approaches developed by the Working Group that you can share with us?

Dr. Greg Miller: Yes. The Working Group has developed two new statistical approaches to commutability assessment. With either approach, the criterion used for the commutability decision is the same for all combinations of measurement procedures in the assessment.

One approach uses the difference in the bias between two measurement procedures for a reference material and for clinical samples. The assessment is based on an error model that allows estimation of various random and systematic sources of error including that from sample specific effects of interfering substances. An advantage of this approach is that the difference in bias between a reference material and the average bias of clinical samples at the concentration of the reference material and its uncertainty are both determined. A reference material is commutable if the difference in bias plus its uncertainty are within the criterion. Commutability is assessed pair-wise for all combinations of two measurement procedures included in the assessment. This approach is suitable for reference materials used as calibrators, as trueness controls, or for proficiency testing.

The other approach is based on the effectiveness of a reference material to fulfill its intended use in a calibration hierarchy to produce equivalent results for clinical samples among different measurement procedures. This approach is only suitable for reference materials used as calibrators. The reference material being assessed for commutability is substituted for the reference material currently used in the calibration hierarchies for the clinical laboratory measurement procedures include in the assessment. The inter-measurement procedure systematic error is determined from the results for clinical samples. A reference material is commutable for measurement procedures that have systematic error within the criterion.

So, this podcast format allows only a brief description of the recommendations and new approaches for commutability assessment. Additional details are available in the three

papers and their supplemental data files. Thank you very much.

Bob Barrett: Dr. Greg Miller is a professor in the Department of Pathology and Director of Clinical Chemistry at Virginia Commonwealth University. He's been a guest in this podcast from *Clinical Chemistry* on assessing commutability and the recommendations from the IFCC Working Group on Commutability. I'm Bob Barrett. Thanks for listening.