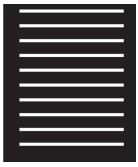
Preface



FOR HEMATOPOIetic cell therapy (HCT) products that are cryopreserved and stored in liquid nitrogen, the critical process of cryopreservation and subsequent thawing represents the single greatest source for loss of viable hematopoietic stem/progenitor cells (HPCs), which are essential for successful engraftment. Cryopreservation is also the least well understood step in HCT product preparation and storage and there are few, if any, detailed published guidelines for interpretation of "cooling curves" (graphs representing product and surrounding chamber temperature over time) generated from controlled-rate freezer devices. In addition, there are no published studies that have systematically investigated the effects of transient alterations in the rate of product cooling, which are sometimes observed during HCT product cryopreservation. Accordingly, it is difficult to specifically define what constitutes an "abnormal cooling curve" and, when abnormal cooling curves are observed, to predict the potential impact on the overall HCT product quality.

This book is primarily written for HCT laboratory personnel, including laboratory directors and medical directors, to help remove some of the mystery of HCT product cryopreservation and anxiety associated with the decisions on what to do with irreplaceable HCT products that appear to have experienced abnormal cryopreservation conditions.

Our primary objectives are as follows:

1. Enhance understanding of the science of the cryopreservation process and operation of common cryopreservation systems.
2. Provide guidelines for the interpretation of abnormal freezing curves, including how to distinguish insignificant product temperature recording artifacts from abnormal cooling conditions that significantly reduce postthaw HPC recovery and functional viability.

3. Describe the laboratory methods used to assess the impact of abnormal cooling conditions on HPC recovery and survival and their specific advantages and limitations.
4. Suggest practical steps to mitigate loss of HPC viability when confronted with an abnormal cooling curve in "real time" and how to avoid "transient warming events."
5. Discuss the voluntary standards and regulatory requirements established to document the integrity and quality of cryopreserved HCT products, including recommendations for validation and verification of procedures used for cryopreservation, storage, and shipment as well as general descriptions of advantages and disadvantages of different storage and transport systems for cryopreserved HCT products.

It is our hope that this book will also serve as a practical guide to assist laboratories in the creation of an effective quality management plan for HCT product cryopreservation and associated processes that will ensure consistent product quality and provide the best clinical outcomes for patients.

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