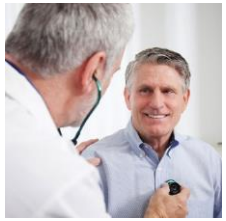
European Federation of Pharmaceutical Industries and Associations

Considerations on Multi-Attribute-Method (MAM) by LC-MS as QC tool

Thomas Pohl on behalf of the working group members



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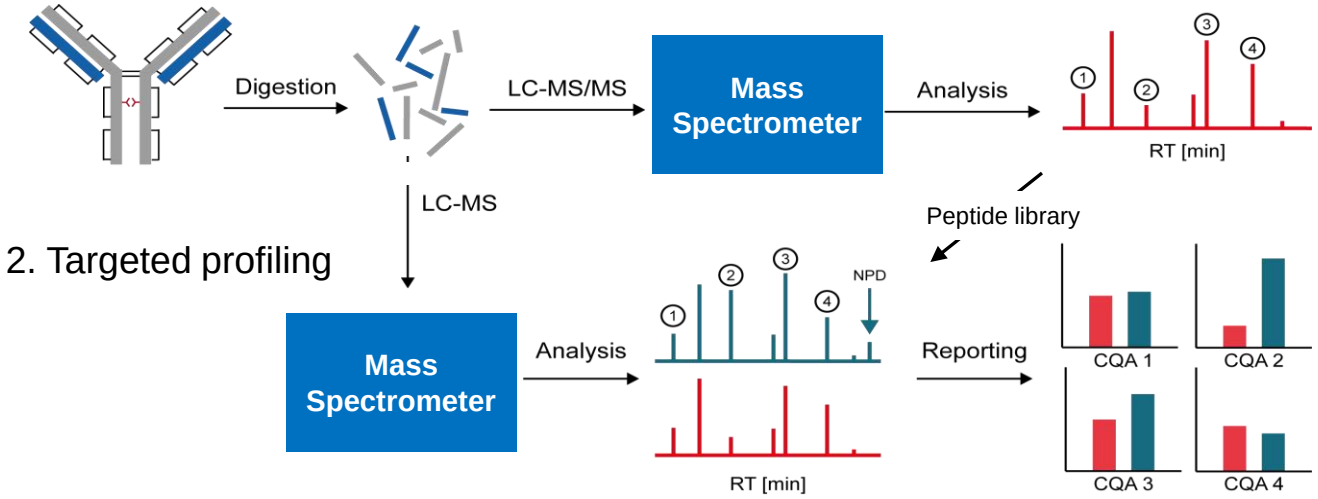
Definition of MAM by LC-MS

1. Initial holistic product characterization



adapted from Rogers *et al.*, 2018

- Quantitative peptide mapping LC-MS to assess relative extent of modification at specific amino acid residue, e.g. % Met34 oxidation
- Addressing multiple product quality attributes (CQAs) within a single method
- New Peak Detection (NPD) to detect 'unknowns', i.e. product variants that were not addressed by initial characterization / are not included in peptide library
- Potential to replace traditional (non-targeted) methods such as CE-SDS, IEX/ciEF/CZE, RP-UV, HILIC glycan mapping

Why this initiative?

- Multi-attribute-method by mass spectrometry (MAM) is well established across the industry in non-GMP environments for product and process characterization purposes
- The majority of pharmaceutical companies and many instrument providers are currently working on the extension of MAM to QC labs
- The use of MAM for lot release and stability testing according to GMP is not well established across the industry due to:
  - ongoing evolution and alignment of best practices across the industry
  - complexity (instrumentation, data sets)
  - limited experience with filing of MAM as a QC method
  - regulatory unfamiliarity with MAM as QC application

Challenges for the implementation of MAM as QC tool

The following areas are, as of today, still considered as major challenges to implement MAM in a QC environment

- Compliance of software
- Extent of method validation package
- Correlation with orthogonal / traditional methods
- Experience in specification setting
- Application of New Peak Detection (NPD)

The primary objective of this working group

Global acceptance
of MAM addressing multiple product quality attributes in a single method for QC release and stability, replacing traditional QC methods (e.g. purity / identity)

- Share and align on best practices across the industry
- Promote & encourage regulatory filing of MAM as QC method
- Reduce regulatory unfamiliarity and obtain HA acceptance

Expected deliverables from this working group

- Present at international conferences
- Publish industry best practices position paper dealing with technical, compliance and regulatory aspects
- Establish connection and interact with major stakeholders working on the implementation of MAM, i.e.
  - Instrument vendors / software providers
  - MAM consortium
  - Regulatory entities e.g. USP, EDQM, EMA BWP, EMA ITF, FDA ETT

Working Group Members

25 participants representing 17 companies

Name	Company
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Ben NIU	Astra Zeneca
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Gwen MANNING	Pfizer
Dietmar REUSCH	Roche
Annick GERVAIS **(Co-Lead)**	UCB
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Questions for the panel discussion

- What are the expected deliverables to accept MAM as stand-alone method that could be applied throughout product development (Clinical Phase 1 up to commercialization) without comparison to traditional methods?
- In case of introducing MAM during product development: What are the expectations in terms of method comparability?
- What are the expectations in terms of specification setting with MAM?
- Do HA see New Peak Detection (NPD) as a requirement during development and/or application in QC environment?
- Is there an interest by EMA ITF / FDA ETT to engage with an industry consortium on this topic?

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Thank you