DEVELOPMENT OF A SECOND-GENERATION LENTIVIRAL VECTOR TO REDUCE COGM WHILE MEETING BOTH VECTOR AND CAR T CELL CQAS

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Lentiviral vectors (LVVs) are often used as the gene delivery tool for manufacturing CAR T cell therapies. There is a growing need for new LVV manufacturing platforms that can reduce cost of goods manufactured (COGm) and meet supply demands of commercial cell therapy products. A major challenge of adopting these new LVV processes into existing clinical and commercial products is matching both viral vector and cell therapy drug product Critical Quality Attributes (CQAs). In particular, vector physical and functional titer readouts may not always be predictive of the transduction frequency that can be achieved by a viral vector in primary cells. Here we present a Quality by Design (QbD) approach to establish a second-generation lentiviral vector for an autologous CAR T cell therapy. Critical upstream process parameters, including relative amounts of plasmids used during the transient transfection step of viral production, were identified that impact the relationship between vector CQAs and CAR T cell CQAs (integrated vector copy number and CAR surface expression). In addition to the interactions between vector CQAs and CAR T cell CQAs, interactions between upstream parameters and downstream unit operations, especially anion-exchange chromatography and sterile filtration, were interrogated. Finally, the tradeoffs between COGm and CAR-T cell CQAs will be discussed in the context of comparability including manufacturing scale results.