University of Minnesota
Facility Design

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Molecular and Cellular Therapeutics
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Overview

- Facility – 40,000 square feet
- ISO Class Production Clean Rooms – 20
- Total Operational Staff – 37
- Major Therapeutic Product Classes Supported – 4
- 18 INDs (14 internal; 4 external)
- Over 900 products produced annually
- Value of Production - $5MM
Our Mission

To Provide World-Class Development and Production of Therapeutic Products, for University of Minnesota Investigators, external institutions, and start-up firms
Molecular and Cellular Therapeutics (MCT) *Est. 1992*

- Translate basic discovery to clinical trials, across a wide array or therapeutic classes
- Develop and manufacture therapeutic products meeting Good Manufacturing Practices (cGMPs) and current Good Tissue Practices (cGTPs)
- Support Phase I/II/III clinical trials of molecular and advanced cell-, tissue-, gene-based, protein, drug therapies for researchers and external contracts
- Manufacturing Units – Cell Therapy, Protein Production Pancreatic Islet Transplant, and Pharmaceutical Synthesis
Production Capabilities

- Hematopoietic Transplant
- Pancreatic Islet Transplant
- Immunoadoptive Therapies
- Cardiac Repair
- Monoclonal Antibodies/Proteins
- Active Pharmaceutical Ingredients (API)
- Xeno (Porcine) Pancreatic Islet Transplant (1)

(1) - Planned for 2009
Upper Level (10,000 sq ft.)
5500 sq ft Clean Space
Core Activities

- Quality and Compliance
- Operations/Quality/Materials Management
- Control of Critical Systems
- Program Budgets/Forecasts/Cost Accounting
- Business Plan Development
- Project Management
- Equipment Management
- Document Change Control
- Process Development/Qualification/Validation
MCT Organizational Structure

- Scientific Director
  - Dr. John Wagner, MD
- Facility Director
  - Randy Tlachac
- Facility Medical Director
  - Dr. David McKenna, MD
- Director of IND/IDE Assistance Program
  - Harvey Arbit, PhD
- Managers
  - Quality Assurance
  - Facility & Materials
  - Operations
  - Finance
Facilities and Services Attributes

- Limited Access – Electronic Card Key
- Controlled Environment Areas (ISO Class 5 and 7)
  - Single pass, isolated differential air pressure rooms, negative pressure capabilities
- Defined Personnel and Process Flow
  - Product/Process Segregation
- Central Alarm Monitoring Critical Systems
- Materials and Inventory Management
- Equipment
  - Calibration & Preventative maintenance
  - IQ/OQ/PQ
- Document Control
- Product Development
  - Project Management
- Regulatory Oversight and Guidance
  - Facility (Type V) Master File
  - CMC Quality Indices
LOWER LEVEL
7,000 Sq ft Clean Space
University of Minnesota Medical Center, Fairview
Clinical Cell Therapy Laboratory

- Established 1979 in support of the Blood and Marrow Transplant Program at the University of Minnesota. Moved to MCT Facility 1996

- Processes more than 1500 human bone marrow, peripheral blood, umbilical cord blood and tissues annually

- Provide translational development expertise for bringing novel cell engineering techniques from research to clinical applications
UMMC Cell Therapy Lab
Clinical Operations - GTP Production

- 3300 sq ft, separate air handling system
- Unclassified space meets the requirements for Class 100,000
- Clinical production not requiring extensive manipulation.
- Processes: cryopreservation, positive and negative selection.
  - Auto/Allo PB, CB & Bone Marrow
- Closed system processes – products in bags; biological safety cabinets
Production Area Characteristics

- Class 10,000 (ISO 7) Clean Suite
- ISO 5 Biological Safety Cabinets
- Single pass, isolated differential air pressure rooms, negative pressure capabilities
- Terminal HEPA Filtration, 20-70 Air Changes/Hr
- Clean Room surfaces, epoxy liquid flooring coved base, reinforced resinous wall surfacing, and epoxy painted veneer plaster ceilings
Process Flow

- Uni-directional workflow
- Production in biosafety cabinets or within closed systems.
- Personnel and product exit through the degowning rooms.
Environmental Controls

- Sanitization
  - Contract for janitorial services
    (non Class 10,000)
  - Programs cleans production suites

- Environmental Monitoring
  - Weekly surface testing
  - Monthly viable particles
  - Quarterly mold and non-viable particles
GMP Product Manufacturing

- Pancreatic Islet Cells
  - Autologous
  - Allogeneic Phase I/II/III
- Hematopoietic Stem Cells
  - Multipotent stem cells
- Immunoadoptive Therapy
  - Allogeneic Natural Killer Cells
  - T Regulatory Cells
  - Mesenchymal Stem Cells
  - Large Multivalent Immunogen Vaccine
  - Donor Lymphocyte Infusions
- Cardiac Repair
  - BM derived MNC
  - Cardiac derived stem cells
- Monoclonal Antibodies/Proteins