Table 1: Qualification and Validation of MS Methods

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Scope:

The use of mass spectrometry (MS)-based methods in Quality Control (QC) laboratories is gaining a lot of attention. However, MS remains less commonly used in QC testing of biotechnology products due to complexity of these products and MS method-specific challenges. Some of the challenges shared previously at this conference include what parameters to qualify/validate, setting up appropriate system suitability and assay criteria, technology transfer between sites, collaborating with vendors on method validation, etc. While the general expectations for demonstrating that the methods are validated or fit for intended use are not different for MS-based methods, there are additional consideration for MS methods due to their complexity. For this round table, we will continue sharing experiences and knowledge on qualification and validation of MS methods, especially for biotherapeutics.

Questions for Discussion:

1. What is the biggest drive to have a MS method implemented in a GMP/QC environment in your company?

2. What MS platforms (e.g. intact mass, subunit analysis, peptide mapping, MAM, etc.) do you use in QC in general? How about for biotechnology products specifically? What quality attributes do you use them for?

3. What stage during the drug development do you consider establishing a qualified and validated MS method?

4. What have been the biggest challenges to qualify and/or validate MS methods? What challenges are unique to biotechnology products?

5. What parameters must be evaluated in method qualification/validation and what parameters must be included in the system suitability/assay acceptance criteria?

6. What are some key elements of the validated/qualified MS method life cycle management strategy? Any unique challenges during MS method tech transfer/cross validation? How do you address them?

7. Have you had successful collaboration with instrument vendors on instrument IQ/OQ/PQ and/or method validation?

Discussion Notes:

1. What is the biggest drive to have a MS method implemented in a GMP/QC environment in your company?

Discussion group members all brought up that one of the biggest drives in their company is to advance new technology such as MAM. A few attendees also mentioned using intact MS as ID assay in QC lab to replace traditional methods.

2. What MS platforms (e.g., intact mass, subunit analysis, peptide mapping, MAM, etc.) do you use in QC in general? How about for biotechnology products specifically? What quality attributes do you use them for?

Mainly three types of MS platform/methods have been implemented in the QC lab among the discussion group, including intact mass for identity testing, QDa method for PTM quantification, and MRM for targeted HCP quantification. No labs among the discussion group have a MAM method in QC yet due to the complex nature of the method.

3. What stage during the drug development do you consider establishing a qualified and validated MS method?

Attendee mentioned approaches include:

- early stage only qualified method in a non-GMP lab, late stage validated method in a QC lab
- For any data shared with regulatory agencies, they ensure the method has been qualified

4. What have been the biggest challenges to qualify and/or validate MS methods? What challenges are unique to biotechnology products?

- Capability in QC lab and CRO, instruments, trained analysts, cost, etc.
- Maintenance/transfer of the MS methods across labs
- Bar is high for skillset/expertise
- Specific for MAM:

- new peak detection is a challenge: what is the criteria applicable in QC labs?

- either too limited regarding the attributes that can be monitored or too complex for method qualification

5. What parameters must be evaluated in method qualification/validation and what parameters must be included in the system suitability/assay acceptance criteria?

Most discussion group members agreed that they follow ICHQ2(R1) and establish criteria for System Suitability. One mentioned standard mAb or standard peptides are used as SS sample. Criteria for RT, peak intensity, and mass accuracy were generally agreed upon as SS criteria that are established. For identity assay using intact mass, one group member mentioned to follow ID assay criteria defined in ICHQ2(R1). In addition, criteria are established for mass accuracy and RT range.

6. What are some key elements of the validated/qualified MS method life cycle management strategy? Any unique challenges during MS method tech transfer/cross validation? How do you address them?

Most discussion group members agreed that instrument change and software can be a challenge.

- How to or do people keep the same acceptance criteria between vendor instrument, including RT, intensity, sensitivity, etc.?

- Different vendor software IQ/OQ/PQ can be a challenge too. One suggestion is using vendor software only for data acquisition but use vendor neutral 3rd party software for data analysis and report.

- In house software allowed? Agency will not say no but software should be demonstrated to be fit for its intended use (e.g. is it validatable) and one should expect review/inspection of the software for its adequacy.

- Need to define criteria for lifecycle management for transfer, instrument upgrade, etc.

- Challenge when newer instrument model is used, and you detect something new

7. How do people generally use the MAM QC method for regulatory applications?

Use of MAM for regulatory applications is increasing even though it is not yet the sole method for monitoring certain attributes. It is still mostly used/seen as an orthogonal method to traditional methods. MAM is also a big topic in emerging technology forum. Sponsors usually have MAM in their plan as back pocket method and for collecting data to gain experience, but continue to use conventional methods as the main/primary QC methods.