Production Assistance for Cellular Therapies (PACT)

A National Heart, Lung, and Blood Institute Program
Traci Heath Mondoro
and
Elizabeth L. Wagner
Genesis of PACT

- Immunomodulation workshop in April 2002
- General recommendations to NHLBI
  - Support for GMP-level facilities
  - Training support for investigators to develop experience with regulatory requirements
  - Develop initiatives to solicit basic and clinical research of cell-based therapies

~PACT - September 2003~
NHLBI Requirement for PACT

- Projects using products manufactured by PACT must fall within the programmatic scope of NHLBI for our mission statement:
  

- Applicants should be prepared to justify how their proposed study fits into the areas of interest of NHLBI.
PACT Organization

3 Manufacturing Facilities & 1 Administrative Coordinating Center

Baylor College of Medicine
Center for Cell and Gene Therapy
Houston, TX

University of Minnesota
Molecular and Cellular Therapeutics
Minneapolis, MN

University of Pittsburgh
Cancer Institute
Pittsburgh, PA

The EMMES Corporation
Rockville, MD
Organizational Structure

- NHLBI awards the contract to PACT facilities and Coordinating Center
  - NHLBI project officers are members of the Steering Committee
- Steering Committee formulates and implements all policy decisions related to the conduct of the PACT group
- External Review Panel is advisory to NHLBI and evaluates the goals and progress of the PACT group on a yearly basis
NHLBI Expectations of PACT

- Manufacture a clinical grade product for investigators lacking a cGMP facility
- Foster partnership of transfusion medicine and hematology with cell-based therapy
- Work with the FDA to facilitate translation to clinical studies
- Provide educational leadership in the field of cell therapy
Application Metrics

Preliminary applications received over time by application origin
# Application Metrics

<table>
<thead>
<tr>
<th>Turn-around Interval</th>
<th>Start-up phase (years 1 &amp; 2) median (range)</th>
<th>Operational phase (years 3 &amp; 4) median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decision to applicant on preliminary application</td>
<td>34 days (3-130)</td>
<td>19 days (2-41)</td>
</tr>
<tr>
<td>Receipt of full application by PACT following approval of preliminary application</td>
<td>110 days (35-267)</td>
<td>142 days (14-484)</td>
</tr>
<tr>
<td>Completion of outside peer-review for full application</td>
<td>24 days (2-79)</td>
<td>19 days (4-58)</td>
</tr>
<tr>
<td>Decision returned to applicant on full application following its receipt</td>
<td>88 days (13-201)</td>
<td>55 days (3-145)</td>
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Turn-around intervals (days) associated with the receipt and evaluation of applications to PACT: start-up period compared with post-start up period
Product Manufacturing Status

43 products approved for production

- 6 completed and delivered
- 18 are in the clinical manufacturing phase
  - 8 of which currently administering product
- 5 are in translational development phase
- 10 pending manufacturing commencement
- 4 manufacturing requests withdrawn
PACT Education Committee

- 11 Educational web seminars on various topics conducted
  - 2009 web seminar topics selected

- 3 On-site 1 ½ day GMP workshops conducted
  - Baylor - April 2006
  - Minnesota - April 2007
  - Pittsburgh - May 2008

- General cell therapy resources for public distribution
  - GMP Presentations (publically available at www.pactgroup.net)
  - Facility SOPs (by request)

- Cell Therapy book near completion
# Web Seminars Conducted

<table>
<thead>
<tr>
<th>Date</th>
<th>Topic</th>
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<tbody>
<tr>
<td>03/31/05</td>
<td>Facility Cleaning and Disinfection*</td>
<td>Cell Processing, Validation, and Performance Qualification</td>
<td>Equipment Qualification</td>
</tr>
<tr>
<td>07/14/05</td>
<td>Biological Product Deviation Reporting*</td>
<td>Chemistry, Manufacturing, and Controls Writing for IND Applications</td>
<td>Staff Training and Competency</td>
</tr>
<tr>
<td>01/19/06</td>
<td>Managing Multiple Specimens in a Cell Processing Facility*</td>
<td>Rapid Release Testing</td>
<td>Packaging and Shipping of Human Cell and Tissue Products</td>
</tr>
<tr>
<td>07/20/06</td>
<td>Facility Master Files*</td>
<td>SOP Development</td>
<td>Development and Operation of a QA System for Deviations from SOPs in a Clinical Cell Therapy Laboratory</td>
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<tr>
<td>10/26/06</td>
<td>Cell Therapy Data Management*</td>
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<tr>
<td>02/22/07</td>
<td>Adverse Event Reporting for 351 Products*</td>
<td>Adverse Event Reporting in IND Studies</td>
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<tr>
<td>07/19/07</td>
<td>Interpreting AABB Cellular Therapy Standards*^</td>
<td>Interpreting FACT Cellular Therapy Standards</td>
<td></td>
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<tr>
<td>10/11/07</td>
<td>How to Survive Audits and Inspections*^</td>
<td>FDA Inspection: Preparation, Inspection &amp; Follow up</td>
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<tr>
<td>02/21/08</td>
<td>Cryopreservation of Cell Therapy Products*^</td>
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<tr>
<td>06/25/08</td>
<td>Training and Career Development Grant Opportunities at NIH*</td>
<td>Overview of Cell Therapy in Lung Biology and Disease</td>
<td></td>
</tr>
<tr>
<td>07/31/08</td>
<td>Validation Processes*^</td>
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</tbody>
</table>

* Slide presentations posted to [www.pactgroup.net](http://www.pactgroup.net)

^ Web seminar recording and Q &A session transcription posted to [www.pactgroup.net](http://www.pactgroup.net)
Publications

- Product-related
  - Abstracts - 11
  - Manuscripts - 9

- PACT-related
  - Abstracts - 3
  - Manuscripts - 6

- Recent publications
  - Endosafe® Study manuscript
    - Published in *Cytotherapy & NIH Pub Central* 08/08
  - “PACT Experience” manuscript
    - Submitted to *Transfusion* 7/08
PACT Projects

- Small volume bone marrow cell selection
  - Study completed; data collected; publication pending

- Cell product shipping validation
  - Data being collected
PACT Application Process

- On-Line Preliminary Application
- Concept Review by Steering Committee
- Full Application invited
- On-Line Full Application
- Reviewers & Technical Liaison
- Review Criteria Points to Consider
- Types of Products
- Budget, Contract & Timeline
Preliminary Application

- Concept review
- Product objectives
- Easily completed in a few hours
- Reviewed by PACT Steering Committee
- Response typically provided in a few weeks
  1) Identify areas which represent problems, and/or
  2) Invite full application
Full Application

- Translational or Clinical
- Detailed information for review
- SOPs and validation information
- Identify any financial support for manufacture
- Identify clinical trial support
- Details of amount of product required
- Clinical protocol identifying intended use and safety monitoring plan
- Proposed timeline and budget
Reviewers & Technical Liaison

- External reviewer assigned
- Technical liaison assigned
- Interactive review initiated
- Review requires detailed understanding of technical requirements
- Review sets the stage for product transfer
- Review assesses feasibility at PACT
Review Criteria

- Scientific merit & relevance to NHLBI
- Funding
- Clinical trial design
- Regulatory status
- Availability of expertise at PACT
- Capacity at PACT
- Timeline - on average 66 days from submission of full application to decision
Budget, Contract, and Timeline

- PACT facility budget development
- Interactive process with applicant
- Contract negotiations with designated facility
- Draft contract developed
  - Intellectual property and/or indemnification
- Development of production task order
- Scheduling of manufacturing tasks
- Scheduling of production
New Initiative

*Support for Cell Therapy Clinical Trials*

PACT has implemented a policy to provide matching clinical trial funding up to 150k based on product manufacturing approval, clinical trial funding need and undergoes programmatic review by NHLBI
Website & Contact Information

- Information and application for manufacturing support available through [www.pactgroup.net](http://www.pactgroup.net)
- Details of application process
- FAQ and updates
- Meeting and review dates
- Education web seminars and workshops
- Announcements
- Links to facilities, regulatory & other resources
- Jamie Winestone or Debbie Wood
  
  phone: 301-251-1161
  email: info@pactgroup.net
Funding

The PACT project has been funded in whole or in part with Federal funds from the NHLBI, NIH under Contract Nos.  
N01-HB-37163  
N01-HB-37164  
N01-HB-37165  
N01-HB-37166
Converging Concepts in Cellular Therapy

- April 23-24, 2009
- Natcher Conference Center, NIH Campus
- Initiated by NIH DTM and NHLBI PACT
- Collaborative effort with representatives from ISCT, AABB, and ISBTc
Future Funding

- The PACT program will continue to be funded via a contract mechanism.
- A full and open competition is anticipated for both the ACC and facilities.
- It is anticipated that the services offered by PACT will be broadened in scope.