Table 24: Advanced Technologies

Facilitator: Chongfeng Xu, *Biogen*

Scribe: Heather Hudson, *Seattle Genetics, Inc.*

SCOPE:

Innovation helps accelerate drug discovery and development, reduce costs and improve productivity. Novel analytical technologies are needed for biopharmaceutical industry to continue to improve development efficiencies, enable better understanding and control of product quality, support the ever-diversifying therapeutic modalities and increase probability of success. Some of the ongoing technology trends include novel analytical instruments and technologies, more specific & sensitive and multi-attribute methods, higher throughput & increased automation, and online/atline/inline process monitoring and control. This roundtable aims to discuss the development and implementation of these technologies, and how the industry is managing the risks associated with introducing novel technologies for release & stability, characterization and PAT applications. Challenges in transferring of new technologies will also be discussed.

QUESTIONS FOR DISCUSSION:

1. What have been some of the recent advanced technologies and strategies being introduced for product release and stability?
2. What are the challenges associated with the implementation and method bridging and how do you address them?
3. What is the current status in your company and where do you see the further applications of Multi-Attribute Method (MAM) going forward? QC, PC or others?
4. What are some of the new analytical technologies you have been using to support C&GT?
5. How are you adopting analytical technologies for continuous manufacturing?
6. Given the concept of real time releases, what's your opinion on technical and regulatory hurdles for the realization of real time release?
7. What are some of the technologies available in your company for Process Analytical Technologies (PAT) in terms of online and at line analysis and do you use them in development or manufacturing setting?

DISCUSSION NOTES:

1. Product Release, Stability, and Characterization:
    a. Native MS used for characterization. Ability to couple online with chromatography and electrophoresis methods. icIEF has been coupled with MS for peak id of chare variants, also with fraction collection capability. Working with vendors for integration solutions.
    b. Fc gamma receptors binding characteristics- redesign how characterization is approach to mechanism of action.
    c. SPR used at Biacore. The technology provides binding, kinetics, affinity, specificity and concentration, without any needs for labels.
    d. Native MS with ammonium acetate buffer: online native SEC-MS for mAb size variants, direct molecular mass measurement for dimer peak at 0.4% or below.

e. Coupling of HIC with native MS, June from BMS will have a presentation at Sciex luncheon seminar today.
f. Can MS detect between empty and full AAV? CDMS is a specialty native MS method enabling the analysis, however, it hasn't been commercialized.
g. Currently focus is on Dev, but challenge is operations and getting equipment GMP qualified.
h. Biggest hurdle for new technology integration into lab
    1. Data integrity
    2. Requires closer relationship between vendors and industry
    3. Guidance for expectations for GMP (support vendors in what industry needs to be able to implement to commercial setting)
i. Most technologies for PAT are still at Dev stage (equipment/implementation/software).
j. Adaptive control- some systems designed to integrate well; some aren't (chromatography systems)
k. Challenge for Analytical vendors: data- customers proprietary, different formats from different customers. Need universal format or standards for vendors to respond to demand.
    1. EX: Biocore- SQL, just implemented EXCEL format for data export
    2. QC space- how much detail is really needed?
l. How much data is the right amount of data?
m. How have people successfully brought new technologies into operational space?

2. Method Bridging
    a. Difficult- dependent on what method is for
    b. How statistical measurement of equivalence is defined, needs focus.
    c. Lab environmental factors influence on results (understand impact on data so good data is recognized)
    d. Using 2 different tests at 2 different labs for the same attribute- should not expect same result, provide side by side performance to show relevance of two method on attribute being measured.
    e. Advance modeling is challenging to explain, especially in a submission.

3. MAM- realistically what else is available beyond MS
    a. Rollout needs very specific definition around what is being evaluated for which CQA.
    b. Roll all out at once vs incrementally. (challenge is if its been filed before, yes, Amgen filed for substitution of identity and purity assasys)
    c. TT challenge still in bringing into QC labs. Needs better training and more awareness for analysts. Challenge in bringing an advance technology like MS into a QC lab and have expertise to execute
        i. Focus is always on advance user
        ii. Data analysis
    d. Industry challenge in balancing production training to follow SOP vs teaching awareness of operators to importance of step being executed.
        i. Critical for PAT
    e. Suggestion/ need: map out QC reference standards for new technologies industry (USP to drive?)
4. GT or CT: Not a lot of information around this question. Vendors don't have clear messaging on what industry needs to support (Cryo EM, RAMEN)

5. Continuous Manufacturing- small molecule used more frequently, biologics behind. DS processing lagging behind. Right analytics in right place. Facility design has much bigger impact on continuous.

   a. How is a continuous batch defined?
   b. Downstream processing alone, or both the upstream and the downstream. Continuous processing in upstream might offer better pQ, such as lower levels of PTMs, reduced levels of Lower pI isoforms and aggregation.
   c. Scale-down modeling for continuous manufacturing not really available.
   d. Fluid dynamics mapping a tool to use as complementary modeling for process information.
6. Collaboration between companies and sharing of information