Small Group Discussion - Session 3a

1. Have you seen differences between results generated using different in silico models? How do you validate in silico models?
2. DC:T cell assays discussion: How do you ensure that you are capturing antigen-specific T cell responses? Assay stimulations can vary from 72 h to 3 weeks. What has been your experience with a) Culture time, b) Control of cell viability c) Number of T cells or CD4+T cells and ratio of DC:T cells in the well, d) Establishing assay sensitivity, e) FBS or defined media, f) Cytokines and growth factors?
3. Impurity concentration threshold: Absolute amount vs % of the API? Appropriate concentration to test individual impurities, e. g., 100%, 10%, 0.5% of API?
4. What improvements to current assays could be made to better reflect clinical immunogenicity?
5. Donor selection discussion: a) Should number of donors be determined by HLA-coverage, assay variability or both? b) Healthy donors vs patient primary cells?

Small Group Discussion - Session 3b

1. What do you think are critical assay attributes when establishing an IIRMI assay? Are there biological readouts of innate immune activation that are more sensitive/relevant than others?
2. In your experience, what have been the main challenges in implementing IIRMI assays to assess the immunogenicity risk of generic peptides? Have there been any strategies that have helped?
3. Excessive dilutions due to formulation inhibitory effects. Strategies to overcome it.
4. What is your statistical analysis approach to analyze the IIRMI data? How do you justify that approach?
5. What criteria do you use to accept/select assay runs and IIRMI data? Should there be a qualifying attribute for donor selection?
6. Your drug product batches show a signal in one or more of the IIRMI assay readouts as compared to the RLD. How do you proceed? Is it necessary to identify the IIRMI(s) to implement controls?