Roundtable Session 2 – Table 13, Cell & Gene Therapy Products: Shared Experiences with Developing Manufacturing Control Strategies

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Abstract:

For successful production of biological products, it is critical to establish and maintain a state of manufacturing control by using effective process performance monitoring and control systems. For Cell & Gene Therapy products, control of input material attributes is difficult; definition of Critical Quality Attributes (CQAs) may not be clear or fully defined; selection of operating conditions, in process controls, and finished product specifications may be challenging due to limited data; and the performance of associated methods may not be optimal since CMC work often lags behind clinical work. Challenges and strategies can be as complex as the products themselves.

This roundtable will discuss experiences, approaches, best practices, and regulatory expectations for the development of process control strategies for Cell & Gene Therapy products.

Discussion Questions:

- Does your company define a Quality Target Product Profile (QTPP) by understanding patient needs and what aspects of the product and process delivers these requirements?
- What are some best practices for understanding CQAs?
- In your experience, where in the manufacturing process is it best to control a CQA?
- How do you make links between CQAs and the manufacturing process?
- What's a good approach for defining input materials tests and specifications?
- How do you use results from risk assessments and experimental work to define Critical Process Parameters (CPP), Normal Operating Ranges (NOR), and Proven Acceptance Ranges (PAR)?
- What changes do you see in the QTPP, CQAs, and PPs as the drug development phase progresses from Phase 1 to 2 to 3?
- How do you enable maximum flexibility during your clinical trials to support wide control strategy limits (specifications /PP etc.)?
- How much characterization data is sufficient for C&GT products? What is the balance between characterization data availability and requirements?
- What are your experiences with post approval changes for process control system?
- How can prior process and product knowledge be leveraged to develop a C&GT manufacturing process control strategy?

Notes:

- In terms of CQAs, companies were focusing on safety, microbial, dosing, activity/potency based on Phase I feedback from health authorities
    - Some experience with working very closely with health authorities to identify appropriate specification ranges based on the challenges around cell and gene therapy products
    - Participants expressed challenges with setting specifications based on limited manufacturing experience/low number of batches
- QTPP can be a moving target in early phases of development
    - QTPP may become more useful proceeding through later clinical phases
    - Participants noted the importance of focusing resources on the most impactful areas depending on phase of the program
- It is important to be able to demonstrate accurate delivery and lack of contamination during in-use studies
- Experience working with CMOs
    - Participants noted challenges they had experienced with CMOs related to availability of information
    - For example, CMO had established tests and specifications for input materials which were not made available for review
- Challenges related to shelf-life
    - Shelf-life can vary between modalities and can, in certain cases, be shorter than the QC testing timeline
    - In these cases, conditional release may be necessary
    - Companies would then follow an established process if something is flagged during QC testing after administration
    - May be necessary to work with agencies to release to the patient even if there is an OOS given the criticality of the situation

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