

PROCESS AND EQUIPMENT SCALE-UP OF CONTROLLED-RATE FREEZING IN CELL THERAPY

Jonathan Rubin, Janssen R&D, USA
jrubin4@its.jnj.com

Scaling-up cryopreservation steps for cell therapies pose significant equipment- and process-related challenges. Often cryopreservation is scaled-out to avoid these issues, but scale-out causes greater intra-batch variation and logistical and regulatory complications. High-capacity controlled-rate freezers (CRFs) can effectively scale-up cryopreservation; however, they have been sparingly used in cell therapy and their comparability to more routinely-used bench-scale CRFs is not well established.

This talk will describe the design and characterization of a high-capacity CRF along with the challenges involved in scaling-up the freeze profile. The 12-fold larger CRF was based, primarily, on the performance of a characterized bench-scale CRF. Temperature mapping studies were performed on both CRFs to establish equivalence. The larger freezer was found to have better temperature uniformity and responsiveness than the smaller CRF. Those differences in equipment performance necessitated re-evaluation of the freeze profiles for two cryopreserved products (bags and vials). The new profiles strode to match cell viability performance from the small-scale CRF and minimize the variation in nucleation times product experienced. The spacing between product in the CRF and design of the product trays and racks played a key role in profile development and freezer performance. This work details the design and characterization of a high-capacity CRF and highlights challenges in process and equipment scale-up.