

PACT

Production Assistance for Cellular Therapies

*PACT - Bench to bedside, cell therapy
manufacturing and facilitating IND submission*

Thursday, November 10, 2011
Robert Lindblad, MD
PACT Coordinating Center (EMMES Corporation)
Rockville, Maryland

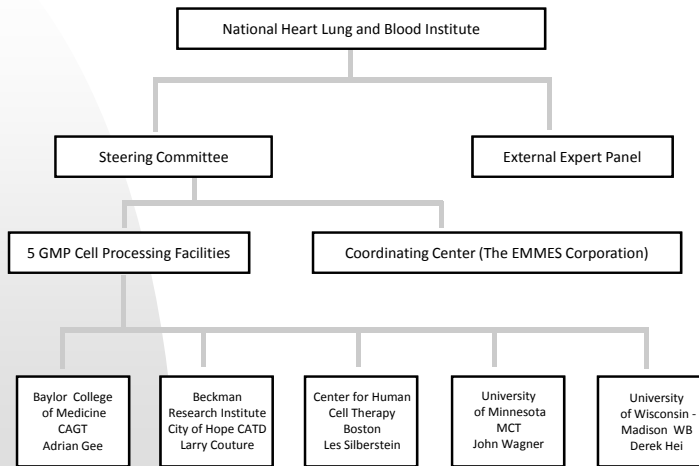
PACT Program

- NHLBI funded initiative
- Began in September 2003
- Renewed in January 2010
- # of facilities, scope, and interest expanded

Objective

Provide assistance with cellular therapy translational research
and the manufacture of cellular therapy products

PACT Organizational Structure



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Application Requests

- Products and Services
 - Products that aid in the repair and regeneration of damaged/diseased tissues, organs, and biologic systems
 - Preclinical/translational studies including animal model work
 - Products of programmatic interest to the Institute and associated with a funded clinical study
 - Proposals possessing procedural advancements to further foster and standardize cell therapies

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NHLBI Scope

- Cardiac repair and disease
- Lung repair and disease
- Complications of malignancy treatment
 - GVHD
 - Post transplant viral infections
- Hematologic disease outside of primary treatment for malignancy



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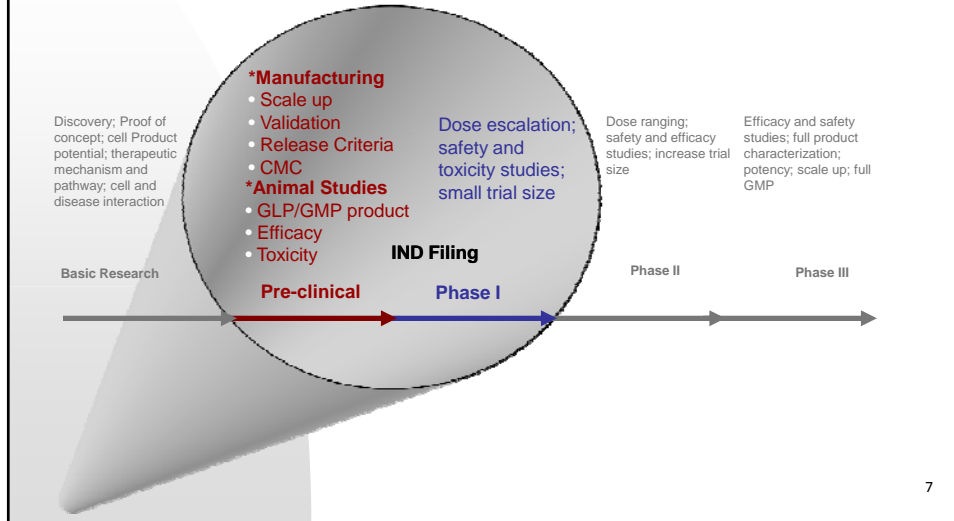
Expanded Interest

- Support for translational work
 - All translational work will be evaluated
- Specific support for GMP translational work not funded through standard NHLBI grant mechanisms



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PACT's Role in Supporting Pre-Clinical Work and Phase I Clinical Trials



PACT Manufacturing Models

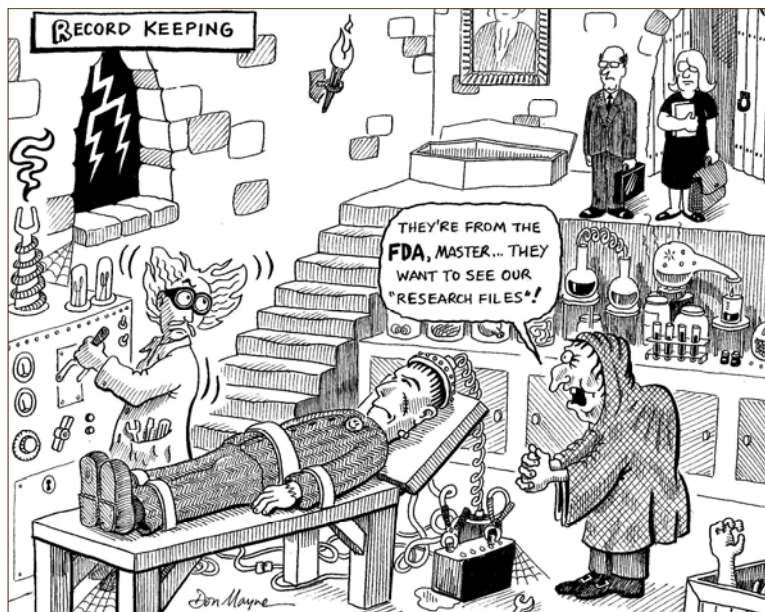
- Centralized Manufacturing
 - Provide single or multiple sites without manufacturing capability with clinical product
- Distributive Manufacturing
 - Manufacturing occurring at multiple sites

PACT Program Status

- 40 ongoing projects
 - 23 - Clinical
 - 12 - Delivering clinical product (cardiac; GVHD; post transplant viral infections; hematological malignancies; X-linked severe combined immunodeficiency [SCID-X1])
 - 17 - Translational (pre-clinical animal studies using hESCs and MSCs for cardiac & lung indications; transduced T cells for Wiskott-Aldridge Syndrome Protein deficiency; stem cells for corneal transplantation)



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PACT and INDs

- Bench to Bedside
 - Process
 - Discovery
 - Animal studies
 - Scale up
 - IND submission
 - Pre-clinical efficacy/toxicity
 - Clinical protocol
 - CMC - manufacturing

Manufacturing and Facilitating IND Submission...

- Pre- Clinical work
 - Provide cells for animal studies
 - Animal models for preclinical studies
- Clinical study protocol development
 - Study product information
- Technology transfer

Manufacturing and Facilitating IND Submission...

- Product development
 - Process Development/Product Scale-Up
 - Product SOPs Development/Batch Records
 - Process/Equipment Validation
 - Product Release Specifications and COA
 - Product Shipping to Clinical Sites

CMC Section Development

- UMN MCT - Shipping Validation
- *Validation of Natural Killer Cell Activation During Long-Distance Shipping*
 - NK cells - prepared from non-mobilized peripheral blood mononuclear cell
 - (MNC) apheresis collections using the Miltenyi CliniMACS® Cell Selection System (CD3+ cell depletion).
 - Cells were incubated in XVIVO 15, without gentamicin and phenol red supplemented with 10% human AB serum (Valley Biomedical) and 1000 U/mL IL-2 in VueLife Teflon bags
 - Temperature stabilizing packs (brought to 33 C) were placed around the product to maintain approximate body temperature within the shipping container.
 - Following round trip flight to Columbus, OH (AirNet), cells were washed and re-suspended prior to QC/lot release testing.
- NK cells can be successfully shipped for use at distant clinical centers

Animal Model Studies

- Indication - Acute Lung Injury
- FDA request
- Pre-clinical animal model work
 - Provided cells for animal studies
 - Allogeneic human mesenchymal stem cells were manufactured by the UMN-MCT



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Animal Model Studies

- Indication - Bronchiolitis Obliterans
- FDA request
- Pre-clinical animal model work
 - Provided cells for animal studies
 - Allogeneic human mesenchymal stem cells were manufactured by the University of Wisconsin-Madison
 - Developed animal model study protocol
 - Development of injured rat model underway
 - Shipping studies underway



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PACT Application Process

- Web based Preliminary Application
- Concept Review by Steering Committee
- Full Application invited (Clinical/Translational)
- Web based Full Application
- Independent Reviews
- Facility and Technical Liaison Assignment
- Budget, Contract & Timeline



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Contact Information

Debbie Wood or Jamie Winestone
Phone: 301-251-1161
Email: pactinfo@pactgroup.net

Website
www.pactgroup.net



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