

## Policy on Gene Transfer Research Trials

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**Applies to:** Any faculty member who wishes to conduct research involving the deliberate transfer of recombinant DNA, (or DNA or RNA derived from recombinant DNA), into one or more human research participants at the University of Virginia.

**Reason for Policy:** This policy will ensure that any research involving the deliberate transfer of recombinant DNA into a human subject will be carried out in accordance with University and Federal policies.

### **Policy**

This policy applies to experiments involving the deliberate transfer of recombinant DNA, (or DNA or RNA derived from recombinant DNA), into one or more human research participants at the University of Virginia.

Oversight of gene transfer research trials is regulated at the Federal level by the National Institutes of Health (NIH), Office of Biotechnology Activities (OBA)/Recombinant DNA Advisory Committee (RAC). All proposed study protocols must be submitted to the OBA in accordance with Appendix M of [“NIH Guidelines: Recombinant DNA and Gene Transfer.”](#) (see procedures section). Final approval of all gene transfer research trials at the University of Virginia is the responsibility of the Institutional Review Board – Health Sciences Research (IRB – HSR), and the Institutional Biosafety Committee (IBC).

The IRB-HSR will:

- Verify that the consent form meets all federal regulations according to 45CFR46 and 21CFR50.
- Verify that all appropriate information as outlined in Appendix M of the RAC application is included in the protocol and consent form.
- Verify that all items as suggested by the IBC and RAC are included in the consent form.
- Verify that complete disclosure of any conflict of interest is noted in the consent form.
- Confirm that approval from all other required review committees or bodies have been obtained. A representative from each required committee or body may be present at the IRB-HSR meeting when final approval is given. If a representative is unable to attend, a written approval from them must be submitted for review at the meeting.
- Confirm that key personnel have completed the IRB-HSR research subject protection training.

The IBC will:

- Verify that all aspects of Appendix M of the NIH Guidelines have been addressed by the principal investigator.
- Confirm that key personnel have completed the appropriate biosafety training.
- Review the mandatory document entitled [“Biosafety Manual and Standard Procedures for the Transfer of Recombinant DNA Molecules into Human Subjects”](#) to confirm that it accurately reflects the protocol and that standard operating procedures are appropriate and accurately described in the manual
- Perform initial and regularly scheduled inspections of clinical facilities where vector distribution, administration and potential subsequent viral shedding may occur to certify the implementation of appropriate work practices and physical controls.
- Assess risks to the environment and the necessity to inform medical care personnel, (e.g., nurses, technicians), of risks, precautions, and recommended health surveillance procedures.
- Verify that Research projects are in compliance with the institution’s health surveillance requirements and data and adverse event reporting requirements.
- Final IBC approval occurs after RAC review.

An *ad hoc* scientific review committee appointed by the SOM VP/Dean will:

- Assess the scientific and medical relevance and merit of the protocol.
- Assess the risk/benefits to subjects and others
- Review the existing knowledge of the disease state and current therapy, route of administration, dose, and vector virulence.

- Recommend information to be provided to family and other caretakers pertaining to potential risks and precautions to be stated in either a separate document or in the consent form.
- Recommend additional information the IRB-HSR may wish to have included in the consent form pertaining to potential risks to subjects.
- Recommend additional information the IBC may wish to have included in the Biosafety Manual and RAC registration.
- Communicate assessments to the IBC and IRB-HSR.

**Additional approvals will be required from the following committees or bodies:**

UVA School of Medicine Clinical Trials Office (CTO) will:

- Review the Case Report Forms to verify they are clear, concise and accurate according to the Protocol, Consent Form and Appendix M.
- Verify that procedures are adequate to oversee management of data.
- Review the Monitoring Plan

**Additional approval may be required by the GCRC Advisory Committee if the subjects will be admitted to an inpatient unit.**

UVA General Clinical Research Center (GCRC) Advisory Committee will:

- Review the document entitled [“Biosafety Manual and Standard Procedures for the Transfer of Recombinant DNA Molecules Into Human Subjects”](#) to confirm it accurately reflects the Protocol, Consent Form and Appendix M.
- Verify that all GCRC personnel who will be working on this protocol have been trained.

**Additional approval may be required by the UVA Cancer Center Protocol Review Committee if the protocol has an inclusion criterion stating the participants must have cancer and the protocol is NOT sponsored by the NIH, ACS, DOD, NSF or a Cancer Cooperative Group.**

UVA Cancer Center Protocol Review Committee will:

- Review the scientific relevance of the study in cancer patients.
- Review the quality of the study design, including entry criteria, patient assessment and follow-up, toxicity assessment and dose modification criteria, and biostatistical analytical plan.
- Verify that the Protocol and Consent Form accurately reflect the study as outlined in Appendix M.

Please Note:

- The RAC requests that the IRB-HSR and IBC provide documentation of Pending Approval. The modifications required prior to final approval must include RAC approval. The protocol must be reviewed by the full board of the IRB – HSR before a pending or approval status is given.

- No study participants may be enrolled until approval to enroll subjects is granted by the IRB-HSR and the PI/sponsor has obtained an IND from the FDA.
- The mechanism for submittal and approval of study protocols is outlined in the procedures section below.

Additional information regarding the review committees or bodies can be found on their Web sites:

- NIH Office of Biotechnology Activities: <http://www.nih.gov/od/oba/>
- IRB-HSR: <http://www.virginia.edu/vprgs/irb/>
- Institutional Biosafety Committee: [https://vprgsecure.web.virginia.edu/bio/ibc\\_webintro.cfm](https://vprgsecure.web.virginia.edu/bio/ibc_webintro.cfm)
- Cancer Center Protocol Review Committee: [http://www.healthsystem.virginia.edu/internet/cancer-research/clinical\\_trials/prc/](http://www.healthsystem.virginia.edu/internet/cancer-research/clinical_trials/prc/)
- GCRC: <http://www.healthsystem.virginia.edu/internet/gcrc/>
- UVA Pharmacy: <https://www.healthsystem.virginia.edu/intranet/pharmacy-services/home.cfm>
- School of Medicine Clinical Trials Office: <http://www.healthsystem.virginia.edu/internet/cto/>

## **D. PROCEDURES**

### **New Application**

1. Write the protocol and consent using the IRB-HSR Protocol Builder application found at [www.irb.virginia.edu](http://www.irb.virginia.edu).
2. The protocol must include an appendix which includes the documents listed in OBA-RAC Appendix M (see Appendix M-I-A), which can be found at [http://www4.od.nih.gov/oba/rac/guidelines\\_02/Appendix\\_M.htm#\\_Toc7255838](http://www4.od.nih.gov/oba/rac/guidelines_02/Appendix_M.htm#_Toc7255838). Appendix M is part of “[NIH Guidelines: Recombinant DNA and Gene Transfer.](#)” The RAC application requires information about the disease under study, vector being used, and nature of the proposal in addition to other items. The NIH review process is open to the public so proprietary information should be withheld.
3. Submit the protocol to the IRB-HSR, the IBC and the SOM Office of Research. The SOM Dean will appoint an ad-hoc committee to complete additional scientific reviews of the protocol.
4. The IRB-HSR will not grant a pending approval until they have received preliminary approval from the IBC.
5. When the Principal Investigator has received a pending approval from the IRB-HSR, he/she should then submit the application to OBA for RAC review. If the RAC review indicates areas of concern (e.g., novel vectors, unresolved health concerns, or other potential problems) the protocol will be selected for public review. RAC currently estimates that this public review process will occur for about 10% of submissions.

6. Following RAC review, submit revised protocol and consent forms, along with a copy of the RAC review comments for full committee review to the IRB-HSR, IBC, SOM Office of Research, and if applicable to the Cancer Center Protocol Review Committee and/or the GCRC Advisory Committee, Verify with each office regarding the number and type of copies required.
7. Personnel from the SOM Clinical Trials Office will review all applicable documents such as case report forms, data and safety monitoring plans etc.
8. After the IRB-HSR has obtained all applicable approvals, the Office of the Vice President for Research and Graduate Studies will be notified. They may ask questions, comment, or place a hold on the protocol.
9. Protocol approval will be given by the IRB-HSR only after the IRB-HSR has received approval and all required documentation from all other committees or bodies.
10. Following IRB-HSR approval, submit the application to FDA.
11. Notify the IRB-HSR 30 days following the FDA submission if the FDA has not put the Investigational New Drug Application (IND) on clinical hold.
12. At that time the IRB-HSR will grant approval to enroll subjects.

#### **Monitoring of Protocol After Approval**

IRB-HSR: Quarterly Status Report for first year, then every 6 months. A copy of the annual report and any other correspondence to the FDA/NIH regarding this protocol should be submitted with the Status Report. Adverse events should be reported to the IBC.

IBC: A copy of the annual report to the FDA/NIH must be submitted concurrently to the IBC. Adverse events will be reviewed and reported to the Office of Biotechnology Activities at the NIH.

School of Medicine Clinical Trials Office: Protocol compliance and periodic review of completion of Case Report Forms.

Cancer Center Protocol Review Committee: (if applicable) 6-month status reports summarizing enrollment data, changes to the protocol and unexpected toxicities.

Gene Transfer Oversight Committee: a group made up of at least one person each from IRB-HSR, IBC, SOM CTO, SOM Research Office, GCRC Advisory Committee and the Cancer Center Protocol Review Committee will meet at least once a year to review this policy and related compliance issues.

For additional information see <http://www4.od.nih.gov/oba/Rdna.htm>

**Policy History**: Implemented January 1, 2002. Revised January 25, 2008