

OVERVIEW

The primary purpose of the Clinical Research Unit (CRU) is to provide infrastructure and resources to support patient-oriented research (POR) conducted by investigators who receive their primary research funding from the NIH. The CRU may also support investigator initiated research funded by other federal, state and local agencies, and by the private sector. The CRU resources are supported by a grant administered by the National Center for Research Resources (NCRR). The Principal Investigator of the CRU is Dr. Daniel Ford, Vice Dean of Research and the team includes the Program Director, Associate Program Director, Administrative Manager, Patient Care Manager, Research Subject Advocate (RSA), and other Core Directors. The Administrative team is available to help any investigator and research team with implementing their study. Any publication derived from research supported by CRU resources should cite the CRU Grant (*M01RR-02719*) as a source of support. Information is also available at the CRU Website (<http://jhbgrc.jhu.edu/>)

Purpose of this Information:

As CRU services may be new to some investigators, it may be helpful to clarify the CRUs expectations of the investigator and the responsibilities of the CRU. The information provided below is a summary of some major considerations. These are given as guidelines for the investigator, once the protocol has been approved by the CRU Advisory Committee and the IRB, and may be adjusted based on protocol specific needs or other appropriate factors.

What to Establish Prior to Protocol Initiation

- Communications with CRU personnel
- Medication Orders/Medical Coverage
- Investigational Drug Management
- Laboratory Processing of Specimens
- Data Management and Analysis
- Special Equipment and Training

Recruitment and Scheduling

- Participant Recruitment
- Scheduling of Participants

CRU Policies Related to Visits

- Explaining CRU Policies to Participants
- Access to the B Building and the CRU

Record Keeping and Investigator's Responsibilities

- IRB approval and Correspondence
- CRU Role in the Informed Consent Process
- Recording Data in the Research Record
- Adverse Event Reporting
- Communications with CRU personnel
- Quality Assurance Reviews and Monitoring

Requirements for Investigators Utilizing the CRU

- Acknowledging the CRU Grant in publications
- Annual Report, Non competitive and Competitive Renewal

WHAT TO ESTABLISH PRIOR TO PROTOCOL INITIATION

COMMUNICATIONS WITH CRU PERSONNEL

Protocol and Equipment Specific Training:

Prior to initiating a study, the investigator and the research team will meet with key CRU staff to determine roles, responsibilities, data collection tools, physician orders, lab processing, protocol time lines and the flow of the research study. The CRU staff will assist the investigator in identifying equipment and supplies the CRU provides what the investigator must supply. It is the investigator's responsibility to obtain any special equipment or supplies not available on the CRU.

In-service:

Once the above steps are completed, the investigator will hold an in-service meeting on the CRU to explain the protocol in detail to the staff. The discussion should include scientific background for the study, specific nursing responsibilities regarding the care of the participants, the conduct of the protocol, testing procedures and scheduling of the subjects. Research participants will not be scheduled for a study in the CRU until the in-service is complete and the study equipment and supplies are available.

Post-Implementation Meeting:

After several subjects have completed the protocol, a meeting will be held with all appropriate personnel to discuss the progress of the study and to problem solve any issues related to the study.

MEDICAL ORDERS/MEDICAL COVERAGE

The CRU abides by the regulations of the NCRR. The NCRR requires medical coverage for protocols. Both entities require medical coverage for protocols. The Principal Investigator who does not have clinical privileges will be responsible for arranging medical coverage for the protocol based on the input from the CRU advisory board.

Physician orders are needed for any activity performed by CRU Nursing Staff. Depending on the protocol these could include orders for medications, infusions, questionnaires, phlebotomy, and study medication dispensed by the pharmacy. Telephone numbers for individuals responsible for medical coverage must be provided to the CRU staff. The CRU staff will assist the investigator in the preparation of these order forms, which may be signed prior to the participant's visit. It's the investigator's responsibility to arrange night, weekend and emergency coverage. As well as

participant coverage while investigator is away. Contact numbers of a responsible member of the investigator's team should be provided to participants.

Intercurrent Illnesses:

In the event that a research participant becomes ill on the CRU, the disposition of the participant will be determined based on the severity of the illness and its relationship to the research. The participant may be kept for treatment in the CRU when the illness is unrelated to the research but is anticipated to be of short duration and not expected to interrupt the research protocol. If the intercurrent illness requires termination of research participation or its interruption for a substantial time, other arrangements for the participant's care should be made. The CRU staff can assist the investigator in transferring the participant to an acute care location.

INVESTIGATIONAL DRUG MANAGEMENT

The Investigator is accountable for the management of any investigational drug. The Maryland Nursing Practice Act prohibits nurses from dispensing medications. Nurses may administer medications or supply packages with pre-labeled research medications to subjects. The CRU recommends that the Investigator work with the JHBMC Research Pharmacy in the acquisition, storage, dispensing and accountability of the research drug. A copy of the Investigational Drug Data Sheet must be in the CRU files and a copy will be placed in the participant's record.

The CRU maintains some routine medications (for example, Tylenol, Milk of Magnesia, Ibuprofen, Mylanta) on the nursing unit. If your study requires special medication or reversal agents, please check with the Nursing Staff to assure the availability of these agents.

LABORATORY PROCESSING OF SPECIMENS

The CRU works with the investigator to determine the most efficient and effective manner of obtaining laboratory data. For routine assays, the CRU can help the investigator set up accounts with external commercial laboratories. Specialized assays may be performed by the CRU Core Laboratory (list of assays is available on the CRU website <http://jhbgcrc.jhu.edu/>). It is the Investigator's responsibility to provide information on the processing and storage of biological specimens for the study.

The CRU staff can obtain, centrifuge and aliquot specimens. To assist with collection organization, labels, special tubes or cryovials should be provided to the CRU staff prior to the collection date.

The CRU can hold specimens in a -70⁰ and a -20⁰ (non-biological) freezer on the Nursing Unit. Specimens are held for no longer than one week at a time. The freezers are not monitored or alarmed. In order to safeguard the integrity of specimens, it is recommended that the Institution relocate specimens to a monitored and controlled environment as soon as possible.

DATA MANAGEMENT AND ANALYSIS

The Investigator is responsible for data management and analysis. Consultation is available from the CRU Informatics Core and the Biostatistician on methods of data management, transfer and analysis. The Informatics Core is responsible for maintaining integrity, security and backups of the data with input from the investigator. Actual analysis is the responsibility of the investigator. The investigator may request assistance from the Biostatistician.

SPECIAL EQUIPMENT AND TRAINING

Each Investigative Team may have special equipment, computers or assessment tools specific to their study . It is essential that the CRU staff is trained and deemed competent to use specialized equipment for data collection. Equipment left on the CRU should be clearly labeled for the study and include written instructions for problem solving. Storage and space on the CRU is limited; therefore, the research team may be asked to provide off-site storage when there are prolonged gaps in recruitment and the equipment is not needed.

RECRUITMENT AND SCHEDULING

PARTICIPANT RECRUITMENT

The investigator is responsible for identifying and recruiting potential participants. Selection of participants for inclusion in the study is the investigator's responsibility.

SCHEDULING OF PARTICIPANTS

Scheduling of participants' visits is individualized per protocol. Researchers will be asked to supply completed demographic information including a study ID number in advance of the research visit. The CRU Nursing Unit Manager, Charge Nurse and Patient Services Coordinator will assist you in this area. Investigators/Coordinators should call for CRU availability. Scheduling will then be performed in order of which requests are received.

- a) **Outpatient Visits:** An investigator may reserve blocks of appointment time in a week if CRU time slots in the same next or same week. Availability is contingent on the availability of equipment, space and staff.

CRU POLICIES RELATED TO VISITS

EXPLAINING CRU POLICIES TO PARTICIPANTS

The investigator accepts responsibility to explain the following CRU policies to research participants.

CRU Inpatient Contract:

The safety of all research participants and staff is of primary importance to the CRU. On admission, participants will be asked to sign a document that describes the rules of conduct for the CRU stay. In the contract, participants are informed of the CRU's smoking policy, (with the investigators consent) no visitor policy, meal provisions, restricted areas, telephone privileges, and the sign in and out process. In addition, participants will be notified of behaviors for which they may be removed from the CRU, such as evidence of non-study alcohol or drug usage or possession, possession of a weapon, sexual harassment or verbal threat of violence, sexual activity and/or gambling. A copy of the contract is available on the CRU.

No Visitors Policy:

The CRU does not allow visitors. This minimizes impediments to data collection and maintains subject confidentiality.

Personal Belongings:

The CRU is not responsible for subject belongings and valuables; The CRU does not have the ability to lock up valuables. Subjects should be instructed to bring in the minimal amount of personal belongings for their CRU stay. A washer and dryer are provided for subject use when participating in a prolonged inpatient protocol. Subjects may bring in laptops and CD players but they do so at their own risk.

Telephone and Internet Access:

The CRU does not provide internet access and subjects are not allowed to use the Center's computer for their personal use. Telephone lines are provided in the inpatient rooms for local usage only. Telephone usage is allowed with a physician's order.

Advanced Directives/Living Will:

It is required by JCAHO and federal law that all inpatients be asked about Advanced Directives. If the inpatient has an advanced directive or living will, it is recommended that a copy be placed on the inpatient medical record or the physician needs to document the participant's desires in a progress note. If the participant does not have a living will/advanced directive, nursing staff will ask if the participant wishes to talk to someone to organize one. Asking participants about this prior to admission will make this discussion more comfortable for the participant. Information packets are available on the CRU and can be included in any information mailed to the participant prior to admission.

Search of Subject Belongings:

CRU Staff do not conduct searches. If this is requested by the Investigator, it is the responsibility of the research team to conduct physical and/or belonging searches. This practice allows researchers the opportunity to directly intervene with their subjects.

Elopement Policy:

Since CRU staff members are accountable for participant safety, all inpatients are asked to sign in and out of the CRU. This information includes the time out, anticipated time of return and the participant's destination. The Investigator will be contacted and if needed, JHBMC Security will be contacted to help locate the participant or escort them back to the CRU.

Weather Policy:

The CRU Weather policy follows the plan of the Johns Hopkins University for weather-related cancellations. Investigators should inform participants to listen to WBAL 1090 for the University's closure. Participants can call the following #410-516-7781. When the University classes are canceled due to weather, the CRU is closed for outpatient appointments. The CRU staff will maintain staffing for inpatients already housed or scheduled to be on the CRU. The Investigator should contact any scheduled admissions to confirm their arrival time and let the CRU staff know what is being planned.

ACCESS TO THE B BUILDING AND CRU

An electronic card access system controls access to the B Building and the CRU. The CRU Administrative Manager will sign the security waiver so researchers have access to the front and back doors of the B Building. Card swipe access to the CRU itself is given only to CRU personnel.

To facilitate subject access for smoking, temporary badges for outside access are available at the nurse's station. The subject must have off unit privileges and sign in and off the unit.

**RECORD KEEPING AND INVESTIGATOR'S
RESPONSIBILITIES**

IRB APPROVAL AND CORRESPONDENCE

The investigator is responsible for obtaining IRB approval for the research protocol and all subsequent protocol or consent form changes. While the study is active, copies of IRB correspondence regarding protocol changes, protocol deviations, unanticipated problems, and any other information concerning the progress or risk/benefits of the should be sent to the Research Subject Advocate (RSA) for the CRU Administrative Study Binder. A copy will be distributed to the assigned CRU staff, and available for reference.

The investigator must ensure that IRB approval remains current throughout the duration of the protocol. If a protocol continues beyond the date of the initial IRB expiration, a renewed copy of the IRB-approved protocol, approval letter and consent form should be submitted to the RSA upon expiration of the current IRB approval.

CRU ROLE IN THE INFORMED CONSENT PROCESS

Informed consent is an ongoing process and must be obtained before any aspect of the research procedure or investigation, including screening, can be done. The investigator is responsible for obtaining consent in compliance with federal and local requirements for each participant prior to entering the study. If this responsibility is delegated to other study personnel, the investigator ensures that they are approved by the IRB to serve in their designated capacity and are fully qualified to explain the study, answer questions and evaluate the participant's understanding of the study before having the participant sign the consent form.

The investigator accepts responsibility for obtaining consent in a manner consistent with the requirements of the IRB, and all Federal and State regulatory requirements. A copy of the signed consent form should be given to the participant, given to the CRU staff for the medical record and the original retained by the investigator.

In the event that concerns about a participant's comprehension of a protocol should occur, the CRU staff will contact the Research team to refresh the consent process with the participant.

RECORDING DATA IN THE RESEARCH RECORD

The research record serves as the primary source document for all data reporting. The investigator will work with the CRU nursing staff on their respective responsibilities for collecting and recording data for each study.

The investigator is ultimately responsible for the accuracy of reported data. All data forms should be completed in their entirety in a neat, legible manner to ensure accurate interpretation of data.

Research record storage is the responsibility of the Investigator. Outpatient records are held on the CRU until the participant completes or leaves the study. At the end of participant study involvement, all records will be removed from the CRU and returned to the Investigator.

Protocol Deviation or Exception to Protocol:

A protocol deviation is defined as a planned or unplanned departure from the IRB approved protocol. In the event of a protocol deviation, a physician's order will be needed to cover the protocol change, (e.g. changing an angiocath size to a smaller gauge needle). The CRU staff will complete a CRU Protocol Deviation and Exception Report Form that includes a rationale for the protocol deviation. If appropriate, a JHBMC Occurrence Report form will be completed as per JHBMC policy. All protocol deviations should be documented in the participant's medical

record. It is recommended that Investigators analyze these deviations to determine if amendments to their protocols would be indicated. Further, it is required that deviations to the protocol be logged and reported to the IRB at least annually, utilizing the appropriate documentation. Planned protocol exceptions or exemptions are not permitted without prior approval from the IRB, as a Change in Research.

ADVERSE EVENT REPORTING

It is the expectation of the National Center of Research Resources that all CRU Investigators notify the Institutional Review Board (IRB) and the sponsor(s) regarding adverse events and Unanticipated Problems (formerly and conventionally known as “Serious Adverse Events”) according to IRB guidelines. Adverse Event reporting is required for all research involving human participants and may be logged and reported at Continuing Review. The intent is to contribute promptly to a body of knowledge about possible harms in order to protect human participants. Unanticipated Problems occurring in the protocol must be reported promptly to the IRB if the event is unexpected, related to the protocol procedures or study article, AND impacting upon the Risk/Benefit ratio of the study.

** Note: Adverse events may require reporting to the Institutional Review Board (IRB), the NIH Office of Biotechnology Activities (OBA) in accordance with gene therapy regulations, the Food and Drug Administration (FDA) in accordance with Investigational New Drug (IND) or Investigational Device Exemption (IDE) regulations, the CRU, JHHS General Counsel’s Office and the JHBMC Risk Manager.*

COMMUNICATIONS WITH CRU PERSONNEL

Data and Safety Monitoring Reports:

The investigator is responsible for regular and timely communications regarding study progress. The investigator accepts responsibility for submitting Data and Safety Monitoring Reports (DSMRs) to the RSA and Biostatistician at regular and pre-arranged intervals. In most cases, the Continuing Review Application submitted to the IRB annually, which contains the basic information concerning the progress of the study and a summary of observed safety issues or protocol deviations, will suffice for Data Safety Monitoring Reporting, unless the nature of the protocol requires more specific or frequent reporting to the RSA.

Changes in CRU Utilization:

In the event that an Investigator wishes additional type of CRU resource or to increase the number of CRU approved visits, a letter requesting the changes must be submitted to the CRU. If a study has been approved but not used CRU resources for at least a year, a letter indicating that the study remains active and will use the resources with the anticipated subject volume must be submitted before the study can continue to use resources.

QUALITY ASSURANCE REVIEWS

The CRU has responsibility to Johns Hopkins Bayview Medical Center, Johns Hopkins University School of Medicine and the NIH to take all reasonable steps to ensure the proper conduct of the study as regards to ethics, implementation of existing NIH policies on the inclusion of women, minorities and children as research participants, and provide oversight evaluation of CRU activities. The main duty is to help the investigator maintain a high level of ethical, scientific, technical and regulatory quality in all aspects of the study.

By signing the CRU application, the investigator agrees to allow the CRU to conduct quality assurance visits. At regular intervals during the study, a representative of the CRU will contact the investigator to review study progress, investigator and participant adherence to protocol requirements and any emergent problems. The following points will be reviewed with the investigator during the quality assurance reviews: informed consent, inclusion and exclusion criteria, adverse event documentation and reporting, and quality of data.

REQUIREMENTS FOR INVESTIGATORS UTILIZING THE CRU

ACKNOWLEDGING THE CRU GRANT IN PUBLICATIONS

The NIH links CRU funding allocations with the number of publications derived from work supported by CRU resources. It is essential that all publications resulting from research supported by any CRU resources cite CRU support. Each investigator receiving support from the CRU accepts responsibility for acknowledging the CRU grant in publications. The proper citation is: “*This research was supported by a grant (M01RR-02719) from the Clinical Research Unit Program of the National Center of Research Resources, National Institutes of Health*”. It should also be noted in the “Methods” section or case report that the research participant(s) was admitted to studies on the Johns Hopkins Bayview Medical Center, Clinical Research Unit. When the article is accepted for publication, or when a reprint becomes available, please provide a copy of the publication to the CRU Administrative Manager.

Annual Report, Budget Process and Competitive Grant Renewal:

The CRU prepares an annual progress report due March 1st, and a non-competitive budget for CRU related activities due September 1st. These reports are submitted to the NIH for review. The NIH uses these to determine funding for the CRU. Investigators will be required to complete the information requested using a web-based reporting module. Each investigator receiving support from the CRU accepts responsibility for supplying the requested information in a timely fashion.

Every 5 years, the CRU must submit a competitive grant. At that time, the CRU will contact all investigators with active protocols for information for the submission. This will include an abstract, a 5 or 10 page description of the research design, and subject enrollment information.

REFERENCES

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21 CFR § 312, Subpart D (2000). (Code of Federal Regulations. Title 21. Food and Drugs. Food and Drug Administration. Part 312. Investigational New Drug Application. Subpart D. Responsibilities of Sponsors and Investigators.)

21 CFR § 812, Subpart D (2000). (Code of Federal Regulations. Title 21. Food and Drugs. Food and Drug Administration. Part 812. Investigational Device Exemptions. Subpart D. IRB Review and Approval.)

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