Commutability of reference materials – perspective of the clinical laboratory

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Disclosure

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Routine diagnostic laboratories

- Industry provided, CE-certified, ready-to-use In-vitro-diagnostic devices
- No manufacturing of working calibration materials in the lab (very few exceptions)
- Relevant reference materials for the clinical lab: EQA- and IQA-samples

Definition

- The **definition** of the term commutability according to the International Vocabulary of Metrology (**VIM**) makes it clear that commutability is not an “absolute”, inherent property of a material, but always a “relative” property attributed to a material in a specific **constellation** related to two or more distinct measurement procedures.

- Commutability: Not an *inherent* but an *attributed* property

- Routine diagnostic procedures may vary greatly in their performance characteristics, especially regarding selectivity and specificity (e.g., different Cyclosporin A-assays).

Routine diagnostic setting

- Formal commutability of a QA material can suggest close between-method agreement of different analytical methods - although results of real patients' samples may differ substantially between platforms.
- This is most evident in the field of therapeutic drug monitoring, where the presence of related drug metabolites is common.
- For a QA material that is spiked only with the respective target analyte - and not simultaneously with the drug metabolites generated from this compound in vivo - commutability can be observed with respect to several routine analytical methods, which in turn indeed differ significantly in their respective analytical sensitivity to metabolites - leading to discrepant clinical results in patient samples.

Manufacturers' perspective

- Commutability of a QA-material related to a wide range of assays in the market is convenient for manufacturers and EQA-provider – since no method-specific target ranges have to be specified.

- However, such "commutable" materials may fail to display specificity-related differences between routine analytical methods.

- Metabolite-free – but thus widely commutable - QA materials may also fail to display specificity issues in long-term assay monitoring by internal QA (e.g., change of cross-reactivity pattern of an assay due to compromised reagents with steric changes of test-antibodies)

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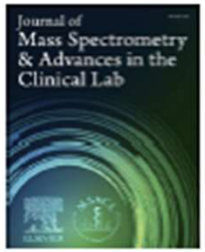

Is commutability of a reference material always desirable?

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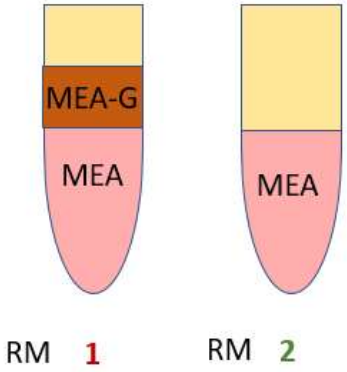
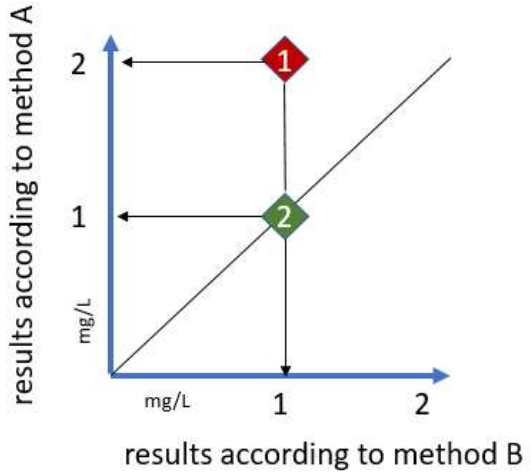


MEA – *measurand*, putative TDM target, undergoing glucuronidation to MEA-G

method A: MEA measurement with cross-detection of MEA-G
method B: selective measurement of MEA



	RM 1	RM 2
method A	2 mg/L	1 mg/L
method B	1 mg/L	1 mg/L

„RM 1 is not commutable“

Conclusions 1

- The relevance and meaning of commutability need to be thoroughly considered in relation to specific diagnostic requirements

- *Nota bene:* high specificity and selectivity may not always be desired clinically (e.g. in group-tests for growth-hormone isoforms; TP, total protein-assay)

Conclusions 2

- It is important to emphasize that commutability in a given *constellation* does not necessarily mean that a material is suitable for its intended purpose in internal or external QA of a clinical laboratory.

- Prudent and correct use of the term and concept of *commutability* is essential for meaningful communication between QA institutions, manufacturers and clinical laboratories.

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Thank you

for your attention