Clinical Research Office (CRO) Welcome Packet

This welcome packet is intended for anyone involved in cancer-relevant clinical research. We hope this packet provides you with the tools you need to get started in research at Northwestern. Please do not hesitate to contact us with any questions or concerns as you become more familiar with CRO and/or University policies and procedures. Sallie Scherer, the CRO Quality Control Manager, is available to answer questions as you navigate this process and can assist in connecting you with the most appropriate CRO personnel, as needed. She can be reached via e-mail at s-scherer@northwestern.edu and by phone at 312-695-1331.
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GETTING STARTED

NU NetID
A NU NetID is your electronic identity at Northwestern. Your NetID will allow you access to systems essential for your participation in clinical research, including NOTIS (Northwestern Oncology Trial Information System) and NU’s electronic Institutional Research Board system (eIRB).

NU faculty and staff are automatically issued NetIDs when they are hired. For more information on how to obtain and activate your NetID go to: http://www.it.northwestern.edu/netid/overview.html.

Registering in eIRB
The NU IRB requires that anyone who plays a significant role in a study be listed on the study’s electronic authorized personnel list (APL). If you will treat and/or consent any subject on a research trial, this will include you. Anyone listed on an APL must be registered with eIRB; in order to register with eIRB, you must complete CITI training.

Once you have a NetID and have completed CITI training you may register with eIRB at the following site: http://www.eirb.northwestern.edu.

Completing CITI Training

Overview of CITI Training:
http://www.research.northwestern.edu/OPRS/irb/education/

Specific Approved CITI Training Options:
http://www.research.northwestern.edu/OPRS/irb/education/initial.html#human

CITI Program Link:
https://www.citiprogram.org/Default.asp

Once you have completed CITI training, please promptly send a copy of your training certificate to Raynette Middleton for our files.
1572s

What is a 1572?
A 1572 is a federal form and is also known as The Statement of Investigator or Form FDA 1572. It is an agreement signed by the investigator to provide certain information to the sponsor and assure that he/she will comply with FDA regulations related to the conduct of a clinical investigation of an investigational drug or biologic. The most recent version of the 1572 is available online at [http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM074728.pdf](http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM074728.pdf).

Who is required to be listed on a 1572?
At minimum, the Principal Investigator (PI) of a study must be listed on the 1572 and must sign the 1572. The CRO requires that all Sub-Investigators (“Sub-I’s”) that have a significant role in the research of a particular study also be listed on the 1572. Only physician investigators with a significant role in the trial should be listed on the 1572. Whenever a new PI or Sub-I is added to a study or no longer participates in the study, an updated 1572 is required.

Other Requirements
The CRO requires that a current (defined as signed within one year of the date the trial is open) Curriculum Vitae (CV) and a current medical license be on file for each PI or Sub-I that is listed on the 1572.

For industry sponsored studies, Financial Disclosure Forms (FDFs) will also be collected for any PI/Sub-I who is listed on the project.

Collecting 1572s & Other Required Regulatory Documentation for the Sponsor of Record
1572s will be collected for each trial using an investigational drug or biologic. 1572s for industrial trials using an investigational drug or biologic will be submitted to the Sponsors of record. 1572s for investigator-initiated trials (IITs) for which NU is considered the Sponsor of record will be collected and the original will be filed and retained in the CRO. The CRO Regulatory Assistant, [Raynette Middleton](mailto:Raynette.Middleton@nu.edu), is responsible for collecting required 1572s, FDFs, and CVs. Please submit all required, original regulatory documentation to Raynette via interoffice mail.

Delegation of Authority Logs & NU eIRB Authorized Personnel List (APL)
The majority of industry sponsors require a current delegation of authority log to be maintained for each of their studies. For cooperative group trials and for NU IITs, the eIRB APL serves as the formal delegation of authority record.
At minimum, the Sponsor delegation of authority log for industry trials and the APL will always list the current PIs and Sub-I’s (as reflected on the 1572), any RN, NP, or PA that treats and/or consents subjects on the study, the current CRO Study Coordinator (SC), the current CRO Data Manager (DM), and designated back-up SC and/or DM, and the Investigational Pharmacist. Additional personnel may be required to be included, but these requirements will vary from Sponsor to Sponsor. Report any changes to your study team to the SC ASAP.
INFORMED CONSENT PROCESS

If you are a faculty and staff member responsible for obtaining informed content, you need to be listed on the eIRB APL as being authorized to obtain informed consent. If you are authorized to obtain informed consent, you need to be aware of some important requirements and guidelines regarding the informed consent process.

Obtaining Written Consent

Obtaining written informed consent from a potential subject is a process, not just a signature on a form.

- The consent document is to be used as a guide for the verbal explanation of the study.
- The consent document should be the basis for a meaningful exchange between the Investigator and the subject.
- The subject's signature provides documentation of agreement to participate in a study, but is only one part of the consent process.
- The consent document must not serve as a substitute for discussion.

The entire informed consent process involves giving a subject adequate information concerning the study, providing adequate opportunity for the subject to consider all options, responding to the subject's questions, ensuring that the subject has comprehended this information, obtaining the subject's voluntary agreement to participate, and continuing to provide information as the subject or situation requires. To be effective, the process should provide ample opportunity for the Investigator and the subject to exchange information and ask questions.

Documentation involves the use of a written consent form containing all the information to be disclosed and signed by the subject or the subject's legally authorized representative (LAR)*. The subject or LAR who signs the consent form must be given a copy as a reference and reminder of the information conveyed.

*Use of a Legally Authorized Representative (surrogate) for obtaining consent for minors or subjects who are cognitively or medically incapacitated requires prior IRB approval.

Explanation of the Research

Investigators (or IRB approved designees) must use the following steps in order to orient the potential subject to the purpose of the research and why he or she might wish to participate:

- **Step One:** The Investigator (or designee as listed in the study's IRB approved eIRB APL) must explain the study to the potential subject verbally, providing all pertinent information (purpose, procedures, risks, benefits, alternatives to participation, etc.), and must allow the potential subject ample opportunity to ask questions.
- **Step Two:** Following this verbal explanation, the potential subject should be provided with a written consent form and afforded sufficient time to consider whether or not to participate in the research. "Sufficient time" can range from hours to days, depending on how long it reasonably takes to evaluate the procedures, risks, potential benefits, and alternative treatments.
- **Step Three:** After allowing the potential subject time to read the consent form, an Investigator listed on the APL should meet with the potential subject and answer any additional questions s/he may have.
Subject Comprehension Assessment
The responsibility of ensuring that a potential subject understands the research and the risks and benefits involved falls upon the Investigator and not upon the potential subject.

- It is critical to the consent process that the Investigator not only fields questions but also asks questions.
- Asking questions can further the discussion, elicit questions from the potential subject, prompt the potential subject to think more carefully about the study, and help the Investigator decide whether the person has adequately understood the study.
- Useful questions will be open-ended and non-directive. Rather than asking for yes or no answers, they ask for explanation because these questions often can be answered in a variety of ways, and do not already contain the correct answer.
- Open-ended questions are often introduced with "what," "where," "how often," "when," and "please describe."

Examples of open-ended questions are:
- "Just so that I'm sure you understand what is expected of you, would you please explain to me what you think we're asking you to do?"
- "Describe in your own words the purpose of the study."
- "What more would you like to know?"
- "What is the possible benefit to you of participating in this study? What are the possible risks?"
- "Can you describe what the alternatives to participation in this study are?"

Required Signatures
1. Once an individual has had all his/her questions answered and has agreed to participate in the study, the subject should sign and date the consent form.
2. The PI/ Person obtaining consent that has oriented and consented the subject also must sign and date the consent form.
   - The PI's signature/Person Obtaining Consent's signature cannot pre-date the subject's signature.
   - It may be appropriate for the Investigator to sign after the subject if the Investigator needs to verify that basic eligibility criteria have been met.
   - The subject must always be provided with a copy of the consent form to use as continual reference for items such as scheduling of procedures and for emergency contact information.

NOTE: The subject is not technically enrolled until both the subject and the PI/POC have signed.

The PI/POC’s signature means that the informed consent process has taken place with the subject and that the subject:
- meets all study inclusion criteria;
- was appropriately consented (as described above);
- understands the requirements of the study; and
- has received a copy of the informed consent document.
Documenting the Informed Consent Process
In addition to the signatures on the informed consent form (ICF), the consent process must also be documented in the subject’s medical record. There must be a written note in the medical record that the subject meets all eligibility requirements, understands the requirements of the study, was appropriately consented, and received a copy of the ICF.

Significant New Findings and Re-consent
Obtaining a signature on a consent form does not complete the consent process. Maintaining informed consent requires that subjects be provided with any new information that arises during the course of the study (such as changes to the research plan, change in risk/benefit profile, the results of related research, etc.) that may affect a subject’s decision whether or not to continue participation in the study.

Unless the NU IRB specifically requires re-consent to be obtained in a particular study, the decision to re-consent subjects is the PI’s responsibility.

IMPORTANT NOTE: You must always use the most current IRB approved ICF. This is obtained via the CRO website. Do NOT an ICF that is not downloaded from the site immediately prior to the consent process.
What is the CTCAE?
The National Cancer Institute developed the Common Terminology Criteria for Adverse Events (CTCAE), which is used for adverse event reporting in oncology clinical trials. All cooperative group trials and many IIT and industry sponsored trials use the CTCAE to report adverse events that occur on a trial. The version of the CTCAE version (usually version 3 or 4) used for reporting will be specified in the protocol.

CTCAE Components and Organization

**SOC**
CTCAE terms are grouped by MedDRA Primary System Organ Classes (SOCs). Within each SOC, adverse events (AEs) are listed and accompanied by descriptions of severity (Grade).

**CTCAE Terms**
An AE is any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medical treatment or procedure that may or may not be considered related to the medical treatment or procedure. An AE is a term that is a unique representation of a specific event used for medical documentation and scientific analyses.

Each CTCAE v4.0 term is a MedDRA LLT (Lowest Level Term).

**Definitions**
A brief definition is provided to clarify the meaning of each AE term.

**Grades**
Grade refers to the severity of the AE. The CTCAE displays Grades 1 through 5 with unique clinical descriptions of severity for each AE.

Accessing the CTCAE
The paper booklet of CTCAE v3.0 and v4.0 are currently out of print, but they can be easily accessed online.

- [CTCAE v 4.0 Quick Reference 5X7](#)
- [CTCAE v 4.0 Quick Reference 8.5 X11](#)
- [CTCAE v 3.0](#)

The Center for Biomedical Informatics (CBMi) at The Children's Hospital of Philadelphia has converted the 190+ pages of the CTCAE v4.02 document into an iPhone application. You can purchase the application for use on your iPhone.

Documenting Adverse Events in the Subject’s Medical Record
For every subject that participates in a clinical trial, it is extremely important that any adverse event they experience during the trial is documented in their electronic medical record, according to the appropriate version of the CTCAE, in a timely manner. There must be a
complete description of the adverse event that occurred and the grade and attribution of each event must be included. This allows the Study Coordinator and Data Manager, and the study PI, to assess the adverse events according to the protocol, make any required dose modifications, and report accurate data in a timely manner.
Overview
The Clinical Protocol Scientific Review and Monitoring System (CPSRMS) provides oversight of all aspects of clinical research conducted at Lurie Cancer Center. Several committees work collaboratively in this effort to form a comprehensive and robust review and monitoring system (see the CPSRMS in a chart overview below). The system is a cancer center requirement mandated through the NIH & NCI. The committees that make up the CPSRMS include: the Scientific Review Committee (SRC); the Data Monitoring Committee (DMC); and the Audit Committee (AC) (committees’ FAQs). The administrative support for the entire CPSRMS is coordinated through the CRO.

Scientific Review Committee (SRC)
All new cancer-relevant studies must receive SRC approval prior to IRB submission.
- Cancer center sign-off in eIRB is dependent upon SRC approval.
- This applies to all study types, e.g., retrospective reviews, lab-based research, industry, and investigator-initiated studies.

SRC responsibilities include:
- reviewing Letters of Intent (if required*) prior to study development;
  *Required for NU investigator-initiated interventional studies
- confirming scientific soundness;
- confirm relevance to cancer center goals;
- ensuring appropriate Data and Safety Monitoring Plan usage;
- reviewing the ongoing scientific progress of all trials; and
- review all protocol revision to existing studies prior to IRB submission.

Please contact Anne McDermott with any questions about the SRC process.

Overview of the Scientific Review Process
Any potential PI that plans to open a cancer-relevant protocol must submit a New Protocol Submission Packet (NPSP) to the CRO’s Scientific Review Coordinator via e-mail. The packet must include the New Protocol Submission form, a copy of the protocol, the ICF draft in editable (Word) form, and the grant (if applicable).

The committee reviews new protocols twice a month (1st and 3rd Wednesdays). The SRC review letter is sent to the PI within one week of review. Review outcomes include:
- Approved - No revisions/minor revisions, proceed to IRB;
- Response and/or Revisions Required Prior to Approval;
- Held for Re-Review
- Substantial Revisions Required (project will be sent to another meeting once addressed); or
- Rejected
Participation as a Reviewer
All cancer center members may be expected to provide peer-review to studies submitted for scientific review. Studies are assigned 1-2 weeks prior to the date of the SRC meeting. The level of review varies with each type of study. Review packets will be sent by the SRC Coordinator via e-mail by the end of the week prior to the review date. If you are asked to participate, attendance at the SRC meeting is strongly preferred (in person or via call-in), 676 N. St. Clair, Suite 1204.

Data Monitoring Committee
This committee conducts on-going safety reviews of all NU IITs based on intervention type and level of risk (as determined at the time of SRC review). Their review includes the following:

- Review of semi-annual summary reports. These are prepared by the study Quality Assurance Monitor (QAM) and are sent to the study PI for review and sign-off. These reports are also submitted to the IRB.
- Review of all SAEs, DLTs, and protocol deviations.
- Review and approval of all data to be released for abstract or manuscript publication.

Protocol Deviations
All protocol deviations that occur on NU IITs must be submitted to the study-assigned QAM using the protocol deviation form. The QAM is responsible for reporting the deviation to the DMC.

If the event qualifies as Promptly Reportable Non-Compliance (PRNC), it must also be reported to IRB.

The DMC may request corrective action.

Adverse Events
All adverse events on NU IITs must be reported to the QAM on the study-specific CRFs/eCRFs. In addition, all Serious Adverse Events (SAEs) must be reported to the QAM as specified in the protocol. If the event qualifies as a UPIRSO, it must also be reported to IRB.

Audit Committee
The internal audit schedule is as follows:
- Comprehensive audits are conducted semi-annually (every June & December)
- Interim audits are also conducted semi-annual (every March & September)
The Audit Committee reviews audit reports & corrective action plans; DMC gives final approval prior to IRB submission.

**Medical Writing Services**

If you or your study team is interested in developing or opening a protocol at NU, the CRO employs a Medical Writer (Ashlee Drawz) to assist with protocol development. These services are available for any cancer-relevant project. Priority is given to interventional trials.

**NOTE:** MW assistance may be requested at any point prior to (or during) SRC review. MW services include amendments, response to FDA, etc. Protocol development workshops are offered by request.

[CPSRMS Activity Flow Diagram (click here for a chart of SRC, DMC, and AC responsibilities and a visual representation of how the committees interact with each other)]
Who do I contact for... (link to CRO personnel organized by department and subject matter)

CRO Staff Phone List (printer friendly alphabetical list)

CRO Organizational Chart

CRO Trial Activation Overview
Many CRO staff collaborate to open trials as quickly as is possible. In order to make the process run as efficiently as possible, please promptly respond to any e-mail sent by the CRO team. The CRO protocol initiation team meets once a week to discuss the status of pending protocols. It is an open meeting and all faculty and staff are welcome to attend (676 N. St. Clair, suite 1206). Additionally the minutes from the meeting are published on the CRO website once a week. For access to these online reports or questions about this meeting, contact Sallie Scherer.

Common CRO Acronyms