Table 2: Platform Analytical Procedures – Does one size fit all?

Scope

For products exhibiting similar structural properties or a common set of quality attributes there may be an opportunity to streamline the analytical tools to control (a) certain quality attribute(s).

In accordance to the Step 3 draft versions of ICH Q14 Analytical Procedure Development and ICH Q2(R2) Analytical Procedure Validation, a platform analytical procedure can be defined as a multi-product method suitable to test quality attributes of different products without significant change to its operational conditions, system suitability and reporting structure. This type of method would apply to molecules that are sufficiently alike with respect to the attributes that the platform method is intended to measure.

Discussion on platform analytical procedure should cover:

- What is the current experience with the concept of platform analytical procedures?
    - What is the understanding around this concept?
    - Which platform analytical procedures are in use already or should be established?
    - Is the use of platform analytical procedure limited to a certain stage of development?
- How to establish a platform analytical procedure?
- Use of an established platform analytical procedure for a new product?
    - What may be the impact on analytical procedure development?
    - What may be the impact on analytical procedure validation?
    - What may be the impact on analytical procedure transfer?
- What are potential benefits or potential risks related to the use of platform analytical procedures?
- What could be special considerations for lifecycle management of analytical platform procedure?
    - With respect to change management
    - Ongoing monitoring
- What is the experience on the regulatory expectance of the use of analytical platform procedures?

Discussion Notes

Introduction. Participants shared their interests in the topic, highlighting needs as well as challenges associated with platform analytical procedures.

Current understanding of platform analytical procedure – how do we describe it?

- Is the concept well understood?
    - Definition proposed in Q2(R2) and Q14 drafts considered appropriate. However, despite of the fact that the drafts provide clarity on the concept, they are silent on how to deal with platform methods.
    - Platform methods apply across classes of products, but also across quality attributes; one needs to define the scope/requirements.
    - Possible gap in the understanding of the concept: *sufficiently alike* [molecules] perceived as a broad term. Risk assessment (*e.g.* of excipients, polysorbates,

formulation components etc.) may be necessary to determine that the attribute is sufficiently alike.
    - Definition of the concept *platform* could be understood as related to the manufacturing process: platform assays are developed for products derived from the same manufacturing process and customised for the processes and host organism used for production. See example of host cell proteins assays: process-specific (ELISA-based) assays *vs* platform (MS-based) assays *vs* generic (kit-based) assays.
- Generic- *vs* platform methods: should there be a difference?
    - Participants noted that if the method did not change and/or used fixed parameters across several products, it should be considered a *generic* method (*e.g.* content by UV determination), whereas a *platform* method would undergo *slight* modifications to turn into a product-specific method.
- Platform methods are primarily used for purity testing.
- What is the degree of modifications allowed to a platform method?
    - Example of platform method for capillary isoelectric focusing (cIEF) analysis of charged variants:
        - necessary to change several parameters in order to apply to different molecules; DoE might be needed to determine where parameters fit best;
        - pH gradient adaptation considered as a typical adjustment for a platform cIEF method;
        - sample-specific aspects (*e.g.* concentration) do not constitute a significant change to the method.
    - Some platform methods require adjustments: there is no "one-size-fits-all" method, each molecule is different.
    - Matrix effects may have significant impact: adjustments to sample preparation would require revalidation.

How to establish a platform analytical procedure?

- **What would be an acceptable qualification**? How many products are necessary to "qualify"/validate a platform analytical procedure?
- The approach depends on the type of method and its intended use (*e.g.* method applicable to all IgG1 products or for all matrixes); this would require different decision points and setting different directions for method development. Method validation follows the Q2(R1) guidance; no full validation is necessary, but rather validation of selected attributes.
- What is the basis to allow setting a platform method?
    - There is no true figure: it depends on a risk-based approach. However, the basic concept behind is that the method works for a defined number of molecules.
    - Some companies define the status of a platform method usually based on 3-5 products; 10 products might be considered in case of new molecule types. No matter the approach taken, a feasibility study needs to be conducted.
- Validation is a major part:
    - If the method was validated on 3 molecules and if the new product is the same kind of molecule, the method can be easily transferred to the new molecule, without full revalidation.
    - Platform method validation report would include either the re-assessment/qualification of specific method attributes as part of a platform qualification protocol (following a risk-based assessment that takes into account method robustness, instrumentation characteristics etc.) or the re-development

from a platform method (*e.g.* detector change) followed by product-specific validation.
    - As regards the regulatory submission: the formal validation (*e.g.* method validation from another project) is part of the dossier, whereas additional data is included to cover the "delta" validation, demonstrating that the method is fit for purpose/applicable to the concerned molecule.
    - AQbD concepts would provide support in defining the method characteristics to address different molecules, matrices etc.
- Example content by UV determination:
    - Requires establishing a generic qualification, followed by product-specific method qualification for each product, *i.e.* demonstration of specificity.
    - Need for repetitive qualifications (if already done for a certain number of different molecules) was questioned. One should re-evaluate the existing validation against a set of acceptance criteria; based on a risk assessment of attributes that require product-specific qualification (*e.g.* specificity, stability-related aspects), one should define a protocol on how to qualify the method for new molecules.

Benefits or potential risks related to the use of platform analytical procedures?

- Establishment of a platform method allows gaining enormous knowledge and helps understanding where time should be invested.
- Use of platform methods should start in early development stages. Platform methods should undergo further refinement to product-specific methods during clinical studies.
- Platform concept is typically used in clinical phase development, whereas full validation is required for MAA/BLA.
- Transition to a GMP lab and then to a commercial lab to run the analysis may be difficult.
- Benefits of platform methods:
    - facilitate high throughput, quicker development times and costs;
    - provide higher knowledge, robustness;
    - allow saving valuable time and resources in method development and quality control;
    - available as a basic form, which allows for tweaks/optimization before it gets locked;
    - easy to transfer to regulatory authorities, if well established procedures.

What could be special considerations for lifecycle management of analytical platform procedure?
How could it "live" in a company as a *master* method? What documentation is necessary? How it is connected to the PQS and to method validation?

- Depending on the specific quality system, documentation might include/require:
    - annexed documents listing specific elements to be defined (*e.g.* UV determination: extinction coefficients, correction for light scattering);
    - establishing product-specific documentation based on a generic one, including qualification to be performed; example: platform method for protein content determination - qualify the method and update SOP.

How is the experience on regulatory acceptance?

- Generally limited experience. Conversations with regulators are ongoing to determine best approaches.
- Participants highlighted that assessors want to see data, and this has to be traceable. If platform methods were used, validation data would be submitted for evaluation. A product-

specific document with appropriate evaluation would have much more acceptance than with a generic document.

- Risk-assessment helps in arguing for regulatory acceptance of a platform method.
- From an assessor perspective, validation data is essential and could be a useful way to facilitate regulatory acceptance. The new concept of platform methods combines knowledge of manufacturing process and of product classes, and it is expected to become widespread in the future.