Table 4: How to Translate Physicochemical Properties into Claims of Safety and Efficacy

SESSION 1:
FACILITATOR: Marta Germano, *Janssen Infectious Diseases and Vaccines*
SCRIBE: Hansjörg Toll, *Sandoz Biopharmaceutical*

SESSION 2:
FACILITATOR: Carl Jone, *UCB Pharma SA*
SCRIBE: Jennifer Römer, *Aalen University*

SCOPE:
A multitude of physicochemical quality attributes can be tested in biological products with the currently available analytical technologies, but they may not all be relevant for control of these products. Establishing their relevance depends on the ability to link such quality attributes to safety and efficacy of the biopharmaceutical product. This can be done by a science-based risk assessment taking into consideration a combination of clinical and nonclinical data obtained with the molecule or other similar molecules or platform products, as well as the published literature.

Physicochemical quality attributes are often tested for characterization of biological products, in support of, for example, comparability assessments. In such assessments, the impact of differences in quality attributes on product safety and efficacy needs to be evaluated, however, depending on the complexity of the biological product and on the extent of prior knowledge, it may not always be clear what differences are relevant.
The roundtable discussion will focus on the following questions.

QUESTIONS FOR DISCUSSION:
1. What risk based approaches are used to identify physicochemical properties and quality attributes, which have an impact on safety and efficacy?
2. How can the impact of these quality attributes on safety and efficacy be assessed?
3. Examples of quality attributes, known to have an impact on safety and efficacy?
4. In the context of comparability assessments:
    a. Do we have sufficient analytical technologies to detect relevant changes in physicochemical properties of biologicals?
    b. What new analytical technologies would be needed to detect relevant changes in physicochemical properties of biologicals?
    c. What are the considerations for proceeding into in vivo studies? When are analytical (physicochemical) results not enough to conclude on comparability?

DISCUSSION NOTES:
For the translation of physicochemical properties into claims of safety and efficacy, the dialog between analytical chemists and the clinical team is of outstanding importance. A miss alignment can be often observed. Here, a common interpretation and explanation of data is a major point.

If no data of necessary quality attributes is available, like for a novel product, literature research and prior knowledge need to be consulted. Examples for prior knowledge are eg. impact of high Man glycan structures on PK behavior of mAbs, aGal structure in Cetuximab, aggregation in EPO,

Rituximab and Infliximab, oxidation in gCSF. Based on this, an initial specification at early stage can be facilitated. With additional obtained information of the product in different stages or additional tools like e.g. plasma and cytokine release assays or blast search of potential protein impurities and epitopes, an appropriate risk assessment is allowed.

For the direct translation of physicochemical properties into safety and efficacy, the linkage of product quality and clinical behavior is important. There is in general a lack of knowledge regarding what happens to the molecules after product administration. Therefore, a common data base of patient studies and the information transfer from regulators of known critical attributes that need to be controlled, would be helpful.

If no literature and data is available at all, the clinical and pre-clinical teams need to be involved and (pre-)clinical tests need to be done at different stages for a better understanding, e.g. by spiking studies of quality attributes of interest in animal studies. This gained information may then be compared to known efficacy data of other biological products. Nevertheless, the translation of physicochemical properties into claims of safety and efficacy is always product dependent and based on the collection and comparison of data and product information.