Temple Clinical Research Institute

TEMPLE UNIVERSITY

Lewis Katz School of Medicine

Temple Clinical Research Institute (TCRI)

Introduction to Clinical Research Funding and Regulations

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Topics

- Overview of Regulations
- Institutional Review Board (IRB)
- HIPAA and Research
- Types of studies and Funding
- TCRI Services
- Compliance Tips

Definitions

Clinical Research: includes all research involving human participants. It does not include secondary studies using existing biological specimens or data collected without identifiers or data that are publicly available.

Clinical Trial: a clinical research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.

Human Subject: a living individual about whom an investigator conducting research obtains 1) data through intervention or interaction with the individual, or 2) identifiable private information.

Why is clinical research regulated?

- Protect participants
- Assure valid data
- Safe & effective
- Prevent & detect fraud & abuse
- Increase transparency

U.S. Regulatory Agencies

Federal Agency	What they do
Department of Health & Human Services (DHHS) - Office for Human Research Protections (OHRP)	Regulates IRBs, promotes human subject protection, oversees federally-funded research
Food and Drug Administration (FDA)	Regulates research testing products under FDA's authority
National Institutes of Health (NIH)	Primary U.S. medical research agency
Office for Civil Rights (OCR)	Enforces HIPAA
Centers for Medicare & Medicaid (CMS)	Clinical trial billing; NCD 310.1
Office of Research Integrity (ORI)	Investigates research misconduct
Dept. of Justice- Office of the Inspector General (DOJ/ OIG)	Investigates & prosecutes fraud, abuse & research misconduct, Sets annual OIG work plan

Which Regulations Apply to My Study?

- Living Human Subjects (HHS/OHRP)
- Identifiable health information (HIPAA)
- FDA-regulated products (FDA)
- Controlled substances (DEA)
- Services billed to Medicare (CMS)
- Federally funded (NIH)

….and more

Human Subject Protection

The Institutional Review Board (IRB) is a committee that carries out the regulations set forth by OHRP and FDA for the protection of human subjects. The IRB assures compliance with:

45CFR46 - OHRP “The Common Rule”

21CFR50, 56, 312, 812 – FDA

ICH E6 GCPs – Unified scientific quality standard for international clinical trials (not a regulatory requirement for U.S. trials)

Human Subject Protection

The IRB reviews and approves clinical research studies to assure that:

- Participants' rights are protected
- Minimize risks
- Informed consent
- Voluntary participation

HIPAA and Research

- Special rules for research
- Protected Health Information (PHI)= any info about health status, provision of health care, or payment for health care created or collected by a Covered Entity (CE) that can be linked to an individual
- Overseen by the organization's privacy board
- HIPAA Authorization vs. Informed consent for research
- HIPAA Waivers

  - Limited Data Set (dates, city/state, age)

  - For Recruitment

  - Preparatory to Research

18 HIPAA Identifiers

• Name	• Certificate/license number
• Address	• VIN; license plate number
• Dates (DOB, admission, discharge, death)	• Device ID or serial number
• Phone numbers	• URL
• Fax numbers	• Biometric ID- finger or voice prints
• Email addresses	• Full face photographs
• SSN	• Internet Protocol (IP) address
• Medical record number (MRN)	• Account number
• Health plan number	• Any other unique identifier

Types of Clinical Research Studies

- Retrospective vs. Prospective
- Interventional vs Observational
- Drug (phase I-III, phase IV)
- Device
- Treatment (behavioral, medical)
- Industry-initiated vs. Investigator-initiated
- Funded vs. Unfunded

Industry – Initiated

- Usually multi-site
- Temple is one of many sites, one PI
- Sponsor creates protocol and study forms
- Sponsor pays Temple for research tests & staff
- Sponsor obtains FDA approval (IND/IDE)
- Sponsor registers study on Clinicaltrials.gov
- Site enrolls, collects data, submits to Sponsor
- Sponsor submits data to FDA for marketing approval

Investigator- Initiated

- Can be single or multi-site
- PI writes protocol and study documents
- Can be unfunded or funded (NIH/profess. org.)
- Temple is the sponsor
- PI obtains FDA approval (IND/IDE)
- PI registers study on Clinicaltrials.gov
- PI enrolls, collects, analyzes data, publishes
- Collaborations may require a DUA or contract

Contract/Budget

1. Confidential Disclosure Agreement (CDA)
2. Contract, Budget and Protocol
    i. Budget Assessment Form
    ii. Device Assessment Form (if applicable)
    iii. Pharmacy
    iv. Conflict of Interest
    v. IRB approval

    Federal, Private or Foundation – usually can not negotiate the budget

National Institutes of Health

- Agency of DHHS
- 27 Institutes and Centers
- Research funded by Congress
- Nation’s foremost research agency
- Provides funding for research nationally and internationally

National Institutes of Health

- Parent Announcements (PA) = unsolicited IITs
- Requests for Applications (RFAs) = solicited, focused topics for research protocol
- Career Development (K), Research Training (T), Research (R)
- Significant dates= application due date(s), scientific merit review, advisory council review, earliest start date
- Ex: application (Jan), SMR (July), ACR (Aug), Start (Dec)
- Contact your research administrator for more information

Drug Trials – Phase I - IV

	Phase	Purpose	Sample Size
PRE-MARKET (IND)	**I**	First time in humans; Establish maximum tolerable dose and side effects	Small N (<100)
	II	Provide additional safety data	Larger N (100's)
	III	Compare treatments, confirm effectiveness for specific populations	Large N (1000's)
	IV	**Post-market**; collect additional data on safety and effectiveness	Several 1000's

Investigational New Drug Application (IND)
Phase I – III trials

- A request for authorization from the FDA to administer an investigational drug or biological product to humans.
- Drug manufacturers apply for an IND in order to test a new drug in humans with the intention of bringing the new drug to market or to test an approved drug for a new indication or patient population.
- Investigators may need to apply for a research IND to study a drug off-label (or if not FDA-approved) in a clinical investigation unless criteria for exemption are met.

Device Trials and Investigational Device Exemptions (IDE)

- The device counterpart to the drug IND
- IDE Holder must comply with 21CFR812 regulations
- Device manufacturers test new devices under an IDE to collect safety and effectiveness data in order to obtain FDA approval, or to test a marketed device for a new indication.
- An IDE allows a clinical investigator to study a significant risk device off-label.
- Post-market trials gather additional safety data in the “real-world” setting.
- Humanitarian Use Devices (HUD) - not research but require IRB approval

ClinicalTrials.Gov

- Online clinical trial registry and results database established in 1997 by the FDA Modernization Act (FDAMA/ FDAAA801)
- Public access to information about current and completed clinical trials
- Supported by the National Library of Medicine and the NIH
- Access at: www.clinicaltrials.gov

ClinicalTrials.gov
A service of the U.S. National Institutes of Health
Developed by the National Library of Medicine

ClinicalTrials.Gov

"Applicable Clinical Trials" are required by law to register and post results.

- Trials of drugs and biological products subject to FDA regulations; controlled clinical investigations other than Phase I trials
- Trials of devices including controlled trials of devices with health outcomes
- Some journals require registration as a condition for consideration for publication
- Sponsor is responsible for registering trial

TCRI Services

- **Clinical Research Administration (CRA)**
  - Confidential Disclosure Agreements (CDA)
  - Negotiate contracts, budgets, amendments
  - Handle check deposits
  - Start-up and IRB invoicing
  - Closeout the financial end of the clinical research study

- **Clinical Research Operations & Regulatory Affairs (CRORA)**
  - regulatory guidance
  - operational support
  - clinicaltrials.gov site administrator
- Biostatisticians (DCS)

Stay Compliant

DO

- Complete required trainings before starting your research
- Obtain approval from IRB before starting research
- Execute a CDA before seeking funding from outside agency
- Comply with HIPAA to protect patient data

DON'T

- Do Not sign any paperwork on behalf of the institution
- Do Not share data without written approvals and/or DUA
- Do Not access PHI for research without IRB approval and HIPAA authorization or waiver
- Do Not access or view patient data in public spaces

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