Roundtable Session 1 – Table 2 – Method Comparability and Method Bridging: Are They the Same Thing?

Facilitator: Birgit Schumauser, *BfArM*

Scribe: Marshall Davis, *Pfizer, Inc.*

Abstract:

During development, for licensure and during the lifecycle of biological products it may be necessary to replace existing methods by alternative / new / modified methods. The terminology used to describe changes of methods is variable. The purpose of this discussion is to try to summarise the understanding of method comparability and method bridging and thus to work out potential similarities and differences between both terms.

Discussion Questions:

Method Comparability

What data do we expect when method comparability is targeted?

Validation data? Analytical results (with statistical evaluation)? Performance comparability?

Is the same method principle expected for both methods?

What is the difference between method comparability and method equivalence?

Is an alternative method the same as an orthogonal method?

What is the role of the samples used?

Method Bridging

Why do we have an additional term to target correlation of results

What is a scenario in which comparability of methods may not be achieved?

Why does a gap exist that needs to be bridged?

How much do precision and accuracy impact the classification

What is the role of the samples used?

Regulatory Support

Is there regulatory support for the two terms method comparability and method bridging?

Where do the terms comparability and bridging occur?

Notes:

What data do you think needs to be provided to show two methods are comparable?

- Sameness of results, you are expecting the two methods to deliver the same results
- Comparability when you change your manufacturing process – you are looking to ensure your results are comparable between the processes and have not changed your PA results
- Critical reagents management: when changing between lots of material you want to see that results are comparable – changing the lot has not altered results
- Comparability between methods = two methods give the same result for the same sample
- Product comparability vs method comparability
    - Product = pre and post production change should show the same result
    - Method = change between methods should produce the same result on the same process? Or is this bridging? How you define this may depend on how different the results are between the methods.

How do you define the difference between bridging and comparability? The group did not form a clear consensus on this topic. However, the key points seem to be the fundamental design of the assay and the difference between the produced results will drive this decision.

Linking MoA-reflective assays for regulatory authorities

- Historical lots
- Stressed samples
- Specificity
- Similar sensitivity, acceptance/equivalence criteria, etc
- **Bridging results are used to move between methods, they often cannot be identical, but you are looking for them to mirror each other. Your stressed samples should move in the same direction, the method delivers sufficiently accurate and sensitive data so as to ensure critical quality attributes are not missed.**

There seems to be disagreement among the participants on the specific definitions between the two terms. Some people are talking about them interchangeably.

Same method run at two different sites on the same sample = comparability

Furthermore, when people talk about comparability, at times they are looking for identical results, whereas at other times they just mean “similar.”

Bridging may not actually be defined within regulatory documents; most participants are referring to institutional practice when they speak of it.

There seems to be a need for these terms to be better defined within the field.

How often does bridging refer to transitioning between lots of material, certain participants do use it this way, while others are saying “bridging” to exclusively refer to transitioning between different methods.

Comparability means a host of different things: method performance, results, etc

What is the role that precision and accuracy play in defining these terms? Is there a minimum level of each you need to see to consider a method comparable?

Superiority also plays a role – better than equivalent (bridging)

An important point for bridging - Ensuring that there is not a large discrepancy in samples that would pass or fail EQ between the two methods.

Should the reported mean between two assays be nearly identical? Group arrives at the conclusion that in comparability, yes. For bridging there could be cases where the means are offset but the historical picture painted by the assay does not change.

Related to above, bridging involves testing historical lots to ensure they would not fail the new acceptance criteria of the new method and do not paint a different historical picture than the previous one.

Movement between different sets of specifications for two methods would imply it is bridging

Comparability: a set of pre-defined criteria that must be hit

- Needs acceptance criteria, difference between the reported results must fall between a certain level of difference