Clinical Research

Resources for Clinical Research

Introduction

UNMC has developed many resources for clinical and translational research through the Center for Clinical and Translational Research (CCTR) as well as partnerships with other collaborators.

Center for Clinical and Translational Research (CCTR)

The CCTR serves as a repository of clinical research resources, policies, education and training opportunities, and has navigators to assist researchers conducting clinical and translational research. The CCTR managed core facilities include the Clinical Research Center, the Electronic Health Record Access Core, The Nebraska Biobank, and the Research Subject Advocate Office.

Clinical Research Center

The Clinical Research Center (CRC) is an outpatient clinical research facility that supports a broad range of clinical trials. The CRC contains exam rooms, procedure rooms, a dental/ENT room, a treadmill room, a phlebotomy room, a coordinator/investigator workroom, and a processing lab. Skilled research nurses in the CRC can also assist with inpatient protocols and serve as monitors for multi-center clinical trials. Facility use and personnel support are available on a fee-for-service basis to researchers.

The CRC can provide research assistance in all aspects of developing and conducting a clinical trial. These services can include but are not limited to:

- Developing and negotiating a budget
- Coverage analysis
- Preparing and submitting IRB documents
- Case report form and order set development
- Study recruitment
- Coordinating study visits and data collection
- Administering study infusions and monitoring patients for adverse events
- Sample drawing/processing and shipping
- Monitoring multi-center protocols and working with the investigator to develop an appropriate monitoring plan.
- Providing research support for pilot studies involving our faculty.
- Providing mentoring and education for new coordinators on campus.
- Assisting with development of advertisements and brochures

Electronic Health Record Data Access Core

The Electronic Health Record Data Access (EHR) core supports requests to assess the available patient population prior to initiating a clinical trial, as well as preparation of de-identified and well-annotated dataset queries of the electronic health record, including both legacy and new Epic data.

Nebraska Biobank

The Nebraska Biobank is a bio-repository of de-identified human biological material (HBM) (serum/plasma, and DNA) isolated from left-over patient blood samples collected at the UNMC/Nebraska Medicine clinics and facilities.

Research Subject Advocate Office

The Research Subject Advocate (RSA) Office was created as one of several mechanisms to ensure the highest level of protection for participants in a clinical research study.

The Research Subject Advocate:

- assists UNMC clinical and translational researchers in developing protocols that minimize research subject risk and optimize benefits.
- facilitates development of consent/assent documents and processes to clearly communicate to potential participants risks and benefits of the research.
- provides education and advocacy to support the safe conduct of clinical research.
- is available to research participants who are directed to the RSA office if they have concerns regarding a research study in which they are participating, or if they have questions about research in general.

Research Clinical Informatics Lead

The Research Clinical Informatics Lead (CIL) is a resource for One Chart and other Clinical Information Systems (CIS). The Research CIL is available to assist with One Chart questions, training requests, workflow development, OrderSet/SmartSet requests, One Chart documentation tool requests, and the use of One Chart to assist with patient recruitment. The Research CIL is primarily responsible for One Chart requests but may also assist in the implementation and development of workflows for other Clinical Information Systems.

The Child Health Research Institute (CHRI)

The Child Health Research Institute aims to create vibrant interfaces between biomedical, genomics and computational approaches to drive innovative clinical and translational studies.

The CHRI is home to the Pediatric Research Office (PRO), a team of research nurses, coordinators, administrators, and support staff that oversees pediatric research being conducted at Children's Hospital and Medical Center and Nebraska Medicine.

More information about the CHRI and the PRO is available on their website.

Investigational Pharmacy

The Nebraska Medicine Investigational Drug Service provides custom pharmaceutical services for the clinical and translational researcher. The Investigational Drug Service Pharmacist is available to address questions or concerns regarding pharmaceutical and investigational agents used in clinical trials. Contact the Investigational Drug Services Pharmacist at 402-559-5255 or view additional contact information on their website.

Study Design, Biostatistics, and Epidemiology Consultation/Resources

The Center for Collaboration on Research Design and Analysis (CCORDA) provides expertise in the quantitative sciences, including biostatistics, epidemiology, and health services research, and coordinates the collaborative design, planning, conduct, analysis and interpretation of laboratory, clinical, and public health research studies.

Requests for CCORDA services may be made by contacting the Center Director or Associate Director or by completing a request for consultation using the CCORDA online request web page. Investigators

who have previously worked with other CCORDA members may contact the center member directly.

Study Data Management Resources

Research Electronic Data Capture (REDCap) software.

REDCap is an open-source clinical research management tool developed by Vanderbilt University, as part of its Clinical Translational Science Award (CTSA). UNMC is one of over 870 institutions in 71 countries that host this program designed to build, manage, and support clinical research including secure on-line surveys and databases. Additional information may be available on the Project REDCap website.

The UNMC Research IT Office (RITO) can orient investigators in its use and hosts the REDCap database.

Clinical Trial Management System

The Clinical Trial Management System (CTMS) is available to UNMC and Nebraska Medicine researchers. The CTMS supports centralized management of therapeutic protocols and subjects. The CTMS allows administrative, regulatory, financial, and clinical functions to interact in a centralized area.

Additional information and training on the CTMS is available through the CCTR training website.

Forte Electronic Data Capture

Forte's Electronic Data Capture System (EDC) is targeted to assist investigator initiated trials (IIT's). The EDC allows a research team to record subject clinical data through forms, customized by the CTMS Analysts, specifically for your study. Forte EDC is validated as 21 CFR part 11 compliant.

Additional information and training on the Forte EDC is available through the CCTR training website.

Centralized Protocol & Data Management Unit of the Fred & Pamela Buffett Cancer Center

Centralized Protocol & Data Management Unit is a shared resource that provides centralized support for protocol development, quality assurance monitoring, coordination of regulatory agency compliance requirements, and evaluation of clinical research at the Fred & Pamela Buffett Cancer Center.

Center for Collaboration on Research Design and Analysis (CCORDA)

CCORDA can establish a research study database for any study on which they are collaborating.

Biobanks and Data Registries

There are a number of biobanks available to investigators:

- The Nebraska Biobank for DNA and serum linked to de-identified health information.
- Disease specific cancer biobanks and data registries

Clinical Trial Monitoring

Data Safety Monitoring

All human subject research should have an appropriate data safety monitoring plan to ensure subject safety regarding the risks, complexity, and nature of the research. Appropriate monitoring may include a data safety monitoring plan, as well as a Data Safety Monitoring Board (DSMB).

What is the researcher's responsibility for data safety monitoring?

The PI is responsible for assuring that the study has appropriate outcome monitoring.

Who at UNMC can provide support for data safety monitoring?

The Center for Collaboration on Research Design and Analysis (CCORDA) will coordinate data acquisition and management for research studies, including data safety monitoring. For more information, see the CCORDA scope of services.

The Data and Safety Monitoring Committee (DSMC) of the Fred & Pamela Buffett Cancer Center monitors cancer trials. Forms for data and safety monitoring are available on the Fred & Pamela Buffett Cancer Center Protocol Review and Monitoring System website.

Site Visits

All external vendors visiting the UNMC/NEMed campus, including clinical trial-related monitoring, are required to register with IntelliCentrics, prior to EACH visit, and check in once arriving on campus. It is recommended that monitors register online (Intellicentrics.com) in advance, to avoid delays once arriving on campus. Following check-in, monitors will be provided with a "Visitor" badge, which must be worn at all times while on campus. Specific registration instructions can be found in the Clinical Research Center Standard Operating Procedures.

Managing Clinical Trials

ClinicalTrials.gov Registry

Required Registration

Registration is required for trials that meet the FDAAA 801 definition of an "applicable clinical trial" that include the following:

- **Trials of drugs and biologics**. Controlled clinical investigations, other than phase 1 clinical investigations, of drugs or biological products subject to Food and Drug Administration (FDA) regulation
- **Trials of devices**.
  - Controlled trials with health outcomes of devices subject to FDA regulation, other than small feasibility studies, and
  - pediatric post-market surveillance required by FDA

"Applicable clinical trials" generally include interventional studies (with one or more arms) of FDA-regulated drugs, biological products, or devices that meet one of the following conditions:

- The trial has one or more sites in the United States
- The trial is conducted under an FDA investigational new drug application or investigational device exemption
- The trial involves a drug, biologic, or device that is manufactured in the United States or its territories and is exported for research

For complete statutory definitions and more on the meaning of "applicable clinical trial," see Elaboration of Definitions of Responsible Party and Applicable Clinical Trial.

Please keep in mind that FDAAA801 regulations apply to “applicable clinical trials” regardless of the funding source or lack thereof.

As a part of the IRB review, the ClinicalTrials.gov identifier (NCT number) will be requested for applicable studies.

Can I register a study after it has started?

Yes, you can register a study on ClinicalTrials.gov after it has started, but initial registration must occur prior to closing subject accrual. Please note that, in general, Section 801 of the Food and Drug Administration Amendments Act (FDAAA 801) requires Applicable Clinical Trials to be registered within 21 days of enrollment of the first participant. The International Committee of Medical Journal Editors and many journals also require registration of clinical trials *prior* to enrollment of the first participant.

Who is responsible for submitting my study to Clinicaltrials.gov?

Whoever is listed as the sponsor/investigator for the study has the responsibility for registering the study with ClinicalTrials.gov. If you need access to ClinicalTrials.gov, have questions, or require assistance with the submission, the Office of Regulatory Affairs can assist you. Call 402-559-6463 with questions.

Epic One Chart

Epic One Chart is used in many ways for clinical trials.

Building a study

Only those designated as Clinical Research Specialists can build and activate studies. Research coordinators must submit a completed Clinical Trial Master Matrix and an IRB number to a Clinical Research Specialist. To reach a Clinical Research Specialist contact the Clinical Research Center or phone: 402-552-2983.

Enrolling subjects

Research Coordinators can enroll patients in active studies using One Chart. The patient's name must be linked to the study to enroll them. Step by step instructions are available in the EPIC Research Quick Start Guide.

Training

Training is provided through the OneChart User Resource Center at Nebraska Medicine.

Advertising a Study

General Guidelines

The IRB has specific requirements for information that can be included in advertisements. See HRPP Policy #3.5 for information.

The following items are appropriate to include in an ad:

- Name and address of the PI and associated institution
- A clear statement that the activity is research
- Purpose of the research
- Eligibility criteria (in shortened form)
- A brief list of potential benefits to the subject, if any
- Time or other commitments required from the subject
- Location of the research, contact person, and phone number for further information
- IRB number

If applicable, you may mention that compensation is available but you may not provide the dollar amount. Avoid words such as "new," "improved," and "better."

The layout of the advertisements must conform to UNMC's requirements regarding the use of logos and brands. Templates are available on the brand platform website, "Brand Wise".

Industry-sponsored research also requires sponsor approval of any advertisement or promotional pieces in addition to UNMC IRB and campus approvals.

Where to Advertise a Study

You are encouraged to post your IRB approved study on the UNMC Clinical Trials database, an online, searchable directory of UNMC based clinical trials. To post a study, follow the instructions listed in the Clinical Trials Database Guide.

Translating Study Materials

Translation services are available through Nebraska Medicine Interpretive Services Office. Staff interpreters translate Nebraska Medicine documents, pamphlets, consent forms, and patient education

materials, including site translation of discharge forms. Research documents including IRB consent forms are translated on a first come first served basis as time allows. To request services, visit the Interpretive Services Request form on the Nebraska Medicine intranet.

The Center for Reducing Health Disparities offers translation services of IRB approved research related documents for a fee. 402-559-2095

Translation services are available at Children's Hospital & Medical Center. More information is available on their website or by calling 402-955-5418.

Recruiting Underrepresented Minorities

Assistance and consultation for recruitment of underrepresented populations may be available through the Research Branch of the Center for Reducing Health Disparities. The CRHD provides services to facilitate health disparities/health equity research including promotion and enrollment in research studies.

For additional information on this and other services provided by the Center for Reducing Health Disparities, visit their website or get in touch with their office.

Phone: 402-559-9660
Email: crhd@unmc.edu

Overnight Monitoring

If a study requires overnight monitoring but your study staff are only working during the day, you may contact the CRC Manager to assist you in determining how best to arrange coverage for your study. CRC staff may be available to address personnel needs outside of business hours.

Cancer Related Trials

Introduction

The oncology Clinical Trials Office (CTO) provides central management and oversight functions for all cancer-related trials that involve human subjects conducted on campus. The CTO is staffed by project coordinators, research nurse coordinators, clinical research assistants, data coordinators, and quality assurance personnel. The CTO staff work alongside the Oncology/Hematology factulty to implement and oversee a diverse range of clinical trials incuding investigator-initiated, industry-sponsored, national cooperative group, and consortium trials.

Special Review Requirements

All cancer-related trials (adult and pediatric) must be reviewed by The Protocol Review and Monitoring System (PRMS) and the Scientific Review Committee (SRC). The SRC oversees the scientific aspects of cancer-related research that involve human subjects conducted by members of the UNMC faculty and personnel.

The SRC is responsible for:

- evaluating all new and amended clinical research protocols for scientific merit and to ensure that there are adequate resources available to successfully complete the proposed research
- monitoring accrual to active protocols to ensure that studies meet their accrual goals and to require a reassessment of recruitment strategies and accrual goals when necessary
- ensuring that there are no competing studies with overlapping eligibility criteria for a specific disease indication
- establishing priority of each protocol based on National Cancer Institute guidelines and institutional priorities
- performing ongoing annual scientific review of cancer center protocols

The function of the SRC is complementary to the Institutional Review Board (IRB) and does not duplicate the IRB's responsibilities, which focuses on the protection of human subjects.

SRC approval is required before the IRB gives final approval or continuation of a protocol submission. If the investigator fails to obtain SRC approval prior to expiration of the IRB approval period, the protocol will be classified as “approval expired” until all requirements are met. Forms for protocol submission are available on the PRMS website.

Data and Safety Monitoring Support

Data and Safety Monitoring

The Data and Safety Monitoring Committee (DSMC) monitors the safety of research participants enrolled in therapeutic interventional clinical research trials sponsored by UNMC faculty as outlined in the UNMC Data Safety Monitoring Plan (DSMP).

Forms for data and safety monitoring are available on the PRMS website.

Audit Reviews

The PRMS Audit Committee (AC) performs audits and provides oversight on all investigator-initiated therapeutic interventional trials with UNMC as the study source (i.e. sponsor). The role of the Audit Committee is to ensure:

- compliance with institutional regulatory guidelines
- confirmation of patient eligibility
- adherence to treatments
- appropriateness of adverse event monitoring and reporting; and 5) adequacy of patient follow-up as stipulated in the protocol.

For a list of all active cancer related clinical trials conducted at UNMC, visit the cancer-related clinical trials page.

The site links each active trial to information on the ClinicalTrials.gov website.

The PRMS website is a useful resource which provides investigators with the most current versions of the SRC, DSMC, and AC Policies and Procedures; Conflict of Interest Policy; submission forms; and meeting dates and submission deadlines.

Drug/Device Trials

Introduction

All clinical trials that use an approved drug or investigational product supplied to the institution from a sponsor must have the protocol reviewed by the Medical Staff Pharmacy and Therapeutics Committee (P&T Committee).

P&T Committee Forms must be attached to the IRB Application prior to submission. Download the forms from the IRB Web site. Complete and save the form, then upload it directly to your electronic IRB application

Drugs

What is an Investigational New Drug (IND)?

A drug permitted by the FDA to be tested in humans but not yet determined to be safe and effective for a particular use in the general population and not yet licensed for marketing. There are three IND types; all require an IND application:

- An Investigator IND is submitted by the physician who both initiates and conducts an investigation and who immediately directs how the investigational drug is administered or dispensed. A physician might submit a research IND to propose studying an unapproved drug or an approved product for a new indication or in a new patient population.
- Emergency Use IND allows the FDA to authorize use of an experimental drug in an emergency situation that does not allow time for submission of an IND in accordance with 21CFR , Sec. 312.232 or Sec. 312.34.3 It is also used for patients who do not meet the criteria of an existing study protocol or if an approved study protocol does not exist.
- Treatment IND is submitted for experimental drugs showing promise in clinical testing for serious or immediately life-threatening conditions while the final clinical work is conducted and the FDA review takes place.

There are two IND categories: Commercial and Research (non-commercial). Once the IND is submitted, the sponsor must wait 30 calendar days before initiating any clinical trials. During this time, FDA has an opportunity to review the IND for safety to assure that research subjects will not be subjected to unreasonable risk.

Research Pharmacy for INDs

All studies using pharmaceutical agents for human administration must use the Nebraska Medicine Investigational Drug Service (Research Pharmacy). Phone: 402-559-5255

Storing Investigational Drugs

All investigational drugs for human consumption must be stored and ordered through the Investigational Drug Service.

Investigational drugs cannot be stored in individual clinics.

Devices

What is a medical device?

Medical devices range from simple tongue depressors and bedpans to complex programmable pacemakers with microchip technology and laser surgical devices. Medical devices also include in vitro diagnostic products, such as general purpose lab equipment, reagents, and test kits, which may include monoclonal antibody technology. If a product is labeled, promoted, or used in a manner that meets the definition outlined in section 201(h) of the Federal Food Drug & Cosmetic (FD&C) Act, it will be regulated by the FDA.

What is a 510(k)?

A 510(k) is a premarket submission made to FDA to demonstrate that the device to be marketed is at least as safe and effective, that is, substantially equivalent, to a legally marketed device (21 CFR 807.92(a)(3)) that is not subject to a Premarket Approval (PMA).

What is a post marketing trial?

A post marketing trial is one wherein the device is approved but the sponsor is required to continue to collect data to satisfy the FDA that the device is safe and effective.

If my study uses a device Nebraska Medicine already stocks, can I use existing inventory to keep my costs down?

No. Study devices are strictly regulated and must be labeled and secured; substitutions of non-study devices, even when identical to hospital stocks, are prohibited. The PI is ultimately responsible for ensuring appropriate storage, security, dispensing, and record-keeping for investigational devices.

Investigational Device Exemption (IDE)

An investigational device exemption (IDE) allows the investigational device to be used in a clinical study in order to collect safety and effectiveness data. All clinical evaluations of investigational devices, unless exempt, must have an approved IDE before the study is initiated.

Information on IDE and exempt devices can be found on the FDA Web site.

Contact SPAdmin for UNMC regulations for IDE, or visit their frequently asked questions page for more information.

Who is responsible for filing the IND/IDE seeking an exemption?

The IND is generally obtained by the PI, their research coordinator, or the Industry Sponsor.

Investigational Device Exemption (IDE). A sponsor must submit a separate IDE for any clinical investigation involving an exception from informed consent under the provisions of 21 CFR 50.24.

For Investigator initiated research, the PI or coordinator generally obtains the IND.

For Industry initiated research, the Industry Sponsor generally obtains the IND.

What is a sponsor-investigator and how do their responsibilities differ from a typical investigator?

A sponsor-investigator both initiates and conducts, alone or with others, a clinical investigation. The role does not include a corporation or agency as the study lead, although a corporation or agency may provide funding to conduct the trial. A sponsor-investigator has the obligations of both an investigator

and a sponsor. An investigator who is also a sponsor must comply with all FDA requirements applicable to investigators and sponsors.

Off-campus Trials

Special Considerations

As the sponsor of a multi-center trial, additional considerations may be necessary, including the following:

- Choosing sites for the trial and ensuring that the sites:
  - have the needed patient population
  - conduct a feasibility assessment, perhaps using the electronic medical record
  - develop recruiting plans for the study
  - consider competing studies
  - have experience conducting similar clinical trials
  - coordinators, whether full time or part time, have a back-up if they are gone
  - have appropriate IRB approvals (Check that human protection training credentials/certifications are current for all personnel involved)
- Checking contract/agreements that may involve multiple entities
- Developing a budget for a large study has much more to consider than a single site study. It could take 2-3 years to get it funded and appropriate prices must be put into the budget.
- Confirming the supply of a study drug
- Assuring collaborators are knowledgeable about responsibilities and adherence to Good Manufacturing Practices (GMP)
- Determining if resources are necessary to have placebo made or study drug over-encapsulated
- Determining the experience of the supplier
- Calculating the drug requirements for the life of the study including expiration dates of the drug
- Making sure there is not a current shortage of the drug
- Determining who will conduct stability testing on the drug during the course of the study
- Identifying where the study drug will be kept
- Participating in a benefit/risk assessment to determine whether or not additional insurance is needed to protect UNMC/Investigator/Study Subjects
- Determining a monitoring plan that includes who will do the monitoring and what will be monitored
- Deciding who will handle data collection and analysis and if they have adequate experience
- Establishing data coordination between sites
- Determining who will be in charge of the clinical coordinating center. This is the point person for the sites to call and to push information out to the sites.
- If lab or imaging will be conducted, determining if centralized laboratories will be used
- Identifying experienced personnel to handle lab samples
- Considering the issues of removing identifiers from the samples and shipping labs or images.

The Nurse Manager of the Clinical Research Center, the Nurse Manager of the Eppley Research Institute, and the Research Pharmacist are available to assist with getting this type of project off the ground.

Veterans Affairs Facilities

UNMC has an affiliation with the Veterans Affairs Nebraska Western Iowa Healthcare System (VA-NWIHCS). The Research Service for the local VA is housed at the Omaha VA at 42nd and Woolworth Avenue. Clinical studies, animal studies, and bench research all occur at the VA.

Regulatory Submission Process

The VA IRB and IACUC are considered subcommittees of the Research and Development (R&D) committee at VA. In order for research to begin at the VA, it must have R&D committee approval as well as relevant subcommittee approvals.

All VA forms for IRB submission, IRB Standard Operating Procedures and other resources are available online through the VA research web pages.

Resources for Researchers

The VA has its own IRB and IACUC for human and animal studies done at VA facilities or with VA resources. The VA also provides a limited number of translational bench laboratories on the Omaha NWIHCS campus.

VA Funding Opportunities

There are Merit and Career Development funding programs unique to the VA with specific eligibility requirements. Contact the local VA Research office at 402-995-3542 or 402-995-3544, or through their research web pages.

Study Personnel

All personnel must be credentialed to do research at a VA site. To start the credentialing process, the PI must complete and turn in the New Personnel Information Form (Rev 05-13).

All persons involved with research require a scope of practice based on the individual and all their roles within research (not protocol specific). Once a year, each individual's scope of practice will require a review for any changes. Scope of Practice for Research Personnel (Rev 07-12).