

SRS#	Prev. SRS#	Wet Bench#	IACUC#	CIRB/COMIRB#
TITLE:				

**SUBCOMMITTEE ON RESEARCH SAFETY
PROTOCOL ACTION FORM**

for

Initial Reviews ♦ Annual/Continuing Reviews ♦ Major/Minor Amendments ♦ Personnel Changes ♦ Closures

VA Principal Investigator	
Name :	e-mail :
Main Investigator (if different from above)	
Name :	e-mail :
Regulatory Contact	
Name :	e-mail :

WHAT SRS ACTION ARE YOU INITIATING BY THE SUBMISSION OF THIS FORM?

(Please check all appropriate boxes)

NEW SUBMISSION/INITIAL REVIEW

ANNUAL/CONTINUING REVIEW

I am submitting this protocol without significant changes* and requesting the SRS to review the same. My RPSS is on file, it is accurate, and reflects my current research.

*non-significant changes include changes not requiring SRS purview such as changing non-SRS related consent wording or adding animal numbers to an existing animal protocol.

*NOTE: If your protocol involves rDNA work, you must submit, along with this document, an **Annual Review of Approved rDNA in VA Research Form** (attached at the back of this document). This includes performance by VA RESEARCH PERSONNEL of PCR for genotyping or cDNA generation for Microarray Analysis.*

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AMENDMENT(S) (check all that apply)

There have been personnel changes as listed in the brief description below.

I am informing the SRS of non-personnel related changes in this protocol as outlined in the in the brief description below:

I wish to make *significant* changes in this protocol by adding or removing the use of any of the agents listed below, as described in attached documents and/or in the brief description below. *Submission of this form with significant changes also requires the submission of an updated RPSS.*

Radiation Materials
 Recombinant DNA
 Controlled Substances

Biohazards
 Hazardous Chemicals

Briefly describe the modifications proposed to amend the existing RPSS:

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CLOSURE - My current research for this protocol is closing.

- All patient activities are complete at all sites
- Data analysis is complete for entire protocol
- Protocol is being closed at COMIRB/ IACUC

IF YOU HAVE NOT CHECKED ALL BOXES ABOVE, YOU SHOULD NOT CLOSE THIS STUDY AT EITHER COMIRB, IACUC, OR SRS.

Yes **Radioactive Materials linked to this study still exist.**
 No If yes, contact the facility Radiation Safety Officer (RSO), to have
 NA materials collected.

Yes **Human Samples (blood, tissue, saliva, excreta) linked to this study
still exist.**
 No If yes, contact Don Lawrence, Safety Officer, to have materials
 NA collected.
***One exception would be samples archived or banked at a Central
Repository OTHER THAN the VA and not involving VA employees
(including WOC employees)***

Yes **Controlled Substances linked to this study still exist.**
 No If yes, contact Don Lawrence, Safety Officer, to have materials
 NA collected.

Yes **Hazardous Chemicals linked to this study still exist.**
 No If yes, contact Don Lawrence, Safety Officer, to have materials
 NA collected.

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TITLE:

ADDITIONAL INFORMATION:

FUNDING SOURCE IN PLACE FOR STUDY: (VA Merit, NIH, Other, No Funding)	
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This study is	<input type="checkbox"/> VA only	<input type="checkbox"/> Multi-site study involving the VA
This study has	<input type="checkbox"/> IRB-Approved Local Enrollment	→ _____ total # enrolled
	<input type="checkbox"/> Veterans Enrolled Locally Since Last Review	→ _____ # enrolled since the previous annual review

VA PERSONNEL INVOLVED IN RESEARCH ACTIVITIES ON THIS PROTOCOL:

Please list all VA personnel (either directly employed by the VA or WOCs with other institutions) who will be performing research activities related to this protocol. Possible Roles include **Main PI, VA PI, Co-PI, Coordinator, Regulatory Contact, or Other**.

<u>Name</u>	<u>Role</u>	<u>Email</u>

Principal Investigator's Signature _____

Date: _____

SRS Chairperson's Signature _____

Date: _____

Safety Officer's Signature _____

Date: _____

Chair R & D Signature _____

Date: _____

Annual Review of Approved Recombinant DNA in VA Research

Subcommittee on Research Safety/Institutional Biohazard Committee

VA PI: _____ COMIRB#/IACUC#/Wet Bench# _____
Associated IACUC# (if wet bench w/o animals) _____

1. Is work utilizing recombinant DNA still ongoing in your laboratory?

YES ___ NO ___

If no, please indicate how materials or animals were eliminated from your laboratory and/or the VA Animal Facility _____

2. If work utilizing recombinant DNA is still ongoing in your laboratory, please indicate the specific categories of work in which this work falls.

___ PCR without cloning (e.g. assessing homozygosity of animal strain)

___ PCR and subsequent cloning of DNA fragments

___ Expression of cloned DNA in cultured cells (not including bacterial cells)

___ Expression of cloned DNA in transgenic mice (e.g. maintenance or production of transgenic animal strains)

3. If you work involved expression of recombinant DNA in cells or animals, please indicate below the source of the cloned DNA, the function of the protein, and if antibiotic resistance is imparted BY EXPRESSION OF THE CLONED DNA (not the vector).

Gene/Protein/Animal Name	Species of gene	Function of Gene Product
_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____

4. If you are working with recombinant DNA in transgenic mouse, please identify the NIH classification* (and brief description) for these recombinant DNA studies:

Gene/Protein/Animal Name	NIH Classification	Brief Description
_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____

*see attached FAQ for information about classifying your animals or rDNA experiments

Chair, Institutional Biohazard Committee (SRS) **Date**

Chair, Research & Development Committee **Date**

Facility Safety Officer **Date**

Transgenic Animals and the Use of Recombinant DNA in Animals

FAQs for Research Subject to the *NIH Guidelines*

1. Under which section of the *NIH Guidelines* does the generation of transgenic rodents fall?

The creation of transgenic rodents falls under one of two portions of the *NIH Guidelines* depending on the containment level required to house the rodents. Experiments involving the creation of transgenic rodents that can be housed under Biosafety Level 1 conditions are covered under **Section III-E-3**. Experiments involving the generation of transgenic rodents requiring BL2, BL3 and BL4 containment are covered under **Section III-D-4**.

2. Under which section of the *NIH Guidelines* does the generation of transgenic animals other than rodents fall?

The creation of all transgenic animals (other than rodents that can be housed under BL1 containment conditions) is covered under **Section III-D-4** of the *NIH Guidelines*.

3. Would the breeding of two different strains of knock-out mice require IBC approval under the *NIH Guidelines*?

The techniques used initially to create knock-out animals involve the stable introduction of recombinant DNA into the animal's genome, and thus these animals are considered transgenic. As the breeding of two different strains of knock-out mice will potentially generate a novel strain of transgenic animal, the work is covered under the *NIH Guidelines* and as such requires IBC review and approval. Sections in the *NIH Guidelines* that cover work with rodents include **III-E-3** for work that requires Biosafety Level (BL) 1 containment and **III-D-4** for work that requires BL2, BL3 and BL4 containment.

4. Is IBC registration and approval needed for the maintenance of a transgenic animal colony?

The maintenance of a transgenic rodent colony (i.e. breeding within a particular transgenic strain) at BL1 is an activity that is exempt from the *NIH Guidelines* and, as such, does not require IBC registration and approval. The maintenance of a transgenic rodent colony at BL2 or higher falls under **Section III-D-4-b** and requires IBC approval. The breeding of all other transgenic animals is subject to the *NIH Guidelines* under **Section III-D-4-a** or **III-D-4-b** depending on the containment level required.

5. Is the purchase and transfer of transgenic rodents exempt from the *NIH Guidelines*?

Under **Appendix C-VI** of the *NIH Guidelines*, the purchase or transfer of transgenic rodents may be maintained at BL1 containment are exempt from the *NIH Guidelines*. The purchase or transfer of transgenic rodents that require BL2 or higher containment is not exempt from the *NIH Guidelines*. These animals are covered under **Section III-D-4**, and purchase and transfer of such animals requires IBC registration and approval. It should be noted that the subsequent use of transgenic rodents may not be exempt from the *NIH Guidelines*. Experiments using transgenic rodents at BL1 are exempt from the *NIH Guidelines* if the experiment does not involve the use of recombinant DNA. If the protocol does involve the use of recombinant DNA or is conducted at BL2 or higher then the work falls under **III-D-4** of the *NIH Guidelines* and as such requires IBC review and approval prior to initiation.

6. Is the purchase and transfer of transgenic animals other than rodents exempt from the *NIH Guidelines*?

No, only the purchase or transfer of transgenic rodents that may be maintained at BL1 containment is exempt from the *NIH Guidelines*. The purchase or transfer of any other animal for research purposes at any biosafety level (including BL1) is not exempt, nor is the purchase and transfer of transgenic rodents that require BL2 or higher containment.

7. Are gene ablation studies covered by the *NIH Guidelines*?

The answer to this question depends on the technique employed in the study. If recombinant techniques are used to knock out the gene, then work would be covered under the *NIH Guidelines*.

8. Who has the responsibility to review the generation of transgenic animals if an institution is generating animals for investigators who are not affiliated with that institution?

The generation (creation) of transgenic animals is an activity covered under the *NIH Guidelines*. The IBC at the institution where that activity is occurring has the responsibility to review and approve that activity (if the institution is subject to the requirements of the *NIH Guidelines*). The subsequent use of the animals by investigators not at that institution would need to be reviewed and approved by the IBC at the investigator's institution if that institution conducts or supports recombinant DNA research that receives NIH support and the activity covered under the *NIH Guidelines*.

9. When a core facility generates transgenic mice as a "fee for service" for Principle Investigators (PIs), is it the responsibility of the PI or the core facility to register the generation of the mice with the IBC?

Section IV-B-7-a-(1) of the *NIH Guidelines* articulates one of the responsibilities of the PI as 'initiating no recombinant DNA research which requires IBC approval prior to initiation until that research has been approved by the IBC and has met all other requirements of the *NIH Guidelines*.' It would be acceptable for either the PI of the core facility or the PI purchasing the transgenic animals to fulfill the responsibility to register the generation of the animals. In many cases, the animals being generated will be subsequently used in experiments that are subject to the *NIH Guidelines*, and the registration of the research with the IBC may encompass both the generation and subsequent experimentation with the animals.

10. When existing transgenic animals at an institution are purchased or transferred to an investigator outside the institution, who should review and approve the use of these animals?

An institution's IBC does not need to review and approve the use of transgenic animals at another institution. If the receiving institution is subject to the *NIH Guidelines* (i.e. conducts or supports recombinant DNA research that receives NIH support), then the purchase and transfer of animals (other than rodents that can be housed under BL1 containment), along with any experiments subject to the *NIH Guideline*, would require review and approval by the IBC at that institution.

11. What are the *NIH Guidelines* requirements for research with large transgenic animals (sheep, pigs, etc.), or research with recombinant DNA microorganisms in such animals?

When conducting recombinant DNA work with large animals, the work is covered under Appendix Q of the *NIH Guidelines*. **Appendix Q** specifies containment and confinement practices when animals are of a size or have growth requirements that preclude the use of laboratory containment of animals. The *NIH Guidelines* include provisions for tracking and inventorying these animals (**Appendix Q-1-B-2** states that a permanent record must be maintained of the experimental use and disposal of each animal). Animal carcasses must be disposed of as to avoid their use as food for human beings or animals unless food use is specifically authorized by an appropriate federal agency (**Appendix Q-1-B-1**). An acceptable method, for example, would be incineration.

12. Are recombinant DNA modifications to the somatic cells of non-transgenic animals subject to the *NIH Guidelines*? Yes, these experiments are subject to the *NIH Guidelines*.

a) **Sections III-D-1-a** through **III-D-1-d** cover experiments using Risk Group 2, 3, 4, or restricted agents in whole animals. See the *NIH Guidelines* for the appropriate containment for such experiments

b) **Section III-D-4-a** covers experiments involving viable recombinant DNA-modified microorganisms tested on whole animals. DNA from any source except for greater than two-thirds of eukaryotic viral genome may be transferred to any animal and propagated under conditions of physical containment comparable to BL1 or BL1-N and appropriate to the organism under study.

c) **Section III-D-4-b** covers recombinant DNA, or DNA or RNA derived therefrom, involving whole animals, including transgenic animals that are not covered by **Sections III-D-1** or **III-D-4-a**. The appropriate containment for these experiments is determined by the IBC.

d) Experiments not included in **Sections III-A, III-B, III-C, III-D**.