Table 4: HOS Analysis for Biotherapeutic Modalities such as Adeno-associated Virus Therapies, Bi-specific Monoclonal Antibodies, Nanobodies, Fusion Proteins, and Vaccines

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SCOPE:
The advent of biosimilars has fostered the development of new technologies for the characterization of the higher order structure of protein drugs such as cytokines, hormones and monoclonal antibodies. As new entities, such as AAV, bi-specific mAbs, and others, enter the therapeutic space (development, manufacturing, and market), these bring new and unique challenges in the field of HOS characterization. This roundtable session will provide attendees the opportunity to discuss the new challenges brought by these new modalities, how current technologies can addressed them, and what new methods or approaches could help filling gaps. Below, a set of questions may serve to stimulate a casual and collegial discussion, during which participants can share their insights and propose answers to these and other pressing questions related to this topic.

QUESTIONS FOR DISCUSSION:
1. What are the new challenges, from a HOS point of view, brought by new modalities?
2. How does the industry determine the extent of acceptable variability in HOS for comparative purposes?
3. Are current available analytical methods for HOS characterization well suited to face these challenges?
4. Which, if any, challenges cannot be met with current methods? Why?

DISCUSSION NOTES:
- Participants described their experience with new modalities. What can we learn from mAbs to apply to new modalities such as viral vectors, bispecific mAbs?
- Process controls assessing. How bispecific are made: single cell vs two cell expression systems.
- Anti parallel Fc fusion calls for specific bioassays to test their binding affinitity and potency.
- Homodimers vs heterdimers require different process control strategies.
- If CQA is in the safety category you can rule it (?) out.
- What are the tricks that are involved?
- Gene therapy: both a challenge and opportunity: initial low quantities of a viral vector is a problem to develop analytic methods.
- Challenge in using AUC to separate empty viral vector vs gene containing because large amounts are required, but not available.
- AV vector are highly challenging from the point of view of HOS because little is known on MOA, it is like flying blind.
- Fusion proteins have their own challenges from the point of view of glycosylation.
- New modalities protein therapies. Do not carry out previous knowledge (intuition?) compared to mAbs.