DEVELOPMENT OF cGMP MANUFACTURING PROCESSES FOR THE LARGE-SCALE PRODUCTION OF CELL-BASED THERAPIES FOR COMMERCIAL APPLICATIONS

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The landmark discovery of induced pluripotent stem cells (iPSCs) ushered in a new era of cell and gene-based therapies and their potentially curative nature for a number of devastating diseases and disorders. This has resulted in a large number of clinical trials being initiated for the use of cell-based therapies for the treatment of various diseases, such as Parkinson's disease, Type I diabetes, and large B-cell lymphoma. Additionally, the recent approval of therapies using immune cells and their success in the clinic are positive indicators of the commercial applicability of cell-based therapies. However, in order to reach the market it is necessary to develop industrialized cGMP manufacturing processes that are scalable, robust and reliable and can meet commercial demands. In addition, for a commercial process it is important to have a good understanding of the critical process parameters (CPPs) and their impact on the critical quality attributes (CQAs) of the final therapeutic product. Lonza has approached the development of industrialized bioprocesses with focus on (1) the development of cGMP manufactured, quality-assured cell bank processes (e.g. iPSC manufacturing process utilizing a robust cell culture system), (2) implementation of computational fluid dynamics (CFD) modeling to aid in scaling culture systems, (3) implementation of process analytical technologies (PAT) to monitor/control the culture conditions and automation to decrease labor and improve reproducibility of the process, (4) utilizing a standard approach to performing process characterization studies based on a failure mode and affects analysis (FMEA) to identify modes of failure, risks and mitigations and aid in commercial readiness, and (5) the development, optimization and qualification of analytical methods to characterize the state of the cultures and support release of cell-based products. Importantly, the development of analytical methods that can demonstrate the characteristics and potency of the final drug product as it relates to its *in vivo* mechanism of action are critical. In this respect, Lonza has developed a library of robust / qualified analytical methods that can be assessed and utilized for different clinical programs in order to support commercial activities. Here, we will discuss how we have applied our unique approach to support the industrialization of cell-based therapies for applications utilizing iPSCs and T-cells..