Analytical Strategies for Cell & Gene Therapies
Francis Poulin, Sanofi, Zenobia Taraporewala, CBER, FDA, Andy Weiskopf, Biogen,
Presentations by: Eric Pastor, Sanofi, Framingham, MA USA

Plen-Shop
Cell and gene therapy products present a number of analytical challenges not encountered with other, more conventional biopharmaceutical products. Beyond standard analytical tools, these therapies often require the use of complex bioassays to assess product potency, confirm product identity, and for in-depth characterization of process- and product-related impurities and residuals. Autologous cellular products, produced as patient-specific lots, present additional constraints due to the limited amounts of material (e.g. for retains and testing) and the short time available for testing. Additionally, the measurement of product potency for cell and gene therapy products often relies upon a matrix of orthogonal biological, biochemical and/or biophysical assays. Difficulties in the development of potency assays can be due to the technical limitations of in vitro systems or the absence of reference standards and suitable reagents. In this plen-shop, we will explore various facets of analytical strategies and discuss effective approaches towards the characterization, lot release, and stability testing of advanced therapy medicinal products.

Questions for Discussion:
1) What are the most challenging analytics for cell and gene therapy products, and what are the solutions being developed by the industry? For example:
   a. Cell therapies
      i. Rapid sterility testing
      ii. Flow cytometry to classify the phenotype of cell therapy products
      iii. New technologies for cell enumerations & viability
      iv. Potency assays
   b. Gene therapies
      i. Capsid, genome & infectivity titer assays
      ii. Potency assays: gene expression vs MOA
      iii. Identity testing implementation in the context of multi-product facilities
      iv. Orthogonal analytics to characterize empty vs full capsids
      v. Biophysical characterization assays implementation in routine QC settings

2) What are the differences in analytical packages for Phase 1 vs Phase 3/BLA?
   a. What are the strategies for implementing cell-based assays reflective of the product’s MOA?

3) Reference standards
   a. What are the uses of universal serotype controls vs internally-developed references?
   b. What analytics are used to qualify reference standards, and how is it protected against drift during re-qualification?

4) Complex cell-based assays are widely used in the testing of cell and gene therapy products, what are the industry’s strategies to reduce assay variability?
   a. Are risk-based approaches to method development widely used, and do they yield more robust/less variable analytical methods?