Small Group Discussion - Session 6a

1. Is there a level of HCPs that might increase the immunogenicity risk? What are the impediments to establishing overall levels of HCP that might be considered “safe” from an immunogenicity standpoint?
2. Are there new/alternative strategies (not discussed in the session) that should be considered when assessing the risk of host cell proteins? What has worked/or not worked in your organization?
3. HCP could modulate the innate immune system. What tools (in silico, in vitro or in vivo studies) do you use to compare the potential immunogenicity risk of two products with different host-cell protein profiles? E.g. ELISAs (+/- LC/MS) can have variable coverage for HCPs.
4. Are there new/alternative strategies (not discussed in the session) that should be considered when assessing impurities? What has worked/or not worked in your organization?
5. What is the lowest and routinely achievable level of total HCPs across your well controlled recombinant peptide manufacturing process(es), and how are they calculated/established?

Small Group Discussion - Session 6b

1. Do you currently have assays in place to assess the potential immunomodulatory activity of impurities in your candidate generic oligonucleotide therapeutic? What assays do you think might help to assess the immunogenicity risk of generic oligonucleotide products?
2. What would be a reasonable way to group impurities to control them? If so, are there reasonable levels for each group of impurities that could be considered as they relate to immunogenicity risk?
3. Do you have thoughts on the role of oligonucleotide impurities in the induction of thrombocytopenia and/or neutropenia? Are there in vitro studies you have tried to assess this risk?
4. What do you think are the differences in impurities that could pose a higher risk of immunogenicity and inflammation for this class of product: Differences in sequence, chemical modifications, backbone, linkages, high order structure?
5. Are there routes of administration for oligonucleotide that have higher immunogenicity/inflammatory risk?