Table 8: HOS in Candidate Selection & Optimization

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SCOPE:
The purpose of this round table is to discuss how Higher Order Structure is used in candidate selection. We will discuss how big a role HOS plays in candidate assessment, what HOS may or may not indicate about the developability of a molecule, and ways in which newer technologies are used in the assessment of HOS.

QUESTIONS FOR DISCUSSION:
1. How do you use HOS in your candidate selection programs? Is it relevant at all? At what stage is it used?
2. How is the connection to formulation development?
3. What are the HOS features that trigger decisions for a molecule moving forward in a development program?
4. What technologies are most commonly used in the candidate selection phase?
5. Which technologies are excluded due to sample throughput but would offer relevant information?
6. What new technologies are emerging that may be useful in candidate selection?

DISCUSSION NOTES:
How do you use HOS in your candidate selection programs? Is it relevant at all? At what stage is it used?
- Before process development. For biosimilar development: target spec collection.

How is the connection to formulation development?
- In case of formulation patent: buffer screening by second virial coefficient

What are the HOS features that trigger decisions for a molecule moving forward in a development program?
- What technologies are most commonly used in the candidate selection phase?

Which technologies are excluded due to sample throughput but would offer relevant information?
- Still NMR. Second virial coefficient determination.

What new technologies are emerging that may be useful in candidate selection?
- Cryo-EM.

Notes:
- 3 Participants including Scribe and Facilitator
- Push for higher ranking of HOS in early development
- Computational approach allows first candidate selection round within one week
- For pool and clone selection the number of methods should be drastically reduced. This is valid for all methods not only HOS. Only high-throughput methods.
- Single cell evaluation by cell sorting with fluorescence detection (best producer with highest titer) for clone selection.
- Yeast display as replacement for mammalian cell protein production.
- Automated decision by algorithm to find balance between