Principal Investigator Support Services for Clinical Research

INSTITUTIONAL RESOURCES

LINDA L. BEEKMAN, RN, MBA
CTO ADMINISTRATIVE DIRECTOR

&

CTO LEADERSHIP TEAM

University of Michigan Comprehensive Cancer Center
CTO Support Services

- CTO is a centralized core to support clinical research conducted by investigators at UMCCC
- Types of studies conducted in the CTO
  - Investigator Initiated
  - Peer-reviewed
  - NCI-CTEP
  - Cooperative Group
  - Industry sponsored
CTO Support Services

- Data Management
- Regulatory
- Finance
- Research Specimen Processing
- Multi-site Project Management
- Information Technology
- Training and Education for
  - All CTO Staff
  - Research Nurse and Coordinators
  - Specimen Processing/Shipping Staff
Investigator Interactions with Regulatory Affairs

KATE ERNSTING
REGULATORY SPECIALIST
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University of Michigan Comprehensive Cancer Center
Regulatory Support

- Role of the Regulatory Specialist
- Regulatory Structure in the CTO
- Requirements to become an Investigator
- eResearch Application – Accepting your role
- Communication of study changes
- UMclinicalstudies.org
New Application Review & Approval Process

- PI submits study
  - Cancer Center Program Director
  - Cancer Center Protocol Review Committee
  - Study Team completes application and PI submits study
  - Concurrent Ancillary Committee Reviews
    - BEU
    - COI
    - IBC
    - IDS
    - RDRC/SHUR
    - TPS

Only sections 1 thru 3-2 are required for Cancer Center Reviews. Only Cancer Center Studies go for Cancer Center Reviews.

- MCRU
- IRBMED
- Study Team conducts research
  - Amendments submitted for all changes prior to implementation
  - AEs/ORIOs reported
  - Continuation Review submitted for study renewal prior to IRB approval expiration or at termination

Application skips over committees that are not required for a particular study

CRAO Office will contact studies that require Billing Plan approval
Amendment Review Process

1. **PI/Study Coordinator**
   - Submits application for research

2. **Cancer Center Program Director/Protocol Review Committee (CCPD/PRC)**
   - If applicable, the application is routed to the CCPD/PRC for review and approval

3. **Ancillary Committees**
   - The application is routed to all applicable Ancillary Committees.
   - The committee members review and approve relevant sections of the application.
   - Changes requested from study team, if necessary

4. **General Clinical Research Center (GCRC)**
   - If applicable, the application is routed to the GCRC for review and approval

5. **IRB Committee Members**
   - IRB Staff
   - The IRB Staff manages the review process using eResearch.
   - The IRB Committees review applications and provide approval.
   - Committee decisions are recorded and stored in eResearch by IRB Staff.

6. **PI/Study Coordinator**
   - Conduct research
   - Report adverse events
   - Submit requests for continuing review
   - Submit amendments

Abbreviations:
- RDRC/SHUR: Radioactive Drug Research Committee/Sub-Committee on Human Use of Radioisotopes
- IBC: Institutional Biosafety Committee
- COI: Conflict of Interest
- TPS: Tissue Procurement Service
- IDS: Investigational Drug Service
- BEU: Biomedical Engineering Unit
Documenting the Consent Process

- All Investigators are responsible for documenting the consent process

- WHERE: CareWeb or MiChart/Epic
  - Consented presented to patient
  - Treatment, side effects, benefits and risks explained
  - All questions answered
  - Patient verbalized understanding
  - Copy of signed consent given to patient
Regulatory Support for Clinicaltrials.gov

Website: clinicaltrials.gov

Regulatory will assist with:

- Registry of Investigator Initiated Studies to NCI website
- Posting the study results:
  September 2008, the ClinicalTrials.gov Results Database allows data providers to report summary results of registered clinical trials and observational studies. Results are reported in a standard, tabular format.
- Abstract & details of the data needed to complete the database
- PIs ARE RESPONSIBLE FOR CONFIRMING AND RELEASING DATA PUT INTO THE NCI DATABASE
Principal Investigator Interactions with CTO Data Management

CINDY REKOWSKI, BS
SOLID TUMOR MANAGER
CREKOWSK@MED.UMICH.EDU,
734.232.0753

University of Michigan Comprehensive Cancer Center
If you are Principal Investigator (PI) for a study, CTO Data Management (DM) will assist with the following:

- Pre-Site/Site Qualification questionnaire completion and visits
  - DM will fill in as much of Site Questionnaire as possible and coordinate completion with relevant departments – IDS, Regulatory and PI
  - DM will schedule and coordinate a site qualification visit with the sponsor to include:
    - Tour of facilities, meetings with PI, review of CTO policies
CTO Data Management

- Feasibility Meeting (review of Feasibility Checklist Handout)
  - CTO Feasibility meeting is triggered by new study appearing on Protocol Review Committee (PRC) meeting schedule
    - DM will review protocol, direct questions to PI as needed such as: expected duration of treatment in study population, number of patients anticipated for accrual, other questions as needed.
    - DM will present study at CTO feasibility to work with finance, clinical teams and regulatory to address logistical issues prior to IRB application
CTO Feasibility Meetings

- **What?** Early discussion of the protocol
- **When?** Triggered by completion of initial study submission in eResearch
- **Who?** Data management, regulatory, research nurse, finance
- **Why?** To identify any potential roadblocks and to share information in order to do our part to get the study open as quickly as possible
CTO Data Management

- If study is an Investigator Initiated trial:
  - DM will work with PI, Biostats, CTO IT and CTO QA to develop case report forms (CRFs) for study – (review CRF development process handout)
Goal: Capture data points required to answer the questions posed by the Primary & Secondary Objectives

- CRF Development Steps
  - PRC Approval triggers the development process
  - Review Standard Forms Sets for required data points
  - Creates Draft CRFs for Review by Statistician
  - Define Standard Reports in Collaboration with Statistician
  - PI Review
  - PI & Statistician Approval of Final CRFs
If study is a sponsored trial:
- DM will work with Sponsor/CRO personnel during trial approval process to handle logistics prior to trial opening –
  - Shipment of study sample kits
  - eCRF/database training
  - Good Clinical Practice (GCP training – this may be required for the entire study team
  - Request Lab/Pharmacy manuals and/or Investigator Brochure (IB)
CTO Data Management

- When Study is ready to open:
  - DM will schedule and coordinate the Study Initiation Visit/Meeting
    - Will identify a day and time that works for all parties involved
    - Schedule a conference room for the meeting
    - Ensure appropriate parties are invited to attend
    - PI is responsible for presenting study and education of study team about study conduct and their individual responsibilities
While patient enrollment, treatment and follow-up are ongoing DM will assist with:

- CRF completion (study data)
- SAE reporting
  - PI will need to review SAE reports, assign attribution and sign the reports
- Work with clinical team to verify patient eligibility for study and complete screening/enrollment paperwork
  - PI will be asked to review and sign-off on patient eligibility
- Assist with protocol related questions from clinical team
- Work with sponsor monitors – schedule visits to IDS, PI meetings with monitor, meet with monitor to review study data
**CTO Data Management**

- While patient enrollment, treatment and follow-up are ongoing DM will assist with (cont’d):
  - Audits – QARC audits if study is investigator initiated, sponsor audits, FDA audits, other institutional audits
  - Facilitate communication between clinical team/PI and sponsor
    - Sponsor’s project manager, medical monitor etc.
  - Address data queries to ensure accuracy and completeness of study data
    - Typically issued for sponsored trials or institutional multi-site trials
  - Complete Data Safety and Monitoring Reports (DSMRs) and meet with PI to hold data safety and monitoring meeting.
    - Submit DSMRs to DSMB coordinator
CTO Data Management

• Study Completion/Closure and Closeout:
  o DM will work with sponsors and PI to identify trials that are ready to be closed and terminated
  o DM will coordinate and schedule sponsored study close-out visits.
  o DM will work with Regulatory Coordinator to coordinate study record retention and data archival

• Studies will not be closed and terminated until ALL data is clean and no further queries will be issued – upon study termination, no further work can be done on the trial
CTO Data Management

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Principal Investigator Interactions with CTO Multisite Coordinators

LIZ VASHER, BSN, RN, CCRP
MULTISITE PROGRAM MANAGER
EVASHER@MED.UMICH.EDU
734.232.0797

University of Michigan Comprehensive Cancer Center
Definition
- Management and oversight of the operational and logistical aspects of multi-centered clinical trials, from Start-up through Close-out.

Scope of Service
- Investigator - Initiated
- Data Coordinating Center at U of M
- Lead PI at U of M
CTO Multisite – Definition and Scope

- Funding Support provided by:
  - Government Sponsored
  - Industry Supported
  - Clinical Translational Resource Allocation Committee (CTRAC)
  - External Sources
    - Example: Multiple Myeloma Research Consortium (MMRC)
CTO Multisite – Study Start-up

- During Protocol Development MSC provide consultation on:
  - Template Multi-site Language
    - Subject Screening & Registration
    - Clinical Monitoring
    - Data Safety Monitoring Procedures
    - Quality Assurance and Audits
  - Review Operational and Logistical Aspects
CTO Multisite – Study Start-up

- Multi-site will Liaison with
  - UM Lead Principal Investigator
  - Industry Supporter
  - MICHRI (IND versus IND exempt)
  - Biostatistian
  - Office of Contract Administration & Office of Research and Sponsored Projects (ORSP)
    - Statement of Work
      - Site Purchase Service Agreements/Sub Contracts
      - Material Transfer Agreement/Data Use Agreements
CTO Multisite – Study Start-up

- **Multisite will create**
  - Regulatory Packet
  - Study Reference Binder

- **Facilitate**
  - Case Report Form Development in Velos
  - Patient Calendar Development in Velos
CTO Multisite – Site Initiations

- For Internal Sites, MSC will:
  - Coordinate
  - Prepare agenda & slides
  - Facilitate
  - Follow-up on issues/questions

- For External Sites, MSC will:
  - Facilitate web-based meeting
CTO Multisite – Manage Study Conduct

- Regulatory Support
  - Maintain Master Trial File
  - Track & Distribute to all Sites
    - Protocols & Amendments
    - Informed Consents
    - Investigator Brochures
    - Safety Letters
  - Review Informed Consent Documents for all Sites
CTO Multisite – Manage Study Conduct

- Central Enrollment
  - Manage for all Subjects
    - Verify Eligibility
    - Obtain Statistician Input & Approval
    - Process Randomization
    - Generate Study Subject Number
    - Notify Site & Study Team of Enrollment
CTO Multisite – Manage Study Conduct

- **Data Management Support**
  - Regular Review of Data
    - Complete & Accurate
  - Issue Data Queries
    - Missing & Discrepant Data
  - Notify Sites of Data Deadlines
    - Abstract Submission
    - CDUS Submission

- **Collaboration with biostatisticians**
  - Provide study data for analysis
    - Define Data Points for Inclusion in Data Abstracts
    - Determine Timeline
CTO Multisite – Manage Study Conduct

- Serious Adverse Events
  - Track & Distribute

- Drug Distribution
  - Oversight of Process

- Data Safety Monitoring
  - Facilitate & Generate Summary Report
CTO Multisite – Manage Study Conduct

• Clinical Monitoring
  ○ Actual Site Visit
  ○ First visit occurs after first 5 patients are enrolled or at one year
  ○ Annual visit every 12 months
CTO Multisite – Manage Study Conduct

- Sample Management (Correlatives)
  - Oversight

- Conference Calls
  - Coordinate & Facilitate

- Study Supporter
  - Updates
Responsibilities
- Lock Study Data
- Coordinate Close Out Activities with Sites
- Conduct Closeout Visits
- Issue Reports
Principal Investigator Interactions with Finance

DAVID BROWNING,
CTO FINANCE MANAGER

University of Michigan Comprehensive Cancer Center
Clinical Research Calendar Review & Analysis Office (CRAO)  
www.med.umich.edu/u/medschool-crao/expectations.htm

- The CRAO will review all of the study-related documents (protocol, informed consent, completed billing calendar, budgets, grants/contracts) and complete a Medicare Coverage Analysis in addition to a billing calendar review. The core documents will be pulled by CRAO from eResearch Regulatory Management (eRRM) and Proposal Management (eRPM), as necessary.
CRAO & MBECT

- All studies require a billing calendar unless all events are standard of care.
- The **Michigan Budget Enrollment Calendar Tool (MBECT)**, formerly known as CT-BECT, CTS and eThority, is a mandatory tool to provide research study teams with one point of data entry for building a clinical research budget, billing calendar, and for submitting and tracking subject enrollment. MBECT is designed to remove current bottlenecks and increase efficiency in these processes.
Billing Calendar Responsibility

- Hem/Onc Finance Team – All non-Ravitz Phase I, Phase II and Phase III studies
- CTO Finance Team – All Ravitz Phase I studies
- Other Divisions & Departments – Request effort estimates from CTO for budget development to ensure accuracy of study budgets for:
  - Data Management
  - Regulatory Specialist
  - Research Nurses & Coordinators
  - Research Specimen Processing
THE PREADWARD PROCESS

Questions?
Ask the CTO Finance Team: David Browning | Kate Harper | Kristen LaVasseur | Molly Mouilleseaux | Sarah Weathers | Brian Zahs
CTO PI Orientation Program

CTO WEBSITE INFORMATION
CTO.MED.UMICH.EDU

University of Michigan
Comprehensive Cancer Center
**Clinical Trials Office**

Our vision is to be the partner of choice in research that changes cancer therapy.

The Clinical Trials Office (CTO) serves as the centralized core facility of all clinical research trials conducted by investigators at the University of Michigan Comprehensive Cancer Center (UMCCC). This includes investigator-initiated (ii), peer reviewed clinical trials, NCI-CTEP approved protocols, pilot transitional institutional studies, cooperative group trials and industry sponsored trials. The CTO offers a broad range of expert services to investigators to help them facilitate the conduct of their studies according to federal regulations and GCPs.

<table>
<thead>
<tr>
<th>Data Management</th>
<th>Regulatory</th>
<th>Multi-Site</th>
<th>Outcomes</th>
<th>Finance</th>
<th>Informatics</th>
<th>Admin</th>
<th>PRC</th>
<th>DSMB</th>
<th>QARC</th>
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</thead>
<tbody>
<tr>
<td>Study startup liaison</td>
<td>Pre-site visit coordination</td>
<td>Eligibility determination</td>
<td>CRF development</td>
<td>Source document development</td>
<td>Monitor visit coordination</td>
<td>SAEs- monitor and report</td>
<td>Data queries</td>
<td>Protocol deviation reporting</td>
<td>CRF completion</td>
</tr>
</tbody>
</table>

*Home page lists available services and descriptions.*
Web site provides links to valuable resources.
CTO PI Orientation Program

CERVANT DASHBOARD REPORTS
CTO WEBSITE >> APPLICATIONS >> CERVANT

University of Michigan
Comprehensive Cancer Center
Multi-Study Report

CC Dashboard Report
A dashboard of accrual and study statistics for the Cancer Center from 2002 to Present.
(Because some studies are coordinated outside the Clinical Trials Office, such as SWOG, etc. data for the present year will be a lower than the actual. Intermediate updates for these studies are occasionally provided, but a full update is done at the end of the calendar year. To know what studies are represented, simply click on that data point to get further details.)

CTO Dashboard Report
A dashboard of accrual and study statistics for the Cancer Center Clinical Trials Office from 2006 to Present.

Review Dashboard (PRC, DSMB, QARC)
A dashboard of accrual and study statistics for the PRC, DSMB, and QARC for 2006 to Present.

Approval Dashboard Report
A dashboard of statistics for studies moving through the approval process from...
Approval dashboard shows the mean time of the various phases in the approval process across the center and programs. Drill-downs are also available to the individual study level.
Interactive center-wide dashboard shows accruals sub grouped by therapeutic and non-therapeutic, plus by gender and race. Drill-downs by program and year available.
An example program drill-down of the CC dashboard.

<table>
<thead>
<tr>
<th>Program</th>
<th>Study</th>
<th>PI</th>
<th>Phase</th>
<th>Opened</th>
<th>Closed</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
<th>2005</th>
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<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
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<tbody>
<tr>
<td>Bone Marrow Transplant</td>
<td>UMCC 2005.109</td>
<td>Mineishi</td>
<td>Phase III</td>
<td>10/17/2006</td>
<td>07/17/2009</td>
<td>1</td>
<td>8</td>
<td>2</td>
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<tr>
<td>Bone Marrow Transplant</td>
<td>UMCC 2006.065</td>
<td>Yanik</td>
<td>Pilot/Feasibility</td>
<td>03/13/2007</td>
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<td>8</td>
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<td>11</td>
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<td>13</td>
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<tr>
<td>Bone Marrow Transplant</td>
<td>UMCC 2006.070</td>
<td>Peres</td>
<td>Phase II</td>
<td>11/30/2006</td>
<td></td>
<td>0</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
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<tr>
<td>Bone Marrow Transplant</td>
<td>UMCC 2011.038</td>
<td>Mineishi</td>
<td>Phase II</td>
<td>11/15/2011</td>
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<tr>
<td>Bone Marrow Transplant</td>
<td>UMCC 2009.095</td>
<td>Levine</td>
<td>Phase III</td>
<td>07/14/2010</td>
<td>11/21/2011</td>
<td>10</td>
<td>0</td>
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<tr>
<td>Bone Marrow Transplant</td>
<td>UMCC 2010.038</td>
<td>Levine</td>
<td>Phase III</td>
<td>09/13/2010</td>
<td>09/15/2011</td>
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</table>
Program dashboard shows monthly accrual comparison vs. targeted by month for CTO coordinated trials. Drill-downs to study details and charts also available.
This report utilizes the patient research calendar information available in Velos eResearch. Information can be filtered by one or more fields.
The visit dates should be confirmed with EWS / Cadence for latest info, but details of visit events will remain consistent.
This report also utilizes the Velos eResearch calendars, but the display is designed in calendar form, friendlier for patient use.
CTO PI Orientation Program

OTHER INSTITUTIONAL SUPPORT

University of Michigan Comprehensive Cancer Center
Cancer Center Research

- WELCOME TO THE FUNDING OPPORTUNITIES CALENDAR
  http://sitemaker.umich.edu/cccresearch/funding_opportunities
  - Internal Opportunities
    - Clinical and Translational Research Allocation Committee (CTRAC):
      http://sitemaker.umich.edu/ctrac/home
      - Funds CTO Infrastructure
      - Translational research projects up to $50,000
    - Clinical Research Committee (CRC):
      http://sitemaker.umich.edu/cccresearchgrants/home
      - Funds IIS Proposals that focus on cancer problems or that have clear cancer relevance. The committee is interested in reviewing not only basic science and translational applications, but also applications directed at clinical (patient oriented) and cancer prevention and control topics.
Welcome to the Funding Opportunities Calendar

http://sitemaker.umich.edu/cccresearch/funding_opportunities

- Funding opportunities are broken down in the left-hand column by the month in which they are due (deadlines).
  - Examples for June:
    - Deadline: June 16, 2012
      Sponsor: NCI/NIH/DHHS
      Amount: $275,000 (direct cost over 2 years)
      Title: Pilot Studies in Pancreatic Cancer (R21)
      Contact: Click here
    - Deadline: June 16, 2012
      Sponsor: NCI/NIH/DHHS
      Amount: $275,000
      Title: Exploratory Studies in Cancer Selection, Diagnosis, and Prognosis (R21)
      Contact: Click here
Research Specimen Processing and Shipping

- Translational Research Lab (TRL)
  - Located on the 2\textsuperscript{nd} floor of the Cancer Center
  - 2 FTEs that support the collection, processing, inventory and shipping of study specific research samples
  - Participate in all sponsor pre-site visits and site initiation visits.
  - TRL staff are trained in GLPs and DOT/IATA certified
  - Phone: 1.734.615.5726
Investigational Drug Service (IDS)

- Located in Central Pharmacy
- FTEs support for Cancer Center
  - 1.6 Clinical Pharmacists & 2 certified technicians
- FY2010 IDS
  - Managed 188 active studies
  - Dispensed 7,809 investigational drugs
  - Participated in 360 audits and monitor visits
Office of Research Sponsored Projects (ORSP)

- Confidential Disclosure Agreement (CDAs)
  - Only signed by ORSP for the University

- Contracts
  - Listed are major sponsors and the ORSP Project Representative who handles that sponsor
    [www.drda.umich.edu/contacts/drda/sponsorassignments.html](http://www.drda.umich.edu/contacts/drda/sponsorassignments.html)
  - Material Transfer Agreement (MTAs)
    [www.drda.umich.edu/projects/transfers/materials_transfer.html](http://www.drda.umich.edu/projects/transfers/materials_transfer.html)
  - Data Use Agreement (DUAs)
    [www.med.umich.edu/i/policies/umh/01-04-342.htm](http://www.med.umich.edu/i/policies/umh/01-04-342.htm)
  - Purchase Service Agreement - Site Subcontracts
CTO PI Orientation Program

KEVIN WEATHERWAX
MANAGER, MICHR IND/IDE ASSISTANCE PROGRAM (MIAP)

University of Michigan Comprehensive Cancer Center
MIAP has been established to provide comprehensive regulatory support, guidance and education services to faculty investigators involved in US FDA regulated clinical research at the University of Michigan.
MICHRR IND/IDE Investigator Assistance Program (MIAP)

Provide assistance to Investigators holding an IND with FDA regulatory responsibilities.

Services Include:

• Guidance/consultation on regulatory strategy
• Assessment for IND applicability
• Assist with Pre-IND FDA meetings
• Prepare and submit IND application to FDA
• Prepare and submit annual reports and IND maintenance documents (amendments, etc.) to FDA
• Safety reporting to FDA
Guidance for Industry

IND Exemptions for Studies of Lawfully Marketed Drug or Biological Products for the Treatment of Cancer

January 2004
MICHR IND/IDE Investigator Assistance Program (MIAP)

Provide assistance to Investigators holding an IND with FDA regulatory responsibilities.

Services Include:

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### IND DECISION WORKSHEET
For Investigator-Initiated Clinical Investigations

**Does Your Study Require an IND Submittal to the FDA?**

**Note:** The following worksheet is intended to help determine whether an IND is required prior to initiating your Investigator-Initiated Clinical Trial.

**Does your study meet ALL of the following criteria for IND exemption?**
Investigations of a drug product that is lawfully marketed in the United States may be exempt from IND requirements provided **ALL** of the following statements are true (per 21 CFR Part 312.2):

<table>
<thead>
<tr>
<th>Investigational Drug and/or Isotopic Name &amp; Manufacturer:</th>
<th></th>
</tr>
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</table>

<table>
<thead>
<tr>
<th>IND EXEMPTION CRITERIA</th>
<th>TRUE</th>
<th>FALSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (a) The investigation <strong>IS NOT</strong> intended to be reported to the FDA as a well-controlled study in support of a new indication for use.</td>
<td></td>
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</tr>
<tr>
<td>1 (b) The investigation <strong>IS NOT</strong> intended to be used to support any other significant change in the labeling for the drug.</td>
<td></td>
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</tr>
<tr>
<td>2 (a) The drug being used in your investigation <strong>IS lawfully marketed as a prescription drug product.</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 (b) The investigation <strong>IS NOT</strong> intended to support a significant change in the advertising for the product.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 (a) The investigation <strong>DOES NOT</strong> involve a ROUTE OF ADMINISTRATION that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 (b) The investigation <strong>DOES NOT</strong> involve a DOSAGE LEVEL that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product.</td>
<td></td>
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</tr>
</tbody>
</table>
Guidance for Industry Investigational New Drug Applications (INDs)—Determining Whether Human Research Studies Can Be Conducted Without an IND
Resources are available at U of M to assist with your IND or IDE
MIAP is here to help with INDs and IDEs

MIAP contacts:

Kevin Weatherwax
Manager, MICHRI IND/IDE Assistance Program (MIAP)
Michigan Institute for Clinical and Health Research (MICHRI)
University of Michigan Health System
2800 Plymouth Rd., Bldg. 400
Ann Arbor, MI 48109-2800
Phone: 734-998-6275  Pager: 734-936-6266, #9912
Fax: 734-998-7318
Website: www.MICHR.umich.edu
kweath@med.umich.edu
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U.S. Halts Research On Humans at Duke
University Can't Ensure Safety, Probers Find
By Rick Weiss
Washington Post Staff Writer

Federal investigation alleges inadequate patient protection
By Leigh Hopper
Houston Chronicle Medical Writer

Clinical trials halted
Feds: Cancer study endangered patients
By Edward T. Pound
USA TODAY

WASHINGTON — In a continuing crackdown on mishandled medical ex-
MICHR Clinical Research Unit

RESOURCES AND SERVICES

CYNDI BOWER
ASSOCIATE MANAGING DIRECTOR

BOWER@MED.UMICH.EDU
734 936 8086
The Clinical Research Facility

- Established 1977, now in state-of-the-art (2009) facility in CVC
- Mission - The enablement of research that would be difficult or impossible to perform without this physical and professional clinical research infrastructure
Michigan Clinical Research Unit (MCRU)

- Main unit located on the central campus, close to the Medical School, the main hospital and the CCC
- Additional off site location at Dominos Farms and service sites in other locations
- Both industry and federally funded studies
- Staffed 12 hours a day – 8am to 8pm
  - Additional evening, weekend and holiday times
  - 7 RNs, 4 LPNs and 4 MAs
  - Laboratory facilities and expertise
Michigan Clinical Research Unit (MCRU)

- **Facilities that support CCC include**
  - 5 ES beds (1 lead lined room)
  - 5 OP /infusion rooms
  - 1 procedure room +1 intake room
  - Hal Lab
  - Core Laboratory

- **Services that support CCC include**
  - Long/intensive procedures eg PK and PD
  - Skin biopsies
  - Acupressure
  - EKGs
  - IVGTs and OGTTS
  - Specimen processing and biobanking

---

**Protocol initiations**

- Other
- Phase III
- Phase II
- Phase I
- Intervention Study
- Population Based

**Biorepository**

- Tissue
- Urine
- RNA
- DNA
- Plasma
- Serum

---

**Number of protocols**

- Grant year 2011 to 2012

---

**Samples**

- Grant year 2011 to 2012
MCRU-2-U – Mobile Clinical Research Team

- One of the first* ‘helicopter’ style research services (est. 2007)
- Most popular/fastest growing service
- MCRU 2U – anywhere within UM campus
- Clinical research nurse – within 1 hour drive (eg home, community center)

a) Activations
- Scheduled
- Just in time

b) Locations
- MCRU drop in
- Cardiovascular Center
- Cancer Center
- Mott Children’s Hospital
- University Hospital
- Taubman Health Care Center

c) Services
- Phlebotomy
- Standard of Care labwork
- Urine
- Health & Physical Exams
- Vitals

* From an infrastructure to a service based business model: 5 years of mobile clinical research at the University of Michigan, *J. Clin. & Transl. Sci.* (in press)
Clinical Studies Active at UMCCC

- UMClinicalStudies
  [www.umclinicalstudies.org](http://www.umclinicalstudies.org)
  - Connects you to clinical and health research studies at the University of Michigan. It allows you to view or sign up for studies that are currently recruiting participants.
  - Posting provided by CTO Regulatory Specialists
MCRU Contact Information

- MCRU website
  http://www.michr.umich.edu/services/mcru

- MICHR Website
  http://www.michr.umich.edu/

Cyndi Bower
Bower@med.umich.edu
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CTO PI Orientation Program

PROTOCOL REVIEW COMMITTEE
(PRRC)
UMCCC Clinical Research Oversight Committees

Protocol Review Committee
- Greg Kalemkerian, MD, Chair
- Greg Yanik, MD, Vice Chair

Data and Safety Monitoring Board
- John Levine, MD, Chair

Quality Assurance Review Committee
- Mark Zalupski, MD, Chair
Organizational Chart

Director
UM Cancer Center
M. Wicha, MD

Associate Director
Translational Research
M. Talpaz, MD

Associate Director
Prevention and Control
TBD

Associate Director
Clinical Research
M. Hussain, MD

Protocol Review Committee
G. Kalemkerian, MD
G. Yanik, MD

Data and Safety Monitoring Board
J. Levine, MD

Quality Assurance Review Committee
M. Zalupski, MD

Clinical Trials Office
S. Schuetze, MD

Biostatistics
Chart Auditors
IDS Auditors
Regulatory Auditors
Protocol Review Committee (PRC)

- Multidisciplinary committee charged with providing peer review of the scientific merit of all clinical trial research conducted at the Cancer Center

- Defines priorities for the use of Cancer Center resources (CTO, space, patients)

- Ensures sufficient scientific progress of supported protocols, including accrual performance

- Goal is to improve the overall quality of clinical research throughout the Cancer Center
Protocol Review Committee (PRC)

- Meets second and fourth Tuesday of each month
- Reviews all therapeutic and non-therapeutic research protocols and amendments that use Cancer Center resources prior to review by IRBMED
- Protocols previously peer reviewed by NCI/CTEP are exempt from review by the full committee and receive an administrative review by the PRC Chair/Vice Chair
Proposal must be formatted consistent with standard clinical protocols (no grant applications)

Protocol must include a protocol specific Data and Safety Monitoring Plan

Biostatistician must be listed as an investigator on institutional trials
PRC Review Outcomes

- Approve without modification
- Approve with contingencies
- Defer pending response and/or revisions
- Disapprove
## PRC Priority Assignment

<table>
<thead>
<tr>
<th>Impact</th>
<th>Score</th>
<th>Descriptor</th>
<th>Strengths/Weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Impact</td>
<td>1</td>
<td>Exceptional</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Outstanding</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Excellent</td>
<td></td>
</tr>
<tr>
<td>Moderate Impact</td>
<td>4</td>
<td>Very Good</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>Good</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>Satisfactory</td>
<td></td>
</tr>
<tr>
<td>Low Impact</td>
<td>7</td>
<td>Fair</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>Marginal</td>
<td></td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>Poor</td>
<td></td>
</tr>
</tbody>
</table>

Non-numeric score options: NR = Not Recommended for Further Consideration, DF = Deferred, AB = Abstention, CF = Conflict, NP = Not Present, ND = Not Discussed
CTO PI Orientation Program

DATA AND SAFETY MONITORING BOARD (DSMB)

University of Michigan Comprehensive Cancer Center
Data and Safety Monitoring Board (DSMB)

- Multidisciplinary committee that provides impartial oversight of the data integrity and patient safety for ongoing investigator-initiated trials
- Reviews protocol specific Data and Safety Monitoring Reports completed by the study specific Data and Safety Monitoring Committees
- Reviews any audit findings resulting from the QARC audit process
## Protocol Specific Data and Safety Monitoring Report

**UMCC Protocol #:**

**DSMC Date:**

**Study Status:**

**Date of Last Report:**

### Protocol Title

---

### Attendance

---

### Protocol Activity

<table>
<thead>
<tr>
<th>Planned Accrual Duration</th>
<th>Global Accrual to Date / Goal: 0 / 0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date First UM Patient Enrolled</td>
<td>UM Accrual to Date / Goal: List multi-stages individually 0 / 0</td>
</tr>
<tr>
<td>Consented Since Last Report</td>
<td>Accrual Since Last Report:</td>
</tr>
<tr>
<td>Eligible Since Last Report</td>
<td>Ineligible Since Last Report:</td>
</tr>
<tr>
<td>Eligibility Exceptions to Date</td>
<td></td>
</tr>
</tbody>
</table>

**Specifically for Phase I and/or Dose Escalating Trials:**

<table>
<thead>
<tr>
<th>Dose Level</th>
<th>Accrual</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

**SAE/UaP Reporting Since Last Report**

- List event, patient study ID number, date of occurrence, and date IRB notified. Attach SAE reports. Attach the updated SAE/UaP spreadsheet summarizing ALL events that have occurred since trial initiation.

1)
2)
**SAE/UaP REPORTING SINCE LAST REPORT**
List event, patient study ID number, date of occurrence, and date IRB notified. Attach SAE reports. Attach the updated SAE/UaP spreadsheet summarizing ALL events that have occurred since trial initiation.

1]  

2]  

3]  

**PATIENTS COMPLETED/OFF PROTOCOL SINCE LAST REPORT**
Provide reason [progression, death, toxicity, completed therapy, etc]. Provide detailed supplemental information for patients off study treatment due to toxicity or death.

**PROTOCOL DEVIATIONS SINCE LAST REPORT**
Include both purposeful and accidental variances in the approved procedures outlined for a study in its IRB approved protocol; provide date reported to Regulatory Affairs or IRB. Attach any protocol deviation forms.

**PROTOCOL AMENDMENTS SINCE LAST REPORT**
Include amendment summary, date submitted to regulatory bodies, and date approved.

**OTHER COMMENTS**

<table>
<thead>
<tr>
<th>Investigator Signature:</th>
<th>Data Manager Signature:</th>
</tr>
</thead>
</table>

| Date: | Date: |
Extent of monitoring and reporting period varies by the phase and complexity of the clinical trial, type of interventions involved and the degree of risk encountered by subjects

- Phase I trials and other high-risk studies require monthly submissions
- Phase II trials require quarterly submissions
- Non-therapeutic trials should be submitted at minimum every six months
<table>
<thead>
<tr>
<th>DSMB Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Continue</strong></td>
</tr>
<tr>
<td><strong>Protocol Revision</strong></td>
</tr>
<tr>
<td><strong>For Cause Audit</strong></td>
</tr>
<tr>
<td><strong>Formal Question</strong></td>
</tr>
<tr>
<td><strong>Closure</strong></td>
</tr>
</tbody>
</table>
DSMB Termination Guidelines

1. Excessive Grade III or IV toxicity
2. Failure of adequate delivery of a therapy due to toxicity, subject noncompliance or technical problems
3. Repetitive and/or excessive protocol deviations by the investigators
4. Failure to comply with a DSMB request
PRC or DSMB Questions?

CARI RICHARDS, MS, CCRP
CLINICAL RESEARCH ADMINISTRATOR

CKRZYZAN@UMICH.EDU
734/647-5232

Protocol Review Committee (PRC)

sitemaker.umich.edu/prc/home

Data & Safety Monitoring Board (DSMB)

sitemaker.umich.edu/dsmb/home
CTO PI Orientation Program

QUALITY ASSURANCE REVIEW COMMITTEE (QARC)

University of Michigan Comprehensive Cancer Center
OBJECTIVES

- **Routine** QARC audits are conducted yearly to assess the study’s overall compliance with the protocol, governing regulations and Good Clinical Practice (GCP) guidelines.
  - Investigator initiated
  - Interventional
  - Not otherwise reviewed

- A ‘**For Cause**’ QARC audit of a specific trial may be conducted if the Associate Director of Research, the Data & Safety Monitoring Board (DSMB), or the CTO Medical Director identifies a need for a more rigorous evaluation of an issue.
Quality Assurance Review Committee (QARC)

**Organizational Chart**

- **Director, Cancer Center**
  - Max Wicha, MD

- **UMCCC Associate Director of Clinical Research**
  - Maha Hussain, MD

- **Chair, Data & Safety Monitoring Board**
  - Bruce Redman, DO

- **Chair, Quality Assurance Review Committee**
  - Mark Zalupski, MD

- **QARC Manager**
  - Monica Orians, CCRC

- **QARC Biostatisticians**
  - 2
- **QARC Chart Auditors**
  - ~100
- **QARC Informed Consent Auditors**
  - 3
- **QARC Investigational Drug Service Auditors**
  - ~30
- **QARC Regulatory Auditors**
  - 2
Quality Assurance Review Committee (QARC)

- **Audit Interval**
  - Initial audit is scheduled one year after the study receives IRB approval. Routine QARC audits occur each anniversary month of initial IRB approval, until the study is closed to accrual.

- **Chart Review (Elements Audited)**
  - 20% of subjects enrolled during audit interval (min. 1) randomly selected for review of eligibility, treatment, toxicities, response, follow up, and recordkeeping. Auditors remain anonymous. Please do not ask who conducted the audit.

  - IDS Pharmacists & Regulatory Coordinators provide corrective and preventive action (CAPA) in response to the audit. PI must acknowledge agreement with these CAPAs in reply to DSMB. PI must draft their own CAPA to chart audit findings.
Quality Assurance Review Committee (QARC)

QARC Results

• **Email Notification:**
  Subject: UMCC 3-23 QARC Letter for review
  Body: Please review QARC letter [November 9, 2011] Click on link [http://XXXX](http://XXXX)

• **Referenced Letter:**
  Dear Dr.

  The Quality Assurance Review Committee (QARC) audited the above referenced study for the interval period of 06/01/2010 through 04/29/2011. This audit has been classified as follows:

  - **Design Review**
  - Informed Consent Review
  - Subject Case Review
  - IDS Pharmacy Review
  - IRB/Regulatory Review
  - Study [followed or did not follow] the study design

  **Possible Outcomes:**
  - Acceptable; Acceptable, needs follow up;
  - Unacceptable; Not Applicable

  You are required to submit a response to audit finding listed below...

  For complete review of the audit final data, click here.

  Send your response to DSMB c/o Cari Richards...by [Month D, YYYY]. [The QARC will verify implementation of your corrective of actions by [Month D, YYYY].]

  The Quality Assurance Review Committee will conduct the next annual audit of this trial in [Month YYYY].
CTO PI Orientation Program

PATTY BEBEE, RN
QARC ADMINISTRATION
MORIANS@MED.UMICH.EDU
734.615.0558

University of Michigan Comprehensive Cancer Center
CTO PI Orientation Program

THE END

QUESTIONS???

University of Michigan Comprehensive Cancer Center