DANA-FARBER CANCER INSTITUTE

HARVARD MEDICAL SCHOOL

Information System Needs of Hospital Based Cell Processing Facility

Cell Therapy Liaison Meeting

September 10, 2009

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History of Cell Manipulation Core Facility @ Dana-Farber Cancer Institute

- 1996 - Established as DFCI Core
  - Located in DFCI
  - Consolidated all clinical cell processing into a single facility
  - Supported DFCI, BWH and Children's Hospital
- 2000 - Established as Core Facility for Dana-Farber/Harvard Cancer Center
  - Support clinical research at all DF/HCC clinical sites

Dana-Farber Cancer Institute

Brigham and Women's Hospital

Children's Hospital Boston

Beth Israel Deaconess Medical Center

Massachusetts General Hospital

Research and Academic Key Interactions

- Joint Program in Transfusion Medicine
  - DFCI, BWH and Children's Hospital Blood Banks
  - Transfusion Medicine Training Program includes MGH and BIDMC
- Center for Human Cell Therapy
  - Support for clinical translation and IND applications for Harvard affiliated investigators
- Harvard Stem Cell Institute
  - Supports development of therapeutic applications of stem cells for various diseases and tissue repair
- DFCI Cancer Vaccine Center
  - Supports development and testing of novel immune therapies for cancer
  - Development of cellular vaccines
  - Development of adoptive cell therapies

Process Volume / Product Type

- Volume
  - Currently supports ~25-30 DF/HCC clinical trials
  - Process ~1200 - 1500 products/year
- Product Types
  - Both PHS Act Section 351 and 361 products
    - Hematopoietic Progenitor Cells
      - FACT accredited laboratory for adult and pediatric stem cell transplant programs at Children's, BWH and DFCI
    - Tumor/Dendritic Cell Vaccines
    - Adoptive Immunotherapy
  - 50% of clinical trials are conducted under IDE/IND (Phase I)
    - Investigator initiated
    - Company sponsored

Regulatory Environment

- FDA
  - Investigational uses of cells and devices
  - cGTP Regulations as of May 25, 2005
- FACT
  - Accreditation of cell processing for both adult and pediatric stem cell transplant programs
- Joint Commission
- DF/HCC Institutional Review Board
- Department of Public Health

CMCF IS Challenges

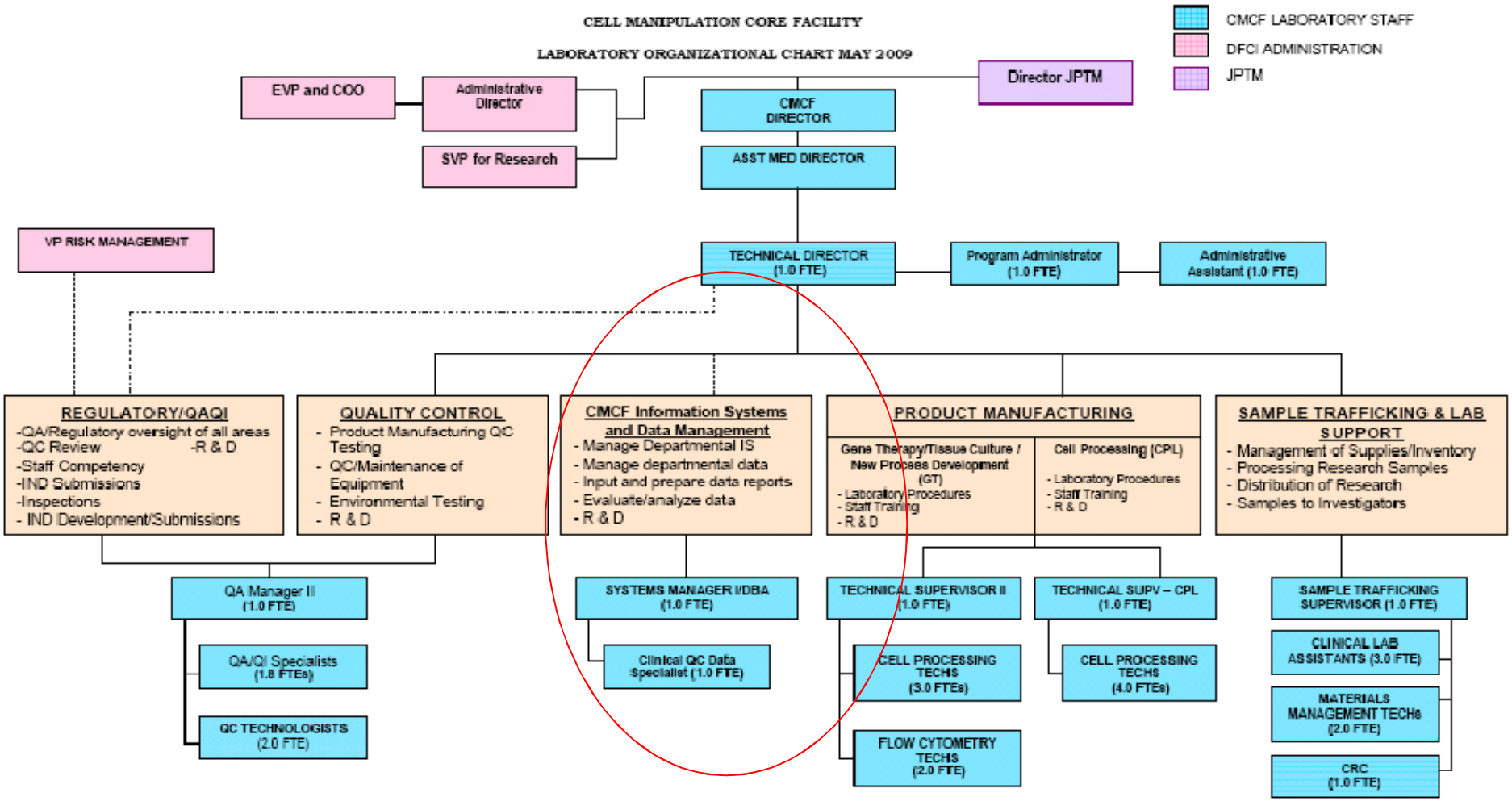
- Academic hospital based cell manufacture site that
  - Is a clean room facility (paperless?)
  - Needs appropriate documentation to comply with multiple regulatory requirements for
    - Product safety
    - Patient safety
  - Produces multiple types of cellular products
    - Simple and complex
    - Genetically modified- viral and non-viral
  - Supports numerous clinical studies with different data capture formats
  - Provide data for IND annual reports
  - Interact with multiple off-site clients
    - Collection
    - Infusion

CMCF Current Operations

- Computer System
  - MISYS (Sunquest)
    - Blood Bank Laboratory System
    - Product Inventory
    - Cell dose data (hematopoietic progenitor cells-related and cryopreserved)
    - Disposition
- Manual Documentation/MS Excel and Access/Filemaker database
  - Physician order for processing and infusion
  - cGTP documentation and checklist
  - cGMP information
    - Manufacture (procedure, data, equipment, cleaning)
    - Material and reagent inventory
    - Environmental
    - QC test results
  - Billing
  - Scheduling
  - Deviations
  - Infusion related adverse events

Current Interactions with other Information Systems

- Clinical Care
  - Chemotherapy Order Entry (COE)
  - Hospital Long-term Medical Record
- Clinical Research
  - QACT (Quality Assurance for Clinical Trials)
    - Documentation of patient consent and enrollment to clinical studies
  - Link to Outcome data
    - DFCI Electronic Data Capture (eDC)
      - Allo and Auto BMT treatment plans, IND and non-IND protocols
      - Provide QA data for transplant service (FACT accreditation)
      - Provide manufacture data for IND annual reports
    - CIBMTR
      - Allo BMT product data
    - Company sponsored clinical protocols


CELL MANIPULATION CORE FACILITY
LABORATORY ORGANIZATIONAL CHART MAY 2009
CMCF LABORATORY STAFF
DFCI ADMINISTRATION
JPTM
EVP and COO
Administrative Director
SVP for Research
Director JPTM
CMCF DIRECTOR
ASST MED DIRECTOR
VP RISK MANAGEMENT
TECHNICAL DIRECTOR (1.0 FTE)
Program Administrator (1.0 FTE)
Administrative Assistant (1.0 FTE)
REGULATORY/QAQI
-QA/Regulatory oversight of all areas
-QC Review -R & D
-Staff Competency
-IND Submissions
-Inspections
- IND Development/Submissions
QUALITY CONTROL
- Product Manufacturing QC Testing
- QC/Maintenance of Equipment
- Environmental Testing
- R & D
CMCF Information Systems and Data Management
- Manage Departmental IS
- Manage departmental data
- Input and prepare data reports
- Evaluate/analyze data
- R & D
PRODUCT MANUFACTURING
Gene Therapy/Tissue Culture / New Process Development (GT)
- Laboratory Procedures
- Staff Training
- R & D
Cell Processing (CPL)
- Laboratory Procedures
- Staff Training
- R & D
SAMPLE TRAFFICKING & LAB SUPPORT
- Management of Supplies/Inventory
- Processing Research Samples
- Distribution of Research
- Samples to Investigators
QA Manager II (1.0 FTE)
QA/QI Specialists (1.8 FTEs)
QC TECHNOLOGISTS (2.0 FTE)
SYSTEMS MANAGER I/DBA (1.0 FTE)
Clinical QC Data Specialist (1.0 FTE)
TECHNICAL SUPERVISOR II (1.0 FTE)
CELL PROCESSING TECHS (3.0 FTEs)
FLOW CYTOMETRY TECHS (2.0 FTE)
TECHNICAL SUPV – CPL (1.0 FTE)
CELL PROCESSING TECHS (4.0 FTEs)
SAMPLE TRAFFICKING SUPERVISOR (1.0 FTE)
CLINICAL LAB ASSISTANTS (3.0 FTE)
MATERIALS MANAGEMENT TECHs (2.0 FTE)
CRC (1.0 FTE)

New CMCF IS Projects

- Electronic Physician Order
  - Biotherapy Order Entry (BOE) System
- Manufacturing Execution System

Biotherapy Order Entry - BOE

- For DFCI/BWH/MGH (Partners) patients only
- Partners IS build and maintenance
- Replace written physician orders
  - Cell Collection
  - Cell Processing
  - Product release and administration
- Link to QACT- Clinical protocol registration
- Develop computerized templates for cellular products dispensed from CMCF
- Develop templates for all cellular therapy treatment regiments and clinical trials

Manufacturing Execution System (MES)

- Build and support by outside vendors
- Requirements
  - Computerized manufacturing record for all cell manufacturing procedures
  - Computerized inventory with bar-coding of all approved reagents and manufacturing components
  - Perform calculations
  - Electronic tracking of reagents, equipments, and products
  - Link clinical information to products
  - Interface with laboratory instruments
  - Interface with other hospital information systems
  - Web-based ordering system (Outside of Partners)
  - Meet and integrate ISBT Label requirements
  - Future 510K licensing

CMCF MES Project Timeline

- 2003- Purchased 1st system but unable to validate due to data lost and stability issues
- 2005- Initiate new search for MES system
  - Obtain consultant
  - Writing systems requirement for Request for Proposal (RFP)
  - Evaluation of RFP and interview vendors
  - Contract negotiation
- 2007- Selected Vendor/signed contract
  - MES used in Pharmaceutical industry
  - System to document “complex” manufacturing procedures
- July 2009- System delivered but awaiting “Sandbox” testing
  - Potential renegotiation
  - Consider another vendor (based on blood banking IS)

MES Projects Obstacles

- Blood Banking based vs. Pharmaceutical manufacture systems
  - Blood Bank based system
    - Good product inventory but not source material inventory
    - Excellent audit history tracking
    - Limited and rigid template builder
    - Ready for new ISBT label
  - Pharmaceutical system
    - Allow flexible template building
    - Excellent cGMP documentation for complex cell manufacturing
    - Difficult to integrate clinical information (considered as customization)
      - Lacking donor-recipient link/tracking/data field
- Batch record reports may not meeting the cell product requirements
- Companies are not Interest in 510K licensing
- Cost- $ 1-2 million (include implementation)

Summary

- There is an urgent need for computerization in cell processing laboratories to ensure product quality and patient safety.
- Integration of necessary clinical information in cell manufacture system is the major obstacle.
- Development of cell manufacture Information System is complex and its investment is expensive.