

Table 5: Biological Consequences of HOS

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SCOPE:

There good amount of data published regards protein therapeutics require a native-like structure in order to minimize interference with the immune system and avoid adverse effects in addition to possible loss of efficacy. Therefore, the Food and Drug Administration (FDA) has recently suggested that the biopharmaceutical industry should invest more effort into the HOS characterization of biological products as early as possible in their development stage. In this round table discussion, we would like to have discussion to share information, data, previous experiences around the assessment of higher order structure (HOS), which involves the analysis of secondary structure, tertiary structure, and particles of proteins and their impacts on safety and activity of protein therapeutics.

QUESTIONS FOR DISCUSSION:

1. Concerns or thoughts around HOS and biological consequences?
2. Any previous work correlating HOS and *in vitro* activity/safety?
3. Any previous work correlating HOS and *in vivo* activity/safety?

DISCUSSION NOTES:

- A small collection of researchers met to discuss the biological consequences of HOS, that included the organizer, the scribe and two additional researchers.
- A number of biological consequences from HOS were discussed, these included the following. The precipitation/aggregation of hemoglobin caused by an amino acid substitution. The aggregation/plaque formation of the Ab peptide and prion proteins, where certain misfolded oligomers (known as "seeds") can induce other molecules to take the misfolded oligomeric form, leading to a chain reaction.
- HOS was defined as everything that occurs after translation, and thus would have the potential to alter the tertiary structure of the protein. It was felt that all techniques were needed as each gives a different view of the protein.