

Recombinant or Synthetic DNA Use in Animals: Understanding which activities require IBC review and approval and how to start the process



What activities are considered Recombinant or Synthetic DNA Molecule Use in Animals?

Generally speaking, any introduction of recombinant or synthetic nucleic acid (rDNA) molecules into an experimental animal falls under the scope of the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)*. Common examples of such activities include: the stable introduction of DNA into an animal's genome to produce a transgenic animal, breeding two strains of transgenic animals to produce an animal with a new genotype, exposing an animal to viral vectors for integration of rDNA molecules into somatic cells, and injecting a cell line or microorganism modified with rDNA molecules into an animal.

It is important to note that any rDNA molecule falls under these guidelines. There are no exemptions based on the level of risk posed by the rDNA molecule used. Be sure to consider fluorescent or luminescent markers, persistently expressed shRNA molecules and any vector sequences that might have integrated into the animal's genome when determining if your animal, animal cells and tissues, or agents contain rDNA molecules.

What activities using Recombinant or Synthetic Nucleic Acid Molecules in Animals require Institutional Biosafety Committee approval?

The Institutional Biosafety Committee (IBC) is charged with reviewing all research using rDNA molecules at Vanderbilt, including animal research, as outlined in the *NIH Guidelines*. However, the required timeline for review differs depending on the specific activity and the animal being used. Broadly speaking, animal experiments are separated into three categories:

1. experiments that require IBC approval before they are initiated,
2. experiments that require IBC notice simultaneous with initiation, and
3. experiments that are exempt from the *NIH Guidelines* and do not require IBC registration,

Knowing what level of review is required for your recombinant DNA use in animals will help you in planning future protocols and committee approval actions.

A representative list of animal experiments using rDNA molecules organized by IBC registration requirements is outlined in this document. A resource table outlining the specific applicable sections of the *NIH Guidelines* to these activities can be found at [this link](#).

Activities that Require IBC Approval Prior to Initiation

- Creation of transgenic or knock-out animals, other than rodents, made by stable introduction of foreign DNA
- Breeding of transgenic or knock-out animals, other than rodents, made by stable introduction of foreign DNA
- Purchase or transfer of transgenic or knock-out animals, other than rodents, made by stable introduction of foreign DNA
- Experiments in which rDNA molecules are administered to a transgenic animal
- Experiments in which viral vectors containing rDNA molecules are administered to any animal (transgenic or otherwise)
- Experiments in which cells modified by rDNA molecules, including cells isolated from transgenic animals, are administered to any animal (transgenic or otherwise)
- Experiments in which microbes modified by rDNA molecules are administered to any animal (transgenic or otherwise)

NOTE: This list focuses on experiments containing rDNA. Do not assume that experiments not listed here are free from requiring IBC approval. For example, experiments in which unmodified microbes are administered to animals also require IBC approval.

Activities that Require IBC Notice Simultaneous with Initiation

NOTE: Activities involving transgenic species other than rodents are not covered under this section. All activities involving transgenic species other than rodents require IBC approval prior to initiation. Please see "**Activities that Require IBC Approval Prior to Initiation**" section.

All of the activities below assume transgenic rodents, such as mice, hamsters, rats, and guinea pigs, which can be housed using ABSL-1 containment.

- Creation of transgenic rodents or knock-out rodents made by stable introduction of foreign DNA, including those made by the Vanderbilt Transgenic Core on your behalf.
- Breeding rodents from two strains (generating a new strain) providing either parental rodent contains the following genetic modifications:
 - incorporation of more than one-half of the genome of an exogenous eukaryotic virus from a single family of viruses; or
 - incorporation of a transgene that is under the control of a gamma retroviral long terminal repeat (LTR); or
 - the rodent that results from the breeding is expected to contain more than one-half of an exogenous viral genome from a single family of viruses

If your animal protocol includes either of the above activities, you will need to register the activity with the IBC. If you have an existing IBC registration, contact the VEHS Biosafety Team to assure that the activity is included in your registration and to determine if further IBC review and approval is needed.

Activities Exempt from the *NIH Guidelines*

NOTE: Non rodent transgenic animals, such as zebrafish or rabbits, are not covered by these exemptions. Information for activities involving non rodent transgenic species can be found in the “**Activities that Require IBC Approval Prior to Initiation**” section.

All of the exemptions below assume transgenic rodents, such as mice, hamsters, rats, and guinea pigs, which can be housed using ABSL-1 containment.

- Breeding rodents from one strain for colony maintenance
- Breeding rodents from two strains (generating a new strain) providing neither parental rodent contains the following genetic modifications:
 - incorporation of more than one-half of the genome of an exogenous eukaryotic virus from a single family of viruses; or
 - incorporation of a transgene that is under the control of a gamma retroviral long terminal repeat (LTR); and
 - the rodent that results from the breeding is not expected to contain more than one-half of an exogenous viral genome from a single family of viruses
- Purchase or transfer of transgenic rodents from a company or academic institution. NOTE: Purchase or transfer of transgenic animals other than rodents is not exempt.

Specific NIH guidance regarding the use of transgenic animals can be found at [this link](#).

Please plan ahead...

If your animal protocol includes (or you plan to add) any of these activities, please note that VEHS will not be able to close out the hazard review of the IACUC review process unless and until the IBC has reviewed and approved the activity. You can minimize the review time required by contacting the Biosafety Officer (Robin Trundy) during the planning stages of your study to get registration and review activities started as soon as possible. Please note that you must have an IACUC protocol under development or that has been previously approved (if adding activities) in order for the IBC review to be initiated. Also note that the IBC generally meets the fourth Tuesday of the month, and there is no expedited review process permitted under the *NIH Guidelines*.

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