CAR T MANUFACTURING: PROCESS MODIFICATIONS FOR A TRANSFORMATIONAL AUTOLOGOUS PRODUCT ON A RAPID PATH TO LICENSURE

Thomas Brieva, Celgene
tbrieva@celgene.com
Eric Law, Celgene
David Hsiung, Celgene
Seth Jones, Celgene
Shiv Misty, Celgene
Sherry Zhou, Celgene
Ryan Glussi, Celgene
Ryan Shorr, Celgene
Kevin Friedman, bluebird bio
Molly Perkins, bluebird bio
Shannon Grande, bluebird bio
Holly Horton, bluebird bio
Kruti Shah, Celgene
Jaymes Fuller, Celgene
Christopher Wiwi, Celgene
Greg Russotti, Celgene

Key Words: Cell therapy, comparability, process change

The transformational impact of CAR T cell therapies on serious diseases demands a rapid path to licensure in order to establish widespread availability to desperate patients. In addition, the complex, labor intensive, and costly patient-specific manufacturing processes for CAR T cell therapies demand process modifications that enable scalability and affordability to maximize availability to patients. There are many options to improve CAR T processes ranging from automation to improved medium composition to simplified closed-system tubing sets. However, the dramatic dose-dependent safety and efficacy activities of these therapies amplifies the need for maintaining product comparability across process changes. This assessment of comparability is challenged by limited knowledge of product Critical Quality Attributes as well as limited availability of patient cells for process development studies. We have developed a comprehensive analytical toolbox that enables the assessment of product impact of process changes along with a risk-based approach to applying a matrix of appropriate tools for each change. This risk-based approach involves the most extensive product analysis for high-risk changes and a relatively restricted product analysis for low-risk changes. In all cases, the product analysis includes assessments of product characteristics that can hypothetically be impacted by the process change. We describe our approach to identifying, prioritizing, and assessing feasibility of process changes along with generating a suitable product comparability dataset to implement the most impactful process changes on an expedited timeline to licensure. We share examples of comparability data and its application to decision making.