



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, III-F, fall into Section III-E. Experiments covered by Section III-E may be conducted at BL1 containment.

Animal experiments covered under the NIH Guidelines for Research Involving Recombinant DNA Molecules



ACTIVITY	MINIMUM BSL	SECTION
CREATION OF TRANSGENIC ANIMALS		
Creation of transgenic rodents	BL1	III-E-3
Creation of transgenic rodents	BL2 or higher	III-D-4-b
Creation of transgenic animals other than rodents	BL1/BL1-N	III-D-4-a
Creation of transgenic animals other than rodents	BL2/BL2-N or higher	III-D-4-b
Creation of recombinant DNA modified arthropods	BL1	III-D-4-a
Creation of recombinant DNA modified arthropods	BL2 or higher	III-D-4-b
Creation of knock-out rodents	BL1	III-E-3
Creation of knock-out rodents	BL2 or higher	III-D-4-b
BREEDING OF TRANSGENIC ANIMALS		
Breeding rodents from one strain (propagation/colony maintenance)	BL1	Exempt (III-F-4)
Breeding rodents from one strain (propagation/colony maintenance)	BL2 or higher	III-D-4-b
Breeding rodents from two strains (generating new strain)	BL1	III-E-3
Breeding rodents from two strains (generating new strain)	BL2 or higher	III-D-4-b
Breeding of transgenic animals other than rodents	BL1	III-D-4
Breeding of transgenic animals other than rodents	BL2 or higher	III-D-4
Breeding of recombinant DNA modified arthropods	BL1	Exempt (III-F-4)
Breeding of recombinant DNA modified arthropods	BL2 or higher	III-D-4-b
Breeding of knockouts (propagation)	BL1	Exempt (III-F-4)
Breeding of knockouts (propagation)	BL2 or higher	III-D-4-b
Breeding of knockouts from two strains (generating new strain)	BL1	III-E-3
Breeding of knockouts from two strains (generating new strain)	BL2 or higher	III-D-4-b
EXPERIMENTS WITH TRANSGENIC ANIMALS		
Experiments with transgenic rodents	BL1	III-D-4-a* (see note)
Experiments with transgenic rodents	≥ BL2 set by IBC	III-D-4-b
Experiments with transgenic animals other than rodents	BL1	III-D-4-a
Experiments with transgenic animals other than rodents	≥ BL2 set by IBC	III-D-4-b
Experiments with recombinant DNA modified arthropods associated with plants	BL1	III-E-2-b-(5).
Experiments with recombinant DNA modified arthropods associated with plants	BL2 or higher	III-E-2
Experiments with recombinant DNA modified arthropods not associated with plants	BL1	III-D-4-a
Experiments with recombinant DNA modified arthropods not associated with plants	BL2 or higher	III-D-4-b

*The purchase or transfer of transgenic rodents requiring BL1 containment is exempt under Appendix C-6. Subsequent use of these animals is also exempt providing the experimental protocol does not involve the use of recombinant DNA. If the protocol does involve the use of recombinant DNA then the research is covered under III-D-4-a. All experiments involving the use of other transgenic animals at any Biosafety Level and the use of transgenic rodents requiring BL2 or higher containment are subject to the *NIH Guidelines*. See above for applicable sections.

EXPERIMENTS WITH R-DNA IN AN ANIMAL (TRANSGENIC OR OTHERWISE)		
Experiments with r-DNA modified microbes in any animal (transgenic or otherwise)	BL1/BL1-N	Not permitted at BL1*
Experiments with RG2 r-DNA modified microbes in any animal (transgenic or otherwise)	BL2/ BL2-N	III-D-1-a
Experiments with RG3 r-DNA modified microbes in any animal (transgenic or otherwise)	BL3/ BL3-N	III-D-1-b
Experiments with RG4 r-DNA modified microbes in any animal (transgenic or otherwise)	BL4/BL4-N	III-D-1-c
Experiments with r-DNA modified restricted agent in an animal (transgenic or otherwise)	BL4/BL4-N	III-D-1-d
Experiments with r-DNA modified animal pathogens in an animal (transgenic or otherwise)	BL4/BL4-N	III-D-1-d
Introduction of less than 2/3 of eukaryotic viral genome into a non-human vertebrate or invertebrate	BL1/BL1-N	III-D-4-a
Propagation of animals containing viral vector sequences not leading to transmissible infection	BL1/BL1-N	III-D-4-a
Experiments with R-DNA involving whole animals not covered by Sections III-D-1 or III-D-4-a	Set by IBC	III-D-4-b
* Other than viruses which are only transmitted vertically, the experiments may not be conducted at BL1. A minimum of BL2 or BL2-N is required.		
CLONING ANIMALS		
Cloning animals	BL1 or higher	Not covered
PURCHASE OR TRANSFER OF TRANSGENIC ANIMALS		
Purchase or transfer of transgenic rodents	BL1	Exempt (Appendix C-6)
Purchase or transfer of transgenic rodents	BL2 or higher	III-D-4
Purchase or transfer of transgenic animals other than rodents	BL1	III-D-4
Purchase or transfer of transgenic animals other than rodents	BL2 or higher	III-D-4
Purchase or transfer of recombinant DNA modified arthropods	BL1	III-D-4
Purchase or transfer of recombinant DNA modified arthropods	BL2 or higher	III-D-4
PLANT EXPERIMENTS WITH ANIMALS OR ARTHROPODS		
Experiments with microorganisms or insects containing recombinant DNA with the potential for detrimental impact to ecosystems.	BL3-P or BL2-P plus biological containment	III-D-5-a or III-D-5-b
Experiments with exotic infectious agents in the presence of arthropod vectors	BL4-P	III-D-5-c
Experiments with microbial pathogens of insects or small animals associated with plants with the potential for detrimental impact to ecosystems.	BL3-P or BL2-P plus biological containment	III-D-5-e
Small animals associated with recombinant DNA-modified plants.	BL1	III-E-2
Experiments with rDNA-modified arthropods or small animals associated with plants	BL1	III-E-2-b-(5).
OTHER		
Transfer of a drug resistance to microorganisms compromising the use in veterinary medicine	Set by NIH (case by case)	III-A-1-a

The *NIH Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines)* are available at <http://www4.od.nih.gov/oba/rac/guidelines/guidelines.html>

For further information about the requirements of the *NIH Guidelines*, please visit the NIH Office of Biotechnology Activities web page at <http://www4.od.nih.gov/oba/> or write to us at oba@od.nih.gov