Roundtable Session 1- Table 6 - Methodologies to Assess / Predict Formulation and In Vivo Stability of Novel Modalities

Facilitator: Claire Bramwell, *Protein Metrics, Inc.*

Scribe: Chris Yu, *Genentech, a Member of the Roche Group*

Abstract / Scope:

The objective of this round table discussion is to comprehensively explore the methodologies, challenges, and regulatory considerations involved in the stability assessment and predictions for novel modalities, such as biologics, RNA based therapeutics, gene therapies and small molecules, to ensure their safety, efficacy, and quality throughout their shelf life.

Questions for Discussion

1. What are the current trends, advancements and requirements for Computational modeling for predicting stability? Does the table have any opinion on emerging in silico methods for stability prediction, such as Machine learning algorithms in stability studies and PK, or AI?
   Notes: Good or effective modeling require good source data. There has been advances in such modeling for biologics, especially when a large amount of empirical data was available. For new modalities, new methods and additional data will be used in machine learning or AI efforts to better inform stability studies.
2. How do current regulatory guidelines and considerations for the stability assessment of novel modalities address the unique challenges posed by the complex nature of these products, and what are the implications for manufacturers in terms of ensuring product safety, efficacy, and shelf-life?
   Notes: Current (existing) regulatory guidelines are helpful for development of new modality investigational products. Gaps exist largely due to lack of specific knowledge, and limited characterization of such products in general. For example,

material characterization and control strategies for cell and gene therapy products could benefit from clarification in regulatory guidelines.

3. How do current and emerging analytical methods, such as mass spectrometry, chromatography, biophysical and biologic assays, compare in their effectiveness for assessing the stability of biologics in formulation and in vivo, and what are the key challenges and innovations driving their development?
   Notes: Current knowledge is built on available methods and empirical data using such methods. Emerging analytical methods (MAM for example) are expected to further enrich our collective knowledge as their adoption in the industry takes hold and their uses expand.
4. What kind of considerations are taken into account when designing stability studies? What are the differences and applications of real time vs accelerated testing and what is the criteria for selecting stability indicating methods throughout the lifecycle of drug development?