Clinical & Translational Research, “What is it and Why Should I Care?”

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What is Clinical Research?
“Human subject” means a living individual about whom an investigator (whether professional or student) conducting research obtains:

1) data through intervention (physical procedures or manipulations of the subject or their environment) or interaction with the individual,

or

2) identifiable private information
Let me ask you a personal question:

How many of you know someone who has cancer or had cancer?

Does anyone know what role MSU has played in helping people with cancer?
In 1978, Barnett Rosenberg and coworkers at Michigan State University discovered that certain platinum-containing compounds inhibited cell division and cured solid tumors resulting from cancer.

This discovery led to “cisplatin” a chemotherapy drug, approved by the FDA in 1978. Cisplatin was the first platinum-compound chemotherapy developed.

1989, MSU developed a second chemotherapy cancer drug, Carboplatin.

Carboplatin vastly reduced side-effects compared to its parent compound cisplatin.
Many people’s lives have been saved as a result of these drugs being developed by MSU.

Michigan State has collected over $160 million in royalties from cisplatin and carboplatin.

These royalties have been used to support other research grants through the MSU Foundation.
What is Clinical Research (NIH)?

• **Patient-oriented research:** Involves a particular person or group of people or uses materials from humans. Examples of types for cancer:
  - Studies of mechanisms of human disease (how cancer causes illness, what causes cancer)
  - Studies of therapies or interventions for disease (cancer disease or cancer symptom treatments)
  - *Clinical trials* (cancer drugs)
  - Studies to develop new technology related to disease (cancer diagnosis techniques)

• **Epidemiological and behavioral studies:** Examine the distribution of disease, the factors that affect health, and how people make health-related decisions. *(Social, environmental, health decision trends and cancer development)*

• **Outcomes & health services research:** These studies seek to identify the most effective and most efficient interventions, treatments, and services. *(analysis of health policies, and cancer prevention and support programs)*
A clinical study involves research using human volunteers (also called participants) that is intended to add to medical knowledge. There are two main types of clinical studies: clinical trials (also called interventional studies) and observational studies. ClinicalTrials.gov includes both interventional and observational studies.
A clinical trial is a type of clinical research in which participants are assigned to receive one or more interventions (or no intervention) so that researchers can evaluate the effects of the interventions on biomedical or health-related outcomes. The assignments are determined by the study protocol.
Investigation: Any experiment that involves a test article and one or more human subjects, and meets certain requirements of the FDA regarding submission\(^1\).

Test Article: Any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation\(^2\) subject to specific regulations. Includes drugs (including botanicals, biologicals, and gene therapy, and genetically derived products that meet the definition of a “drug”), and medical devices for human use.

\(^1\) Food and Drug Administration under section 505(i) or 520(g)
\(^2\) Sections 351 and 354-360F of the Public Health Service Act (42 U.S.C. 262 and 263b-263n)
For clinical investigations or research involving devices, the definition of “subject” includes the use of specimens, even if the specimen is unidentified. While such research is not considered “human subjects” under the DHHS regulations, such research would be considered “subjects” under the FDA regulation for certain types of research.
Types of Clinical Trials (FDA)

**Treatment trials** test new treatments, new combinations of drugs, or new approaches to surgery or radiation therapy. (Cisplatin, carboplatin, radiation treatments for cancer)

**Prevention trials** look for better ways to prevent disease in people who have never had the disease or to prevent a disease from returning. These approaches may include medicines, vaccines, vitamins, minerals, or lifestyle changes. (Lifestyle and dietary changes to prevent cancer; flu vaccines to prevent the flu)

**Diagnostic trials** are conducted to find better tests or procedures for diagnosing a particular disease or condition. (Cancer early diagnosis methods so early treatment can be most effective)

**Screening trials** test the best way to detect certain diseases or health conditions. (Identifying those at risk prior to development of cancer; genetic testing for cancer genes)

**Quality of Life trials** (or Supportive Care trials) explore ways to improve comfort and the quality of life for individuals with a chronic illness. (Treatment and management of pain resulting from cancer)
Sponsor-Initiated vs. Investigator-Initiated

- Sponsor-initiated is defined as an individual or agency who initiates and takes responsibility for the research. The sponsor does not actually conduct the investigation (e.g. MSU is paid for providing services, but has no direct input on or influence over the research design or protocol). (Pharmaceutical company asks MSU physician to enroll subjects in the company’s cancer clinical trial)

- Investigator-initiated is an individual who both initiates and conducts an investigation, and assumes all of the sponsor responsibilities defined in the regulations. (MSU investigator has cancer study idea, asks for funding in support of this research)

  - If study is investigator-initiated, the requirements include both those applicable to the investigator and a sponsor.
New Drug Development Timeline

Pre-Clinical Testing, Research and Development
- Initial Synthesis
  - Range: 1-3 years
    - Avg.: 18 mos.
- Animal testing
  - Range: 2-10 years
    - Avg.: 5 years

Clinical Research and Development
- Phase 1
  - Range: 2 mos.–7 years
    - Avg.: 24 mos.
- Phase 2
- Phase 3
  - Range: 2 mos.–7 years
    - Avg.: 24 mos.

NDA Review
- NDA Submitted
- NDA Approved
- Range: 2 mos.–7 years
  - Avg.: 5 years

Post-Marketing Surveillance
- Adverse Event Reporting
- Surveys/Sampling/Testing
- Inspections

30 Day Safety Review

FDA Time

Sponsor Time
What is Translational Research?

The act of transitioning knowledge from one venue to another:

Bench $\rightarrow$ Bedside
What and Who are Involved In Clinical Research?

- Principal Investigators
- Sub-Investigators
- Ancillary Services
- Study Staff (Coordinators, Nurses, Data Managers)
- Administration (Contracts, Budget & Billing)
- Other Compliance staff (IRB, Human Subjects Liaisons)

The Process
High Level Process Overview of Clinical Research

Decision to Pursue
- Confidential Disclosure Agreement (CDA)
- Protocol Feasibility

Study Closeout

Study Pre-Award
- Parallel Processes
- Budget Preparation
- Clinical Trial Agreements and Negotiation
- Regulatory Reviews

Study Start-Up and Management
- Financial
- Contractual
- Regulatory
Protocol Feasibility Overview

• Clinical Research is a BUSINESS and must be run accordingly!
  - Involves money, regulation
  - Doing it right means more business
  - Doing it wrong means out of business
    • Legal, regulatory, financial ramifications

• A Business best achieves goals by starting with a STRATEGIC PLAN
  - Why are you in the business of clinical research?
  - What is your market?
  - What are your research fixed operating costs, and how will you fund them through clinical research?
  - How will you attract and retain high-quality staff?
Feasibility Overview
(i.e. Project/Needs Assessment)

- Know your subject base and have recruitment plans
  - Payment is generally based on completed subject visits
- Be aware of project logistics and your available resources
  - Labor needs (study coordination, financial management, PI)
  - Space, equipment, service needs
- Be aware of financial obligations of the study
  - Labor costs
  - Equipment or test costs, other fees
  - Subcontracts
- Use of business tools
  - Operational Budgets
  - Project Budget Templates
  - Break-Even Analysis
  - Clinical Research Management Systems
• Study Effort/Personnel Costs
• Upfront/Start Up Costs
• IRB fees
• Per subject (variable) costs
  - pharmacy, imaging, labs, regulatory prep and amendment fees, Safety report review fees, supplies, record archiving

• Ongoing Administration Expenses
• Facilities and Administrative Costs (F&A) assessed on all items except IRB fees
Simultaneous Institutional Evaluation (Pre-Award)

Department / College Approvals

- Budget Review, Negotiation & Coverage Analysis
- Contract Review by Appropriate Office
- Submit IRB Application
- Additional Required Reviews?

Obtain All Needed Institutional Reviews &/or Approvals, CGA Account Setup, & Notify All Parties
Clinical Research Billing Compliance (CRBC) Office within the Office of Regulatory Affairs

• They Conduct required prospective Medicare Coverage Analysis
• They Develop detailed study budgets for clinical research studies generating billable events (billing compliance plan)
• They Negotiate budgets directly w/ Sponsors and Clinical Research Organizations (CRO’s) to ensure

  ✓ Initial sponsor budget often does not cover internal study budget expenses
    ▪ Sponsors culture is profit-oriented, offering the lowest budget possible
  ✓ MSU as a non-profit cannot subsidize for-profit entities because it jeopardizes our tax status

• They Review informed consent cost language, and review & negotiate payment terms and obtain local Medicare Administrative Contractors approval if needed
Who Processes Agreements at MSU

- All **Industrial Sponsored** Clinical Trials & Research Agreements are handled by **MSU Business Connect**, Randy Sheets

- All **Federally Sponsored or Non-Profits** Clinical Trials & Research Agreements are handled by the **Office of Sponsored Programs**, Fred Salas

- Appropriate application of the clinical trial F&A cost rate
  - 26% of direct costs for Industrial Sponsored clinical research
  - 53.5% for federally sponsored investigator-initiated research
Financial Management

• Post-Award
  - Track sponsor payments; review for accuracy
  - Invoicing sponsor for line items
  - Payables to service providers per billing compliance plan
  - Labor distributions & effort reporting
  - Study subject stipends and 1099
  - Subrecipient Monitoring

• Close Out
  - Study closeout of finances
Vice President for Research & Graduate Studies

Clinical & Translational Sciences Institute (CTSI)

Biomedical Research Informatics Core (BRIC)
- Research Collaboration
- Data Mgt. & Informatics, Access to Software Tools & Data Security
- Data oversight throughout study lifecycle

Develop New Opportunities With Research Partners

Office of Clinical Research (OCR)
- Biologic Sample Collection & Processing
- Subject Recruitment & Retention Strategies
- Research Process Navigation Project Feasibility / Needs Assessment
- Post Award Financial & Invoicing Support
- Access to Clinical Research Personnel & Facilities
- Access to Clinical & Translational Sciences Institute (CTSI) Biomedical Research Informatics Core (BRIC)
- Office of Clinical Research (OCR)
Current CTSI projects:
visit us at ctsi.msu.edu
Office of Clinical Research (OCR):

Assists research investigators with the development, implementation, management, and completion of clinical research conducted at MSU and through its community partner network.

Project feasibility
- Research subject availability
- Resource needs assessment

Study logistics & management support
- Research process navigation
- Connection to internal & external resources
- Subject remuneration processes

Recruitment & retention
- Recruitment & retention strategies
- ResearchMatch & other social networking resources
Post award management consultation

- Payment receipt & tracking assistance for per-patient & milestone payments
- Processes for paying external entities
- Internal payment allocation per initial cost projections

Clinical research space & personnel

- Study coordination
- Research exam rooms, laboratory equipment
- Biological sample collection, processing, shipping
Biomedical Research Informatics Core (BRIC):

Provides research data management services to clinical research studies.

**Research collaboration**
- Data collection consultation
- Utilize best practice guidelines for defining variables
- Address evolving technical requirements
- Help investigators comply with CFR 21 Part 11

**Data oversight throughout study lifecycle**
- Database Creation
- Testing electronic versions of your study instruments
- Ongoing surveillance of data quality & reporting
- Prepare data for analysis
Software solutions
- Web-based Data collection software (REDCap, OpenClinica)
- Mobile & offline options
- Tailor existing software to streamline study workflow
- Create novel software

Data Security & Storage
- Live data stored on encrypted redundant backup drives
- Redundant power sources to protect against power service interruptions
- Servers housed in HIPPA - Class security facility
Clinical and Translational Sciences Institute

Funding

Clinical and Translational Research (internal funding)
CTSI Pilot Project/Seed Grant Program - Funding is Available for pilot clinical and translational projects. Applications accepted at anytime.

MSU/Sparrow Center for Innovation and Research
Spring 2015 Letter of Intent Announcement for Center for Innovation and Research – Research Support and Translation Support. Call due date: January 14, 2015 by 5:00 p.m.

SciVal Funding
SciVal® Funding is a subscription service provided to the MSU research community to help faculty identify funding opportunities based on specific terms and criteria. Faculty profiles in the MSU Scholars database can be linked to the SciVal Funding tool to allow faculty to set up automatic alerts of funding opportunities that match their expertise.

MSU Office of the Vice President for Research and Graduate Studies (VPRGS)
The office facilitates and expands scholarship, research and economic development by providing leadership, resources, coordination, oversight and innovation. View their Funding Opportunities Database.

NIH Funding
The NIH Guide for Grants and Contracts is the official publication of the NIH.
Tools available for Researchers

**MSU Scholars**
Use the MSU Scholars site to search for expertise, identify research opportunities, and facilitate collaborations. [read more...]

**Search for MSU Core facilities and services via eagle-i**
eagle-i allows MSU researchers to discover needed core laboratory services, reagents, animals, specimens, etc. that are available on campus and nationally. Secondly, it allows us to expose our own resources to external researchers who need them. [read more...]

**ResearchMatch**
ResearchMatch is a national recruitment registry that brings together researchers and people who are interested to learn more about research studies via a secure website. Researchers at Michigan State University and its affiliates can use this tool for feasibility assessment and recruiting. [read more...]

**REDCap**
REDCap is a secure web application for building and managing online surveys and databases. BRIC adds additional custom functionality through REDCap's plugin system; for example, expanding the output of available real-time reports, and automating email activity reminders. [read more...]

**Great Lakes Research into Practice Network (GRIN)**

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**Events & Workshops**

- Interactive Workshop - Getting to Know PCORI: From Application to Closeout
  - Thu, 02/19/2015 - Fri, 02/20/2015
  - Thu, 05/07/2015

- Technology and Aging?
  - Thu, 02/19/2015

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**Announcements**

- CBPR Partnership Academy: Call for Applications
  - The Detroit Urban Research Center is pleased to announce the Community-Based Participatory Research (CBPR) Partnership Academy, a nationwide...
CTSI Tools & Resources

- **ResearchMatch** - National Online participant registry that brings together researchers and people interested in research participation via a secure website.

- **Eagle-i** - National resource discovery platform; search for MSU core laboratory services, reagents, animals, specimens, etc. as well as those available across the country.

- **REDCap** - A secure web application for building and managing online surveys and databases.

- **Clinical research staffing for hire**

- **CTSpedia** - A knowledge base for clinical and translational research; collection of wisdom, tools, educational materials useful to clinical and translational researchers.

For more information, please go to [CTSI.msu.edu](http://CTSI.msu.edu)
What is ResearchMatch?

• A secure place for volunteers and researchers to get connected.

• simple goal - to bring together two groups of people who are looking for one another: (1) people who are trying to find research studies, and (2) researchers who are looking for people to participate in their studies.

• Once you sign up and get added to our registry, a researcher will contact you if they think you’ll be a good match for their research study.
What is ResearchMatch?

• A free and secure disease-neutral registry developed by major academic research institutions across the country with the mission of helping today’s research studies make a difference for everyone’s health

• A complementary recruitment tool to help address the problem of research studies ending too soon because of a lack of volunteers

• A way for volunteers of any age, race, ethnicity, or health status to indicate their interest in participating in research

• Sponsored by the NIH National Center for Advancing Translational Sciences (NCATS)
What is ResearchMatch?

- 102 participating institutions
- 38 partnering organizations
- Over 71,600 volunteers
- 900 in Michigan

What is eagle-i?

MSU-CTSI has recently joined the eagle-i network for resource discovery. Joining eagle-i offers multiple benefits for MSU.

- First, it allows our own MSU researchers to discover needed core laboratory services, reagents, animals, specimens, etc. that are available locally and nationally.

- Secondly, it allows us to expose our own resources to external researchers who need them.
Below you'll find links to summary lists of participating resource providers at this institution and other useful links. The summary lists are linked to more detailed information, but many users may prefer to use the search application for a more interactive experience.

Resource Provider Summary Lists:
- View only Core Laboratories
- View only Laboratories
- View All Resource Providers

Useful Links:
- SWEET (data entry tool, login required)
- eagle-i project technical documentation and source code
- Public SPARQL Endpoint
- List of all Resource eagle-i IDs in this Institution

This institution proudly participates in the eagle-i Network. Use the search bar above to search more than 50,000 biomedical research resources currently listed in eagle-i from 25 institutions. Not sure what you're looking for? Choose "Browse Resources" at the top of the page to see organisms, instruments, reagents, services and more.

To learn more about the eagle-i Network, resources and institutions, please visit www.eagle-i.net.
Refine Your Search

Resource Location

All Institutions
Show only resources in core laboratories

Resource Type

All Resource Types
Database (1)
Instrument (33)
Organism or Virus (2)
Protocol (17)
Reagent (36)
Service (90)
Software (32)
Core Laboratories (35)

Results in the eagle-i Network

"proteomics"[X]

1 - 10 of 322

Show: 10 Results per Page
Sort by: Highest Relevance

Proteomics analysis service

...Related Technique: Protein expression profiling...Resource Description: The Proteomics Core will provide a comprehensive array of services pertaining to the design, performance and analysis of proteomic studies. The core not only offers the ability to implement...

Type: Material analysis service - Service
Location: Harvard University - BIDMC Genomics, Proteomics, Bioinformatics and Systems Biology Center

Proteomics analysis service

...Related Technique: Protein expression profiling...Resource Description: Proteomics analysis services include: • protein identification • protein mass measurement • protein quantitation • modification site mapping (phosphorylation)...

Type: Material analysis service - Service
Location: University of Pennsylvania - Proteomics and Systems Biology Core (Penn)

Proteomics Overview

...Uses: Protein expression profiling...Resource Description: An overview of mass spectrometry based proteomics...

Type: Protocol - Document
Location: Oregon Health and Science University - Proteomics Shared Resource Core Laboratory

Proteomics services

Resource Description: Protein isolation, blotting and hybridization, Western blotting, immunoblotting and immunoprecipitation, protein determination assays, microsome preparation, amino acid analysis, column........Related Technique: Protein expression profiling...

Type: Material analysis service - Service
Location: Jackson State University - Molecular and Cellular Biology Core Laboratory

Proteomics methods development


Questions?