Table 2: Best Practice for Analyzing and Interpreting Routine Biophysical Assays (DLS, CD, DSC)

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Scope:

Several biophysical assays are routinely used to characterize biotherapeutic products. These characterization tools contribute to a deeper understanding of the products manufacturability, stability, safety, and efficacy. How we analyze and interpret the data can influence not only our product understanding but how we represent this data in regulatory filings. The objective of this round table is to define the best practices for analyzing and interpreting routine biophysical assays and possibly find alignment align between biopharmaceutical companies, academia and regulatory agencies.

Questions for Discussion:

1. If you could pick one best practice for analyzing and interpreting data for DLS, CD and DSC, what would it be and why?
2. CD: When collecting spectra on a perturbed/changed modality and comparing to its reference, how much does the spectra need to change from your reference to be considered different? And on the flip side, how different can the spectra for your perturbed sample be and still be considered the same as your reference?
3. DLS: Do you compare your data to a size standard?
4. DSC: Do you report delta H values for larger or complex molecules, if so, why?
5. DSC: Are you identifying each thermal transitions?
6. How are these methods used for characterization of nucleic acid structures, RNA and DNA for newer vaccine/therapeutic models (gene therapeutics, RNA vaccines, etc)? How best to apply these methods or design experiments for biophysical characterization?

Discussion Notes:

CD: Half the group uses automated CD and the other half uses manual, all agreed that cleaning the cell is was the challenge, but the automation tends to clean the cells more reliably which removes some of that error. Consensus that each sample is loaded on the cell 2-3 times with 3 scans each and CSA (Jasco protocol) or system suitability is used prior to each sample set. Near-UV-CD was used by all and Far-UV CD was used by half for comparability.

DSC: Malvern used by all and the std from Malvern is used, one person mentioned the RNAase A was the previous std by Malvern and has stockpiled it due to the new std from Malvern. The Tms and delta H are used and filed for comparability. A few are currently working on domain

(CH2 CH3 and FAB) characterization and currently report the apparent Tms and non-apparent Tm (shoulders).

Both CD and DSC, characterization of bispecifics or mixed mAbs discussed and if they should be analyzed separately and then together and the possible issues with analyzing and interpreting data when mixing 2 mAbs.

No one in the group besides myself currently uses DLS for product characterization.

Both MM-IR from Red Shift and Tyko (unfolding technique using heat and FL detection)

On a side, two of us briefly discussed our available full-time positions.