

Table 6: Selected and Non-Aggregating Proteins - HOS in Candidate Selection and Optimization in Biologics Discovery Space

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Scope:

Candidate selection is the single most important discovery milestone marking the end of the discovery activities and the beginning of the clinical testing phase of an experimental drug. This decision point is reached after a comprehensive data package is assembled on the lead molecule and evaluated by a group of experts in various disciplines including discovery sciences, manufacturing, drug safety, drug metabolism, regulatory, legal, commercial, as well as clinical.

Questions for Discussion:

1. What is candidate selection in antibody drug discovery?
2. What type of methods can be applied to monitor HOS attributes during the candidate selection?
3. Aggregation can occur during all phases of production and controlling the levels of aggregate in the final product can be challenging. What would be the best exercise to optimize candidate selection in early discovery stage?
4. In addition to aggregation, significant degradation pathways, such as oxidation, deamidation, isomerization, and peptide bond cleavage are also evaluated early, typically at multiple temperatures. HOS is a matter in candidate selection and optimization in biologics discovery space?

Discussion Notes:

Q. What type of methods can be applied to monitor HOS attributes during the candidate selection?

In discovery automated-, sensitive, and robust biophysical methods are needed:

* Utilization of AUC for the aggregate or molecular size determination: Marina Feschenko – AUC low throughput not easy to transfer to QC; not good for screening tool at all. Good for characterization tool.

* CD: far- and near-UV CD for secondary and tertiary structure characterization; automation is needed; to monitor HOS in Discovery area, discussed about 96-well automated CD system from Applied photophysics

*MMS: automated IR system for the protein secondary structure characterization from RedshiftBio

* Digital liquid – FTIR system for secondary structure characterization

* DSC for structural thermal stability – Malvern 96 well based automated system