ISCT
INSTITUTE OF TRAINING
& DEVELOPMENT

ISCT Clinical Cell Therapy Leadership Micro Course

Course Overview

The Cell Therapy Leadership training micro-course is an 10-hour on-demand course, curated by world-renowned leaders in Cell and Gene Therapy for Principal Investigators, Clinical Development Scientists, and Industry professionals involved in translational research, product development, and clinical trial sponsorship.

Learn how to effectively navigate the complexities of bringing CGT products from bench to bedside, with comprehensive insights into critical areas such as IND submissions, clinical trial design, GMP standards, Quality Assurance, Technology Licensing, and patient access.

What You Will Learn

- Key considerations for translating research to clinical manufacturing
- Essential components of IND submissions and CMC requirements
- Key considerations for study design, product release criteria, and safety to support clinical decision-making and regulatory approval
- Understand the role of correlative studies in assessing gene transfer, immunogenicity, and toxicity
- Manufacturing cell and gene therapies under GMP guidelines best practices
- Viral vector production methods, regulatory challenges, and release testing for clinical use
- Develop and qualify release tests according to GMP standards
- Learn how to create and manage scientific teams for successful cell therapy product delivery
- Key regulations and guidelines for establishing quality systems in early product development
- Strategies for interpreting regulatory requirements to accelerate development and enhance reproducibility
- Insights into the cost structure of CAR-T and gene therapies
- Academic-to-industry partnerships, IP protection, and commercialization strategies

Course Overview

Pre-Clinical Development (60 mins)

Gabriela Plesa, MD, PhD, *University of Pennsylvania, Pennsylvania*
David DiGiusto, PhD, *Independent Consultant, DiGiusto Consulting LLC, Massachusetts*

In this session, speakers will address the hurdles to translating a variety of cell therapy products with a focus on manufacturing considerations and particular issues related to the translation of T cells, and iPSCs.

Learning Objectives:

- Historical overview of T cells products development.
- Challenges to be considered for translating a product from a research bench to clinical manufacturing.
- Pre-clinical data package for regulatory submission.
- Creating and Characterizing iPSC and iPSC-derived products.
- Developing data to support the proposed use of Regenerative Medicine Products.
- Animal modeling – pre-clinical safety and efficacy.
- Example of bench to bedside translation.
- Understanding gene editing for pre-clinical development.

IND Development (30 mins)

Elizabeth Hexner, MD, *University of Pennsylvania, Pennsylvania*

This section will cover the format, topics, inclusions, and strategies for filing an Investigational New Drug (IND), with focus on the non-clinical and clinical data expectations required by the eCTD format. The session will also include a discussion of translating the early phase R&D product into GMP, including the development of specifications pertinent to the Chemistry, Manufacturing and Controls (CMC) of the IND.

Learning Objectives:

- Learn the CTD/eCTD modular format and available opportunities for FDA interaction during IND development.
- Learn the components of the IND submission, the clinical research protocol and the related and required monitoring plans.
- Understand the components of the CMC and how to develop and present those components for inclusion in the IND.
- Recognize the importance of gathering appropriate previous human and preclinical data to support the IND.
- Recognize the importance of working closely with the GMP facility for tech transfer related to product manufacturing and release.

Study Design, Conduct and Analysis of Clinical Trials (50 mins)

Noelle Frey, MD, MSCE, *University of Pennsylvania, Pennsylvania*
Nirali Shah, MD, *National Cancer Institute, Maryland*
Wei-Ting Hwang, *PhD, University of Pennsylvania, Pennsylvania*

Learning Objectives:

- Confirmatory & Exploratory Analyses.
- Choosing manufacture and product release criteria.
- Biomarkers & Surrogate Endpoints.
- Choosing the right trial endpoint.
- Stopping rules.
- Safety considerations.
- Including replacements.
- Addressing Missing Data in Clinical Trials.
- To review specific trial design issues from scholar presentations.
- Unique pediatric-specific considerations.

Correlative Studies (30 mins)

Joseph Fraietta, *PhD, University of Pennsylvania, Pennsylvania*

Lectures will encompass a discussion on the importance of immune correlative studies for immune-based therapies, along with associated challenges.

Learning Objectives:

- To understand the importance of correlative studies in accurately assessing aspects such as
    - Delivery and efficiency of gene transfer.
    - Target specificity.
    - Immunogenicity and toxicity – genotoxicity: insertional mutagenesis.
    - Long-term versus short-term expression.

Cell Manufacturing (30 mins)

Andrew Fesnak, MD, *University of Pennsylvania, Pennsylvania*
Emily Hopewell, PhD, *Indiana University, Indiana*

These lectures will cover basic principles and practices for the manufacturing of non-genetically modified cell and gene therapy products according to GMP. Examples from instructors experiences will be used to provide context for the interpretation of federal regulations.

Learning Objectives:

- Principles of GMP as applied to manufacturing operations.
- Therapeutic applications of cellular products.
- Raw materials specifications and vendor selection.
- Working with primary cells from patients and patient-specific product manufacturing.
- Optimization of manufacturing environment.

Manufacturing and Analytics of Viral Vectors (30 mins)

Johannes (Han) van der Loo, PhD, *Children's Hospital of Philadelphia, Pennsylvania*
Kenneth Cornetta, MD, *Indiana University, Indiana*

This session will highlight current challenges associated with the manufacturing of viral vector products. Moreover, Dr. van der Loo will describe the regulations and standards that governs the production, and Dr. Cornetta will describe release testing requirements for viral vectors intend for *ex vivo* or *in vivo* clinical use.

Learning Objectives:

- To understand the basic differences between types of viral vectors, manufacturing methods, and applications.
- To understand issues associated with the manufacturing of viral vector products, including scale and lot-to-lot variability.
- To understand and appreciate the facilities and equipment needed to support GMP manufacturing.
- To understand the basic regulatory requirements governing the manufacture and release of viral vector products.
- To understand the value of adopting a risk-based approach in GMP manufacturing.

In Process and Release Testing (30 mins)

Andrew Fesnak, MD, *University of Pennsylvania, Pennsylvania*
Emily Hopewell, PhD, *Indiana University, Indiana*
Steven Highfill, PhD, *National Institutes of Health, Maryland*

These lectures will cover basic principles and practices for in-process and release testing of non-genetically modified and gene-modified cell & gene therapy products according to Good Manufacturing Practices. Examples from instructor experiences will be used to provide context for the interpretation of federal regulations.

Learning Objectives:

- Principles of GMP as applied to testing; comparison of in-process and release testing.
- In-process testing and setting metrics for success.
- Developing and qualifying appropriate release tests (compendial vs product specific).
- Potency assays.

Team Science/ Building Cross-Functional Teams (30 mins)

Anne Chew, PhD, *University of Pennsylvania, Pennsylvania*
Nirali Shah, MD, *National Cancer Institute, Maryland*

Drs. Maus, Chew, and Shah will address the various ways of forming a translational science team and discuss how they set up and what works in a cell therapy program.

Learning Objectives:

- To understand how to create a multi-functional scientific team that addresses all of the requirements for creating, qualifying and delivering a cell therapy product to the clinic.
- How to motivate and keep the team together during the lengthy translational stages of product development and when collaborating with industry partners.
- Career development opportunities for cross-functional team members.

Quality Assurance Development (30 mins)

Steven Emanuel, PhD, *University of Pennsylvania, Pennsylvania*
Stephen McKenna, MS, *University of Pennsylvania, Pennsylvania*

This section will introduce the regulations, guidance, and make recommendations for establishing Quality System elements consistent with the needs for early phase clinical studies.

Learning Objectives:

- • Understanding what constitutes a Quality System.
- • Understanding compliance requirements for cell therapy products.
- • Understanding the role Quality System plays in product development.
- • Developing Quality Systems appropriate to the stage of the project.

Clinical Trial Case Studies: Delivery of Cell Therapy Products (Infusion) (30 mins)

Lester Lledo, MSN, DNP, *University of Pennsylvania, Pennsylvania*
Elizabeth Hexner, MD, *University of Pennsylvania, Pennsylvania*
Rayne Rouce, MD, *Texas Children's Hospital, Texas*

This session will focus on the nuances and issues related to delivering various cell and gene therapy products to patients including shipping, storage, infusion, managing product-related adverse events and reporting.

Learning Objectives:

- To understand the issues related to shipping cell and gene therapy products - Manufacturing Issue.
- To understand the issues related to the storage of cell and gene therapy products-Manufacturing Issue.
- To understand the issues related to infusing of cell and gene therapy products, including routes of administration and monitoring.
- Define adverse event reporting structures: from clinical sites to sponsor and sponsor to FDA.
- Approaching risk mitigation strategies after an unexpected adverse event.

Strategies for Regulatory Success: A Fireside Chat (30 mins)

Peter Marks, MD, PhD, *Center for Biologics Evaluation and Research, FDA, Maryland*

This Regulatory Affairs Case Studies discussion will focus on real-world experiences in developing and interpreting the regulatory requirements for cell and gene therapy. This session will be interactive, and the scholars will have extensive opportunities to ask questions of the faculty with respect to their specific project proposals.

Learning Objectives:

- The concept of holistic product development.
- The importance of forward planning and thinking about how to make a product reproducibly.
- The importance of early and continued discussions with the agency in reducing development time.

Evolving Financial Models for CAR-T and Gene Therapies (30 mins)

Krishna Komanduri, MD, *Helen Diller Family Comprehensive Cancer Center, California*

Learning Objectives:

- Understanding what goes into the actual cost of delivery of a clinical product reimbursement.

Protecting and Licensing Your Technology (30 mins)

Mark Engleka, PhD, The Penn Center for Innovation, University of Pennsylvania, Pennsylvania
Denene Wambach, Esq., University of Pennsylvania, Pennsylvania
Haig Aghajanian, PhD, Co-Founder and Head of Research at Capstan Therapeutics, Pennsylvania

This session will focus on academic/industry partnerships in the cell and gene therapy space, the goals of such partnerships, the transition of cell & gene therapy projects and technology from an academic setting into industry, and the establishment of academic/industry partnerships which facilitate this transition, with a focus on intellectual property and contractual considerations for commercialization. Personal experiences, strategies and lessons learned in making this sometimes challenging transition will be shared. We will also discuss the goals of academic/industry partnerships in the cell and gene therapy space.

Learning Objectives:

- To understand your options for engaging with industry to advance your technology and to fund additional research in your lab to develop new and useful technologies.
- To understand intellectual property and strategies for protecting and maximizing value of your inventions.
- To understand the licensing process for setting up robust relationships with the commercial partners.
- To understand how technology you played a role in developing will be used and commercialized by industry.
- To understand the potential scope of an academic/industry partnership revolving around gene and cell therapy technology (manufacturing, process development, assay development, quality improvement, technology transfer, research and development, etc.).

Hot Topics and Controversies in Cell Therapy (30 mins)

Rayne Rouce, MD, *Texas Children's Hospital, Texas*
Krishna Komanduri, MD, *Helen Diller Family Comprehensive Cancer Center, California*

This session will focus on specific challenges to patient accessibility to cutting edge therapies. While many life saving therapies have been developed in the area of cell and gene therapy of the past decades, patient accessibility remains an obstacle for many agents. In this session we will discuss the root causes of some of these obstacles, how they directly impact specific populations, and highlight innovative potential solutions.

Learning Objectives:

- Describe how insurance coverage practices can impact clinical outcomes in the setting of CAR T cell therapy.
- Understand underutilization and disparities in access (in both trials and post-approval settings).
- Discuss strategies to decrease regulatory burdens for onboarding.
- Describe the potential (and challenges) of decentralized/"home brew" cellular therapy as one solution.