

## FAQs for Research Subject to the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines): Genetically Modified (Transgenic) Animals and the Use of Recombinant or Synthetic Nucleic Acid Molecules in Animals*

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

The creation of transgenic rodents falls under one of two sections 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**.

### 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*.

### Would the breeding of two different lines of knock-out mice require IBC approval under the *NIH Guidelines*?

If the technique used to create the knock-out mice involves the stable introduction of recombinant or synthetic nucleic acid molecules into the animal's genome, the animals will be

considered transgenic. As the breeding of two different lines of knock-out animals will potentially generate a novel line of transgenic animal, the work may be covered under the *NIH Guidelines* and require 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. Certain breeding experiments are exempt under **Appendix C-VIII** the *NIH Guidelines*. This exemption covers the breeding of two different lines of transgenic rodents or the breeding of a transgenic rodent and a non-transgenic rodent with the intent of creating a new line of transgenic rodent that can be housed at BL1 if:

- (1) both parental rodents can be housed under BL1 containment; and
- (2) neither parental transgenic rodent contains the following genetic modifications: (i) incorporation of more than one-half of the genome of an exogenous eukaryotic virus from a single family of viruses; or (ii) incorporation of a transgene that is under the control of a gammaretroviral long terminal repeat (LTR); and
- (3) the transgenic rodent that results from this breeding is not expected to contain more

than one-half of an exogenous viral genome from a single family of viruses.

### 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 line) that can be housed 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.

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

Under **Appendix C-VII** of the *NIH Guidelines*, the purchase or transfer of transgenic rodents that may be housed under BL1 containment are activities that 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 research does not involve the use of recombinant or synthetic nucleic acid molecules. If the protocol does involve the use of recombinant or synthetic nucleic acid molecules then the work falls under **III-D-4** of

the *NIH Guidelines* and as such requires IBC review and approval prior to initiation.

### 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.

### 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 the work would be covered under the *NIH Guidelines*.

### 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 an investigator not at that institution would need to be reviewed and approved by the IBC at that investigator's institution if that institution conducts or supports research with recombinant or synthetic nucleic acid

molecules, receives NIH support for such research, and the activity covered under the *NIH Guidelines*.

**When a core facility generates transgenic mice as a "fee for service" for a Principal Investigator (PI), 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 or synthetic nucleic acid molecules 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.

**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. receives NIH support for research with recombinant or synthetic nucleic acid molecules), 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.

**What are the *NIH Guidelines* requirements for research with large transgenic animals (sheep, pigs, etc.), or research with recombinant or synthetic nucleic acid-modified microorganisms in such animals?**

When conducting research with recombinant or synthetic nucleic acid molecules in 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.

**Are recombinant or synthetic nucleic acid modifications to the somatic cells of non-transgenic animals subject to the *NIH Guidelines*?**

Yes, these experiments are subject to the *NIH Guidelines*.

• **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

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- **Section III-D-4-a** covers experiments involving viable recombinant or synthetic nucleic acid-modified microorganisms tested on whole animals. Recombinant or synthetic nucleic acid 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.
  - **Section III-D-4-b** covers recombinant or synthetic nucleic acid, 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.
  - Experiments not included in **Sections III-A, III-B, III-C, III-D, III-F**, fall into **Section III-E**. Experiments covered by **Section III-E** may be conducted at BL1 containment.

**For further information about the requirements of the *NIH Guidelines*, please email: [NIHGuidelines@od.nih.gov](mailto:NIHGuidelines@od.nih.gov).**