

Physikalisch-Technische Bundesanstalt Braunschweig and Berlin National Metrology Institute



Standardisation of Metabolomics

& other suggested topics

EMN-TLM workshop 2021

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Background

Metabolomics

The study of the set of metabolites present within an organism, cell or tissue.

Over the last two decades targeted and untargeted metabolomics has become an invaluable tool in biomarker discovery, molecular pathway discovery and disease understanding.

Barriers exist in realising the full potential of this enabling technology for the production of routine clinical data.

Lack of:

- Standards
- Matrix CRMs •
- QA/QC procedures •
- Meeting quality standards/regulations •

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	Characteristic	Research	Testing	ckgro
	Focus	Control & experimental group	Individual patient	Bac
	Technology	GC/LC-MS/MS	GC/LC-MS/MS	
	Uses	Biomarker discovery	diagnosis	ent
	Sample	Flexible	fixed	Curre
	Stats considerations	Study design and proper controls	Reference ranges, Z- scores,	
	Analytical validation	Optional	Required	unity
	Clinical validation	Not required	Required to support diagnostic claims	Comm
	Regulatory framework	Not required	Required	
	Future trends	Network modelling, AI, multi-omics	Increasing, reduction of biomarker panels to targeted tests.	Project Concep

Adapted from Kennedy et al. J Mass Spectrom. 2018;53:1143–1154

Approach

Engagement

NMI activities for clinical metabolites

Current NMI approach

2021-10-11

- Exact matching Isotope Dilution Mass Spectrometry
 - Manual gravimetric preparation of calibration materials
 - Manual gravimetric preparation of sample and calibration blends



Current Approach

> Community Engagement

On-going activities

US NIH-National Cancer Institute (2018)

•To identify, catalog, harmonize and disseminate QA/QC best practices for untargeted metabolomics.

•To establish mechanisms to enable the metabolomics community to adopt QA/QC best practices.

•To promote and support systematic training in QA/QC best practices for the metabolomics community.

•To encourage the prioritization and development of reference materials applicable to metabolomics research.



https://epi.grants.cancer.gov/Consortia/mQACC/

Metabolomics Quality Assurance and Quality Control Consortium (mQACC): Reference and Test Material Working Group

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Plasma Reference Material Suite



The suite of plasma reference materials comprises different metabolic health states: type 2 diabetes, hypertriglyceridemia (high TG), and young, normal African-American (AA).

Standards and Reference materials group

https://dgmet.de/research/working-groups/standards/



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Proposed activities

The following will need to be addressed to deliver on the concepts of standardisation of metabolomics.

Targeted metabolomics

- Development of Multiparameter reference methods
 - Automation of preparation of standards, calibration and sample blends,
 - IDMS approaches for multiplexed measurements
 - New approaches for the characterisation of multiplexed solution CRMs
- Prioritisation of disease marker panels
- Untargeted metabolomics

2021-10-11

- Identification of "beacon molecules"
 - use of AI to map molecular and analytical space
 - Investigation of approaches for "fit for purpose" global standardisation
 - Impact of integrating approaches into current QA/QC practices







biocrates



Quality Assurance & Quality Control Consortium (mQACC)



Cells

- Quantification of cell surface and membrane proteins.
- Antibody binding measurements
- Mass cytometry
- Imaging
 - Metal based imaging

- Multiplexed reference measurement procedures
 - Steroids, metabolites, drugs, proteins
 - Micro-sampling strategies (DBS etc.)
- Reference methods for priority proteins
- Protein structure/activity
 - Cross linking
 - Metal incorporation
- Viral measurements
 - Viral genome : protein stoichiometry
 - Viral load measurements (CMV)



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