



GENERAL CLINICAL RESEARCH CENTER

Protocol Submission Procedures

To submit a research study to the General Clinical Research Center:

- Please read these **Protocol Submission Instructions** carefully
- Prepare the 5-page protocol (GCRC version) per the instructions
 - Use Arial 11 pt font only
 - Margins = 0.75 inches left, 0.50 inches right, 1.0 inches top and bottom
 - Five page limit (title through statistical analysis sections – items 1-9)
- Submit the protocol and other required documents in one of two ways:
 - Via e-mail as attachments, or
 - Delivered to the GCRC on removable electronic media (CD, DVD, or USB drive)

Who May Submit a Protocol?

The VCU GCRC is available to all VCU Health System and VCU faculty members who want to conduct patient oriented research. Each project conducted on the VCU GCRC must include at least one full-time faculty physician with admitting privileges who assumes overall patient responsibility. Studies must receive approval from the Institutional Review Board (IRB) and the VCU GCRC Advisory Committee.

Writing and Submitting a Research Study (Protocol) *see Protocol Layout

Research protocol application instructions and forms for the VCU GCRC are available from the GCRC web site download page (<http://www.vcuhealth.org/crc/proiinfo.htm>). The Administrative Director (Doris Rice, 804-828-9230, drice2@mcvh-vcu.edu) can answer questions regarding research budget, protocol format, or utilization of GCRC resources.

Investigators must submit the proposed research study (protocol) including the VCU GCRC forms, the IRB approved patient consent form plus one copy of the IRB approval letter. Submission per the e-mail instructions (see e-mail instructions below) is preferred. The protocol may also be submitted to the GCRC on removable electronic media such as CD, DVD, or USB drive. Please follow the protocol format included in this guide and be sure to include the VCU GCRC Gender/Minority table (Targeted/Planned Enrollment Table), Justification Form, and the Data and Safety Monitoring Plan (DSMP).

Approval from the Radiation Safety Committee and/or the Investigational Drug Committee may be needed if the protocol involves the use of radiation therapy or investigational drugs and copies of those approvals must be sent with the protocol submission forms.

Prior to submitting a protocol, investigators are strongly encouraged to discuss study design and statistical analysis with the biostatistician (Dr. Chris Gennings, 828-9824, cgennings@vcu.edu). Additionally, the VCU GCRC staff can assist with special nursing, dietary, and/or database needs prior to submission. Please refer to the GCRC Protocol Submission Checklist to ensure that your application is complete.

Protocol Review Process

Once a research project has been submitted, the proposal is distributed to each member of the Advisory Committee from which two or three primary reviewers are assigned. Investigators may be invited to be present at the Advisory Committee meeting to discuss their application. The study

design of the protocol is carefully reviewed by the committee to determine: 1) safety; 2) scientific merit; and 3) the need for VCU GCRC resources. For approval by the Advisory Committee, protocols must be hypothesis-driven with clearly defined hypotheses and specific aims, have a detailed biostatistical plan, meet appropriate gender/minority requirements, and include a Data and Safety Monitoring Plan (see DSMP below). Protocols should be submitted at least ten days prior to the Advisory Committee meeting which is held on the **third Wednesday of each month**.

Procedure for Changes to a GCRC Approved Protocol

The same procedures used to submit or initiate a study are followed for changes to a VCU GCRC approved protocol. Any consent or protocol changes must be forwarded to the GCRC. If the changes are minor, a one-page addendum may be submitted as long as the addendum has been approved by the IRB and is accompanied by the new consent form and IRB approval letter.

Protocol Layout (please use the following numbering convention)

- 1. Title
- 2. Investigators (including co-investigators)
- 3. IRB Approval Number (if known)
- 4. Hypothesis
- 5. Specific Aims
- 6. Background and Significance
- 7. Preliminary Progress/Data Report
- 8. Research Method and Design
- 9. Statistical Analysis - see Statistical Analysis Instructions
- 10. References - see Human Subjects Instructions
- 11. Human Subjects Concerns (items 1-4) - see Human Subjects Instructions
- 12. Data and Safety Monitoring Plan - see DSMP instructions
 - **Study Monitoring Process**
 - 12.1.1 Responsible individual for data and safety monitoring
 - 12.1.2 Content of review
 - 12.1.3 Frequency of monitoring
 - 12.1.4 To whom are the results of the review reported
 - **Adverse Event (AE) Reporting**
 - 12.2.1 List of graded anticipated adverse events included in human subjects concerns (see Human Subjects Instructions - item 1)
 - 12.2.2 Reporting process for anticipated AE's
 - 12.2.3 Reporting process for unanticipated AE's
- 13. Inclusion of Children - see Children Inclusion Instructions
- 14. Gender and Minority - see Gender/Minority Instructions
- 15. GCRC Justification Table - see Need for GCRC Instructions

In addition to Items 1-15 above, please provide the following documents:

- You may be asked to provide a recent CV to assist in the review process
- IRB Training certificate (provided or on file) for all investigators

Note: The maximum length of the protocol submission (Title through Statistical Analysis - items 1-9 above) is 5 pages.

Protocol Format Requirements

- Use only Arial 11 pt font
- No more than 15 characters per inch type density

- No more than six vertical lines per inch
- Margins = 0.75 inches left, 0.50 inches right, 1.0 inches top and bottom
- Five page limit (title through statistical analysis sections - items 1 through 9)

Statistical Analysis / Data Management

Provide details of biostatistical design and analysis. The investigator may contact the VCU GCRC's Systems Manager (taro@mcvh-vcu.edu) and Biostatistician (cgennings@vcu.edu) to set up free computer and biostatistical consultation, respectively.

Human Subjects Instructions

Under each criterion, indicate whether the information relates to the primary research site, or to a collaborating performance site(s), or to all sites.

(Related NIH URL: <http://grants1.nih.gov/grants/policy/hs/index.htm>)

1. Risks to the Subjects

Human Subjects Involvement and Characteristics: Describe the proposed involvement of human subjects in the work outlined in the Research Design and Methods section. Describe the characteristics of the subject population, including their anticipated number, age range, and health status. Identify the criteria for inclusion or exclusion of any sub-population. Explain the rationale for the involvement of special classes of subjects, such as fetuses, pregnant women, children, prisoners, institutionalized individuals, or others who may be considered vulnerable populations.

Sources of Materials: Identify the sources of research material obtained from individually identifiable living human subjects in the form of specimens, records, or data. Indicate whether the material or data will be obtained specifically for research purposes or whether use will be made of existing specimens, records, or data.

Potential Risks: Describe the potential risks to subjects (physical, psychological, social, legal, or other) and assess their likelihood and seriousness to the subjects. Where appropriate, describe alternative treatments and procedures, including the risks and benefits of the alternative treatments and procedures to participants in the proposed research.

2. Adequacy of Protection Against Risks

Recruitment and Informed Consent: Describe plans for the recruitment of subjects and the process for obtaining informed consent. Include a description of the circumstances under which consent will be sought and obtained, who will seek it, the nature of the information to be provided to prospective subjects, and the method of documenting consent. The informed consent document should be submitted to the PHS only if requested.

Protection Against Risk: Describe the planned procedures for protecting against or minimizing potential risks, including risks to confidentiality, and assess their likely effectiveness. Where appropriate, discuss plans for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects. In studies that involve interventions, describe the plan for data and safety monitoring of the research to ensure the safety of subjects.

3. Potential Benefits of the Proposed Research to the Subjects and Others

Discuss the potential benefits of the research to the subjects and others. Discuss why the risks to subjects are reasonable in relation to the anticipated benefits to subjects and others.

4. Importance of the Knowledge to be Gained

Discuss the importance of the knowledge gained or to be gained as a result of the proposed research. Discuss why the risks to subjects are reasonable in relation to the importance of the knowledge that reasonably may be expected to result.

Note: If a test article (investigational new drug, device, or biologic) is involved, name the test article and state whether the 30-day interval between submission of applicant certification to the Food and Drug Administration and its response has elapsed or has been waived and/or whether use of the test article has been withheld or restricted by the Food and Drug Administration.

Data and Safety Monitoring Plan (DSMP)

Persuant to federal requirements for more comprehensive documentation of the process followed to ensure the safety of human subjects enrolled in patient oriented research, a Data and Safety Monitoring Plan (DSMP) is now required of all protocols submitted to the General Clinical Research Center (GCRC). In coordination with the Massey Cancer Center and the Office of Compliance at VCU the GCRC has developed the following format for a DSMP. Given the diversity of research protocols performed on the GCRC, we recognize that a common document (DSMP) may not be applicable to all investigators. However, the essential elements contained in this template should provide sufficient structure to enable the investigator to comply with these new regulations.

With regard to the DSMP, the following essential elements are identified:

Study Monitoring Process

12.1.1 - Indicate who will be responsible for data and safety monitoring during the study. (e.g. an external Data and Safety Monitoring Board, study team, or the PI only). In many cases, the PI/study team will perform much of the data and safety monitoring, with periodic review by the GCRC Audit Committee and by a Research Subject Advocate (RSA) who functions as an independent compliance officer.

12.1.2 - Indicate the content of the review (e.g. protocol compliance with inclusion/exclusion criteria, gender and minority, adverse events. See below).

12.1.3 - Indicate the frequency of monitoring. A suggested strategy might be that each protocol will undergo its initial review by the study team after 10% of the anticipated enrollment or at least 3 subjects have been enrolled, with follow-up review at intervals to be dictated by protocol risk as determined by the GCRC Advisory Committee. For low risk protocols, annual review may be adequate whereas high-risk protocols may require quarterly review.

12.1.4 -To whom are the results of the review reported? In the case of the GCRC, it is suggested that reports be submitted to the GCRC RSA. The RSA is an independent compliance officer, as mandated by NIH, supporting research at the GCRC. Additional GCRC RSA contact information may be found on the GCRC web site (General Information – Staff).

Adverse Event (AE) Reporting

12.2.1 -Provide a list of anticipated adverse events, graded as mild, moderate, or serious (see AE Grading Scale below). In most cases these have been identified in the consent form and in item 1 of the human subjects concerns. It may be helpful to identify those

potential AE's which are of sufficient concern to include as study outcomes and warrant capture in the protocol database.

12.2.2 -Indicate the process by which anticipated AE's will be reported. Serious anticipated adverse events should be reported to the GCRC and may be reported to the IRB. Adverse events should also be retained in a study binder for review by the study team and the GCRC RSA.

12.2.3 -Indicate the process by which unanticipated AE's will be dealt. It is assumed that all unanticipated AE's will be reported to the IRB as required by 45CFR46.103(b)(5)(i). This should include a grading and attribution scale and a mechanism for reporting these events to the IRB and GCRC. All serious unanticipated adverse events should be reported within 2 days to both the IRB and the GCRC (http://www.vcuhealth.org/crc/Pdf_Docs/vcu_ae.pdf).

Adverse Event (AE) Grading Scale (Suggested GCRC Adverse Event Grading Scale)

These grading scale definitions are used by the GCRC, and may be helpful in categorizing the risk of AE's in your research protocol. However, as stated earlier, the PI is ultimately responsible for determining the definitions (and reporting requirements) of the protocol.

Mild Severity:

- Transient laboratory test alterations
- Discomforts noted but without disruption of daily activities
- No therapy, or only symptomatic therapy, required

Moderate Severity:

- Laboratory test alterations indicating injury without long-term risk
- Discomfort sufficient to modify normal daily activity
- Specific therapy required (i.e., more than symptomatic)

Serious*:

- Laboratory tests indicating a serious health threat or permanent injury
- Incapacity, inability to work, inability to perform normal daily activity
- Hospitalization required or prolonged
- Emergency treatment required
- Life-threatening events
- Death

*NOTE: The term serious is used in place of severe, a term that is used in many Protocols. There is an opinion that a minor or moderate event can be "severe" but not harmful to the patient, such as a transient pruritic rash that is "severe", but not serious.

Inclusion of Children

If Children (defined as individuals under the age of 21 years) are to be excluded from the study, please provide justification for their exclusion.

Minority and Gender

The NIH policy is that women and members of minority groups and their sub-populations must be included in research projects involving human subjects, unless a clear and compelling rationale justifies their exclusion. Cost is not an acceptable reason for exclusion except when the study would duplicate data from other sources. Women of childbearing potential should not be routinely

excluded from participation in clinical research. This policy applies to research subjects of all ages. Address the inclusion of women and members of minority groups and their sub-populations in developing a research design appropriate to the scientific objectives of the study. Describe the composition of the proposed study population in terms of gender and racial/ethnic group, and provide a rationale for selection of such subjects. Provide a compelling rationale and justification for requesting any exclusions noted above. When proposing Phase III clinical trials, show whether clinically important gender or race/ethnicity differences are to be expected, and the trial should be designed to accommodate any differences. Please fill out the tables as directed below.

For planned studies, indicate the expected study composition using the categories noted below. For ongoing studies, provide the number of subjects enrolled in the study to date cumulatively according to the following categories. If there is more than one study, provide a separate table for each study.

(Helpful links: <http://www.census.gov/> and <http://www.cdc.gov/health/diseases.htm>)

(Note: Total Planned Enrollment in example below is 196)

Example: Total Planned Enrollment Table

TARGETED/PLANNED ENROLLMENT: Number of Subjects			
Ethnic Category	Sex/Gender		
	Females	Males	Total
Hispanic or Latino	5	5	10
Not Hispanic or Latino	127	59	186
Ethnic Category Total of All Subjects*	132	64	196
Racial Categories			
American Indian/Alaska Native			
Asian			
Native Hawaiian or Other Pacific Islander			
Black or African American	75	31	106
White	57	33	90
Racial Categories: Total of All Subjects *	132	64	196

*The "Ethnic Category Total of All Subjects" must be equal to the "Racial Categories Total of All Subjects."



General Clinical Research Center

Contact Information

Email: Jennifer Economy jeconomy@mcvh-vcu.edu
Fax: 804-828-5002
Phone: 804-828-0228

Protocol Submission Checklist

Send the following using the contact information provided above:

- 1) GCRC Version of the protocol - the GCRC version of the protocol is 5-pages or less in length (Title through Statistical Analysis -see Protocol layout above).
- 2) Full Length Version of the protocol - If a longer version of the protocol exists, please e-mail and provide 3 hard copies of that version as well (grant/industry/multi-center/other).
- 3) Justification for GCRC Resources form (MS Excel file)
- 4) IRB Approval Letter* - (must be dated)
- 5) Consent Form* - (all IRB approved versions, must be dated)
- 6) Financial Agreement* (if applicable) - If the protocol is a D (industry sponsored) study, then a copy of the financial agreement with the sponsor must also be submitted.

***Note:** Copies of the original IRB Approval Letter, Consent Form, and Financial Agreement (if applicable) should be faxed to the GCRC (804-828-5002).