Human Subject Research

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Human Subjects Protection Training

Required Human Subjects Protection Training

All research personnel planning to conduct human subject research are required to complete Web-based training on human subject protection and good clinical practice (GCP) on the Collaborative Institutional Training Initiative (CITI) website.

Instructions and registration for the CITI Training Program are also available through the UNMC Institutional Review Board (IRB) website on their CITI pages.

Additional training in clinical research is available for trainees, faculty, health providers, and research personnel at the annual Clinical Research Symposium coordinated by the Clinical Research Center (CRC). View the schedule and registration details on the CRC's website.

Training for Clinical Coordinators

Required training

- CITI Training: Good Clinical Practice Course available through the UNMC Institutional Review Board (IRB) web site at unmc.edu/irb/resources/citi.
- Clinical Trials Master Matrix (CTMM)/billing grid training is required for access to the secure drive where centralized Clinical Trials folders are stored. Training is provided upon request by contacting the Senior Research Billing Associate at 402-559-4939.
- Coverage Analysis instruction is required for clinical coordinators. Schedule training through the Clinical Research Manager at 402-552-6601 or the Senior Clinical Trials Analyst at 402-552-7817.
- One Chart Electronic Health Record training is required for all clinical coordinators to have access to One Chart in order to perform duties such as chart review, order entry, patient enrollments, and study visit/orders linking. Access requests may be completed in the IT Service Requests portal. Coordinators may sign up for training in Apollo or reach out to OneChartTrainingRequests@NebraskaMed.com for assistance.

Recommended training

- The Clinical Research Coordinator’s Workshop is available on the CCTR website. Recommended for all new clinical coordinators. A live training program is scheduled annually as well. For information and access to the workshop materials, contact the Research Subject Advocate Office, 402-559-6941.
- Clinical Coordinator Orientation is available on request from UNeHealth. Coordinators receive an overview of the contract and negotiation process and learn best practices to speed study start-up.
- IRB Orientation is available upon request by contacting the IRB Office at 402-559-6463. The session is tailored to the needs of the attendee based on the type of research conducted and their role in studies. The session includes specific information on the IRB submission process, post-approval submission requirements, informed consent training, and orientation to the electronic IRB application submission system.
- The IRB Education Series offers educational sessions for new and experienced clinical personnel. Topics range from an orientation level to research subject compensation, tips for a trouble-free IRB review, and more. For a schedule, visit the IRB Education Series webpage or contact the IRB Education Coordinator at 402-559-6463.

Institutional Review Board

Introduction

The UNMC Institutional Review Board (IRB) reviews all human subject protocols conducted by anyone on the premises of UNMC, Nebraska Medicine, Children's Hospital & Medical Center, Nebraska Medicine - Bellevue, and the University of Nebraska at Omaha (UNO) or conducted by UNMC or UNO faculty or students for adequate human subjects protection. The IRB serves as a resource for questions regarding clinical research and human subject protections at UNMC. IRB review and approval is **required** before human study protocols can be initiated.

- **Exempt, expedited, or full board.** Human research studies are classified as either exempt, expedited, or full board. There are several types of research considered exempt, such as quality improvement and health outcomes data where results are shown in aggregate without individual identifiers. Exempt and expedited research is discussed further on the IRB website.
- **Adult versus pediatric protocols.** Separate IRB boards review and approve adult and pediatric protocols. The adult IRBs meet on the first and third Thursday of the month (with the exception of January and July when the board meets only on the third Thursday). The UNMC-Children's Hospital & Medical Center Joint Pediatric IRB meets on the fourth Tuesday of the month. Deadlines and meeting dates for IRB meetings can be found on the IRB website.

If research involves both adult and pediatric populations, the IRB Office assesses which IRB will review the study based on the majority population and other considerations. Nevertheless, all IRB applications, adult as well as pediatric, will be submitted electronically using the online RSS-Research Support System. For questions, contact the IRB staff.

Studies classified as exempt or expedited are reviewed either by IRB Staff or IRB members outside of a convened meeting.

Key Contacts

The **Office of Regulatory Affairs (ORA)** can answer questions and assist with the IRB submission process.

402-559-6463
irbora@unmc.edu

Submission and Approval

All research involving human subjects conducted on site at UNMC, Nebraska Medicine, Children's Hospital & Medical Center, Nebraska Medicine - Bellevue or UNO, or conducted by their employees or representatives at other sites, must receive approval by a designated IRB before the research may commence. Human subject research includes all research conducted with a human subject as defined as "a living individual about whom an investigator (whether professional or student) obtains: 1) data through intervention or interaction with the individual or 2) identifiable private information."

Research involving data or human biological materials (HBM) with subject identifiers also requires IRB application and approval. A complete listing of included and exempt research can be found in the UNMC Human Research Protection Program (HRPP) Policies and Procedures Manual, Policy #2.6.

Not all work on human specimens constitutes Human Subject Research. The NIH rules can be complex, and useful information can be found on the NIH website.

There may be exemptions to requirements for human subject research rules, but the investigator cannot make that final determination, which must be made by the IRB. Contact the IRB staff for guidance whether your project requires IRB review and approval. HRPP Policies and Procedures, Policy #2.6.

Submitting an Application

All IRB applications are submitted online using the Research Support System (RSS). Use your UNMC NetID or Nebraska Medical Center email username and password. If you are unsure of which IRB application to complete, please contact the IRB Office.

The application requires an initial review and approval of scholarly merit and resource use by an authorized department member, such as the chairperson, an authorized delegate, or appointed review committee of the PI's department or division, prior to submission.

Instructions are in the IRB's Procedures webpage.

The IRB charges a fee for review of full board or expedited industry sponsored studies. The Commercial Fee Form can be downloaded from the IRB website.

Additional Committee Reviews

Depending upon the nature of the research, proposals may be subject to additional review and approval by one or more of the following groups before obtaining IRB approval:

- **Fred & Pamela Buffett Cancer Center Scientific Review Committee (SRC):** The SRC must review and approve all cancer-related research involving human subjects conducted by members of the UNMC faculty, trainees, and members of the Fred & Pamela Buffett Cancer Center.
- **Pharmacy and Therapeutics Committee (P&T):** The P&T committee ensures the safety, accurate dispensing, and control of both investigational and marketed drugs. Upon request of the IRB, the P&T also reviews research involving the administration of agents such as vitamins or other chemicals not classified as drugs. If your protocol requires administration of any medication to human subjects, you must check the P&T box in the IRB electronic application.
- **Radioactive Drug Research Committee (RDRC):** The RDRC reviews human subject protocols involving research with radioactive drugs.
- **Conflict of Interest (COI) Committee:** When an IRB application is submitted and the PI indicates that he/she or other Responsible Personnel on the application have a financial interest, the IRB must review the financial interest and a COI management plan must be developed. If the financial interest is:
  - *Not Significant*, the COI management plan must be reviewed and approved by the IRB Executive Chair before IRB final approval.
  - *Significant Financial Interest*, the COI management plan must be reviewed and approved by expedited review or the full IRB before the protocol qualifies for final approval.
- **Sponsored Programs Administration (SPAdmin)/UNeHealth** reviews all grants and contracts funding human subjects research, including the study protocol, IRB application, consent documents.

Final IRB approval will not be given until SPAdmin or UNeHealth has a fully executed contract (for industry-sponsored research) and all other reviews and the institutional requirements have been met.

Additional Documents to Submit

The following documents, as applicable, should be submitted with the IRB application:

- Planned subject recruitment material which must be approved and stamped

- Pharmacy and Therapeutics (P&T) Committee Investigational Drug Study Registry and/or Marketed Drug Form
- Performance site approval for all non-UNMC, NEMed, UNO and Children's Hospital & Medical Center sites
- Copy of all questionnaires, surveys, assessment tools, and other relevant materials
- Detailed protocol
- Investigator's brochure
- Grant Application
- IRB Review Fee Form for all commercially sponsored research projects
- UNMC Disclosure of Potential Conflict of Interest Form for the Principal Investigator as well as any responsible personnel if a financial interest has been declared in the IRB Application for that individual(s)
- Clinical Trial Master Matrix/Billing grid. This document identifies protocol scheduled procedures and source of payment for each of the procedures. This research billing "matrix/grid" must be submitted for any study that includes clinical care conducted at NEMed/NMB/UNMC/UNMC-Physicians clinics or facilities irrespective of funding.
  - **Where can I find information regarding the Research Matrix/Billing grid?** See the SPAdmin Clinical Billing website.
  - **Who do I contact to help develop my billing "matrix"?** The Senior Research Billing Analyst will assist with completion of the matrix/billing grid as well as review it prior to IRB submission, including Coverage Analysis if indicated. Investigators/Coordinators who have questions or would like assistance with matrix completion may contact 402-559-7421 or see the SPAdmin Clinical Billing contact page.

Research Involving Children or Adolescents

UNMC and Children's Hospital & Medical Center have a Joint Pediatric IRB. Deadlines and meeting dates for the Pediatric IRB can be found on the IRB website.

Biomedical and Behavioral-Social Science studies have an adult and pediatric application. All other applications types are the same for adult and pediatric study populations. If you are unsure of which application to complete, please contact the IRB Office.

Assistance Preparing the Application

The UNMC IRB in the Office of the Vice Chancellor for Research is available to assist investigators from initial submission to study completion. If you have any questions regarding the IRB application, contact the IRB office.

The Clinical Research Center (CRC) has research personnel who can prepare your clinical trial IRB application and all forms required for submission on a fee-for-service basis. See the CRC website for information about this service.

The Pediatric Research Office (PRO) staff can prepare your clinical trial IRB application and all forms required for submission for Pediatric Studies at UNMC and Children's Hospital & Medical Center. The PRO charges a fee for this service. For more information, please see the PRO website .

Compliance and Regulatory Requirements for Human Subject Research

The Compliance Office and Officer answer questions related to research compliance. A listing of compliance areas and responsible officers is available on the academic affairs compliance website.

Managing risks associated with potential conflicts of interest begins with establishing a culture of transparency. UNMC utilizes a Web-based system called **COI-SMART** to assist in the disclosure process. COI-SMART identifies potential conflicts of interest, documents them, and when necessary, establishes plans to manage the risk.

Developing a Budget

Considerations for Preparing a Budget

For studies that require a grant or contract, the Investigator or representative is responsible for generating and/or negotiating the budget with the sponsor.

Initiation costs and Personnel time for start-up

- **Determination of feasibility using electronic health record access core.** Potential eligible patients can be identified to ensure the study is likely to meet recruitment goals by applying to the Electronic Health Record Core.
- **Regulatory Document Preparation.** IRB application fee and personnel costs for preparation of documents for industry-sponsored trials.
- **Coverage Analysis.** The Finance Analyst is available to evaluate and verify conventional or "standard" care versus research costs and can or cannot be billed to a third party payer (either private insurance or Medicare). This is important for compliance as well as budgeting. Fees related to Coverage Analysis may be required; current rates may be found on the Clinical Research Center website.
- **Data Storage.** Data storage needs and costs vary with the type of data stored, HIPAA-compliant versus non-compliant, and duration. Consult the Research Information Technology Office (RITO) to develop a data storage plan and estimate. (phone: 402-559-9072)
- **Drug and Device.** Investigational devices may require additional clinical care costs for implantation. Devices with IDE must be submitted to Centers for Medicare & Medicaid Services (CMS) for a Coverage Determination.
- **Sample size analysis by a biostatistician.** Biostatistics consultation for study design, sample size calculation, and preparation of a biostatistical analysis plan can all be determined through consultation with the Center for Collaboration on Research Design and Analysis (CCORDA). Contact by phone: 402-559-9436.
- **Spanish language translation fees.** Spanish language translation of study materials is available through the NEMed Interpretive Services Office; however, if materials are needed rapidly, other translators may be contracted through the Center for Reducing Health Disparities.
- **Salaries.** The Clinical Research Center is available to contract clinical research support, contact the CRC 402-559-85555 for an estimate. Biostatistician salaries can be obtained

from CCORDA as above.
- **Time from the Electronic Health Record Core** to obtain patient lists for on-going recruitment, contact the EHR director for an estimate.
- **Benefit rates** for each type of personnel can be found on the Sponsored Programs website.

Study related fees

Salaries and Effort

- **Investigator and Staff Time.** Principal investigators and key personnel are usually budgeted as FTEs.
- **Clinical personnel** who provide professional review services (e.g., Pathology or Radiology reviews) may require contracted professional fees. See Clinical Trial Professional & Technical Fee Billing Procedures Policy #8008 for guidelines on cost recovery for professional fees. Include salary and benefits, for all effort necessary (actual visits, preparation time, paperwork, queries, etc.).
- **Personnel time** needed to complete the study, including recruitment, study visits, preparation of IRB annual review, serious adverse event submissions, and changes of protocol.
- **Biostatisticians** and other collaborators.
- **Consultants.** This can include budgeted time and travel.
- **Research Pharmacy and Study Drugs.** The sponsor may provide the study drug whether the trial is investigator-initiated or not, however, the research pharmacy will charge for services provided. These could include consultation on obtaining the right drug or formula, submission of IND forms, subject randomization, study initiation, blinding, drug preparation or storage, and/or dispensing fees. The route of administration will determine if drug administration fees are required. Contact the research pharmacist at 402-559-5255 or download the price calculator.
- **Research IT Office or CCORDA** support of study database.

Supplies

- **Study drug or placebo** may be required for investigator-initiated study.
- **Study Devices.** Costs may be required related to obtaining, storing, maintaining, and/or training to use devices.

Travel

- **For the subject,** investigator or study personnel, or consultants.
- **Study personnel** may need to travel to the subject to obtain data or samples.
- **Subjects may require assistance** with travel to and from the study site, including bus passes or cab vouchers if local, or if distant, federally approved gas reimbursement or gas cards.

Other expenses

- **Core Facility Use and Equipment.** Fees for campus core facilities can be found on the individual core website. A full directory of core facilities is available on the VCR website. Include costs for device calibration requirements.
- **Clinical Research Center Use.** Fees for CRC facilities and staff are on the CRC website.
- **Biological Production Facility.** Fees for studies utilizing cell products.
- **Pathology Fees.** For studies requiring submission of pathology slides to a central reviewer.
- **Shipping Expenses.** If samples must be shipped in dry ice, additional shipping costs will be required.
- **Subject Stipends.** IRB typically allows up to $20/hour for participation in trials, which can include recovery or travel time. This can be provided by a check that is generated by the State of Nebraska or gift cards.
- **Postage.** Send follow-up messages or documents through the mail.
- **Record Retention Costs.** Costs of storing records during or after completion of study.

Clinical Care costs

- **Facility Fees.** There may be room charges depending on where the study is performed.
- **Clinical tests or procedures** performed during the research study may be required (e.g., EKG, lung function testing).
- **Other supplies** needed (i.e., gowns, use of hospital owned equipment, glucose testing, IV fluids). One Chart-Price Inquiry can be used to locate these fees.

Overall budget considerations

- **Cost of Living Increases.** Prices often increase over the duration of the grant, 3-5% annually, although these cost of living increases may not be allowed in NIH grant applications depending on the funding agency.
- **Indirect Costs.** Current F&A rates can be found on the SPA website.

Who are my key contacts for questions about budgeting and sources for fee information?

- Your Department Administrator
- Clinical Trials Analysts, & Research Billing Senior Associate
- Sponsored Programs Administration
- One Chart-Price Inquiry
- UNeHealth, for industry-funded clinical research

What is the Clinical Trials Master Matrix/Billing Grid (CTMM)

Completion of the Clinical Trials Master Matrix/Billing Grid can assist you with budget preparation in that it sets up the budget table for the study.

A research billing “matrix” must be submitted for any study that includes clinical care conducted at Nebraska Medicine/UNMC clinics or facilities. The matrix/billing grid guides investigators through determining costs associated with a clinical trial; it is stored on a secure drive and access must be requested from the Senior Research Billing Associate.

Where do I find hospital-based charges?

Hospital-based charges can be found in One Chart, under the separate Price Inquiry tab.
Instructions on using Price Inquiry can be found in the “Tips & Tricks” in the Epic modules of the Learning Center.

What requires a professional fee?

- Any hospital or clinic visit (office visit) where a physician, nurse practitioner, or physician’s assistant would examine a patient
- Any consultation
- Any test that requires test review and a written report from one of the following departments, among others: Radiology, Cardiology, Pathology.

Are there fees for Children’s Hospital & Medical Center facilities and services that I need for my study?

Yes. Questions regarding clinical research fees may be directed to the Pediatric Research Office.

How can I determine if study procedures, tests, items, which are “standard of care” can be billed to Medicare/insurance?

No costs for procedures completed solely for research purposes may be billed to insurance. Medicare Qualifying Criteria are outlined in NCD 310.1 “Routine Costs of Clinical Trials.” If the study meets the qualifying criteria, routine costs and costs for diagnosis and treatment of adverse events can be billed to Medicare.

If the study does not meet the qualifying criteria, nothing can be billed to Medicare, not even routine care costs. Coverage analysis is performed to verify that research procedures listed as paid by insurance are “standard of care” and can be billed to a third party payer (either private insurance or Medicare).

Coverage analysis also compares the matrix/billing grid, informed consent document, and preliminary budget to ensure that all costs are known. This process ensures that the final study budget reflects the true cost of the research project. For additional information, see the SPA Clinical Trials Billing FAQ.

The coverage analysis makes a general judgement on insurance coverage for participation in clinical trials based on Medicare rules. When a patient is identified for potential participation in a clinical trial, insurance pre-authorization is put in place to review the patient’s insurance policy and coverage. Information on the Insurance Pre-authorization process can be found at unmc.edu/cctr/resources.

Who initiates the insurance pre-authorization process?

It is the research coordinator or study staff’s responsibility to initiate the insurance pre-authorization process with Nebraska Medicine patient financial counselors.

Coverage Analysis

Performing Coverage Analysis

Clinical Trials Analysts perform coverage analyses for drug/biologics related clinical trials. Faculty/Coordinators who have questions or would like assistance can contact the Clinical Research Manager or the Senior Clinical Trials Analyst at 402-552-7817.

Is a coverage analysis required for all industry sponsored trials?

A coverage analysis is required for all adult, full board clinical trials. It should be completed for any study involving billing of clinical care at the same time of the, trial regardless of funding. The IRB may also require coverage analysis for specific trials.

The results of the coverage analysis are shared with the IRB to determine if subjects will be placed at additional financial risk as a result of study participation.

Coverage Analysis Fees

There is a fee for coverage analyses for industry funded research. Contact the Clinical Research Manager for the fee amount.

What can be charged to the sponsor in an industry-sponsored trial?

Charge time and effort for activities, including all persons involved (investigator, coordinator, research assistants, etc.). Also include supplies needed to conduct the study. If hospital services are used you should charge for them. You can also meet directly with the manager of the CRC to discuss budgeting.