Production Assistance for Cellular Therapies

Educational Web Seminar

Regulatory Requirements For Clinical Research Protocol Development

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Learning Objectives

- Introduction of clinical research protocol
- Reference to PACT mechanism to explain clinical research
- GLP awareness and compliance: regulations
- Non-Clinical perspective
- How do non-clinical and clinical development influence each other
- Type and timing of non-clinical studies
- Regulatory hurdles faced during development of Cardiac Stem cells

What is a research protocol?

- A detailed plan that sets forth the study:
  - Objectives
  - Aims
  - Design
  - Methodology

Why do we need a research protocol?

- Scientific validity
- Subject safety
- Replicate the science if necessary
- Regulatory requirements

PACT's Mission

- PACT assists translational research community to obtain clinical grade cellular products manufactured under cGMP conditions.
- PACT facilitates transition of laboratory research developments into clinical grade products for use in IND- enabling studies.
- Provides assistance with the manufacturing of cellular therapy products and regulatory expertise to address all aspects of the translational process.

Good Lab Practice (GLP) Awareness & Compliance

- GLP makes sure that the data submitted are a true reflection of the results that are obtained during the study.
- GLP also makes sure that data is traceable.
- Promotes international acceptance of tests.

Food and Drug Administration, 21 CFR part 58 good laboratory practice regulations; final rule. 52 Federal Register, 33,768–33,78

The Fundamental Points of GLP

- **Resources**
  - Organizational Requirements
  - Personnel Requirements
  - Facilities Requirements
  - Equipment Requirements
- **Rules**
  - Protocols
  - SOPs
  - The Study Director

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7

The Fundamental Points of GLP

- **Characterization**
  Knowledge of material and test items used during study e.g.
  - Identity
  - Purity
  - Composition
  - Stability
- **Documentation**
  - Raw Data
  - Study Report
  - Archives

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8

Non-Clinical Perspectives

- Non-clinical studies are conducted to support clinical trials
- Demonstrate safety (Tox studies)
- Model selection: Animal studies must demonstrate that the vaccine is likely to clinically benefit humans.
  - Enable selection of a protective dosage for humans
- Identify a marker of immunity that predicts protection and can be measured in both animals and humans.
  - Mechanism of protection: is it known?
- Pivotal animal studies
  - Demonstrate efficacy
  - Bridge immune responses to human immune responses

How do Non-Clinical and Clinical Development Influence Each Other?

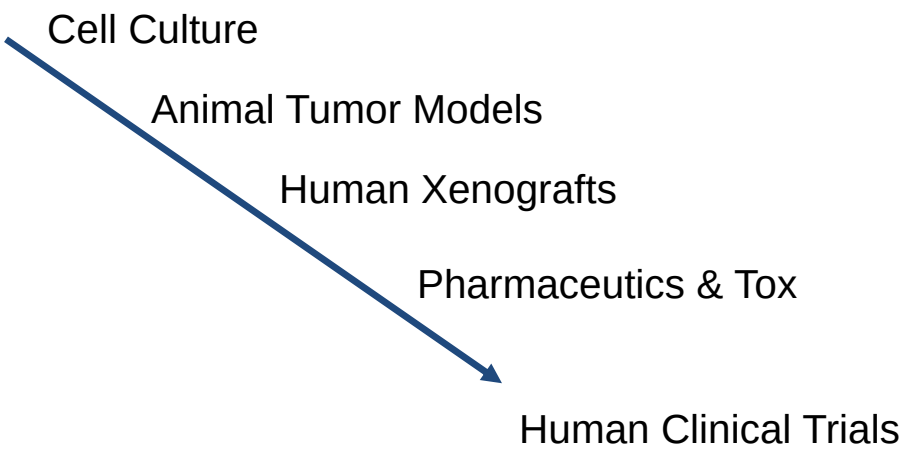
- How do you get from non-clinical studies into the clinic?
- What types of non-clinical studies are needed to continue clinical development?
- What role do non-clinical studies play in clinical trial design?

Non-Clinical Studies M3

- Safety pharmacology
- Pharmacokinetics
- ADME (absorption, distribution, metabolism, elimination)
- General toxicology
- Local Tolerance
- Genotoxicity
- Carcinogenicity
- Reproductive toxicology
- Special studies

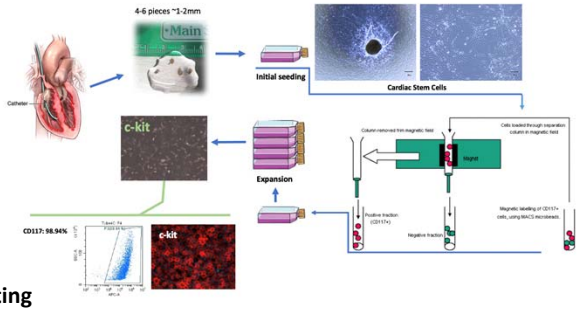
ICH M3 Timing of Nonclinical Safety Studies for the Conduct of Human Clinical Trials for Pharmaceuticals (FDA, 1997).

Pre-Clinical Drug Development



Development of Cardiac Stem Cells – Validations

- Transport of endomyocardial biopsies (EMB)
- Temperature monitoring
- Starting material size and weight
- EMB digestion – enzyme concentration and time optimization
- Culture and expansion
- Magnetic selection
- Culture and expansion
- Cryopreservation
- Storage stability
- Shipping
- Thawing of cells
  Preparation of infusion
- Shelf life testing
- Administration device testing



I have great idea & strategy but do I have…….

- The <u>appropriate</u> patient population
- Collaborating within and interdisciplinary faculty
- Facilities/Cores to conduct the study
- Supportive clinical staff
- Time/administrative buy in
- Funding
- Legal/contractual issues


Thank you