



The ACC Connection

Volume 2, no.4, October 2006

WELCOME to the fifth edition of the *ACC Connection*, a quarterly newsletter designed to help researchers with questions regarding animal research at the University of Connecticut Health Center. Our fifth issue is designed to help you become familiar with the regulations involving recombinant DNA.

Federal Regulations – Recombinant DNA Work

All work with recombinant DNA must adhere to the *NIH Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines)*. This federal guideline can be found on the ACC website and can also be found at the following web link: <http://www4.od.nih.gov/oba/rac/guidelines/guidelines.html>. When institutions receive NIH funding for research involving recombinant DNA (rDNA) molecules, they must follow the provisions for containment and biosafety oversight set forth in the *NIH Guidelines*. Compliance with the *NIH Guidelines* is mandatory; failure to adhere to the *NIH Guidelines* can result in suspension or termination of NIH funding for this type of research or lead to a requirement for prior NIH approval of any or all rDNA projects at the institution. Compliance with the *NIH Guidelines* is critical to the safe conduct of research and to the fulfillment of an institutional commitment to the protection of staff, the environment, and public health.

Categories of Experiments Covered by the NIH Guidelines

The *NIH Guidelines* has established 6 categories of experiments utilizing rDNA:

III A: Requires IBC approval, RAC review, and NIH Director approval prior to initiation of experiments

These types of experiments cannot be initiated without submission of relevant information on the proposed experiments to the Office of Biological Activities (OBA), publication of the proposal in the Federal Register for 15 days of comment, review by the Recombinant DNA Advisory Committee (RAC), and specific approval by the National Institutes of Health (NIH). These types of experiments would include the deliberate transfer of a drug resistance trait to microorganisms that are not known to acquire the trait naturally.

III B: Require OBA approval and IBC approval prior to initiation of experiments

These types of experiments require containment conditions that will be determined by OBA. Types of experiments would include those that have a deliberate formation of rDNA containing genes for the biosynthesis of toxin molecules lethal for vertebrates at an LD₅₀ of ≤ 100 ng/kg.

III C: Requires IRB, IBC, and RAC review before participant enrollment

Any experiment involving the deliberate transfer of rDNA, or DNA or RNA derived from rDNA, into human research subjects would fall into this category.

III D: Requires IBC approval before initiation of experiments

This group would include using Risk Group (RG) 2,3,4, or restricted agents as Host-Vector systems; experiments in which DNA from RG2, RG3, RG4, or restricted agents is cloned into nonpathogenic prokaryotic or lower eukaryotic host-vector systems; experiments involving the use of infectious DNA or RNA viruses or defective DNA or RNA viruses in the presence of helper virus in a tissue culture system; experiments involving whole animals and plants requiring RG2 or higher containment; and experiments involving >10 liters of culture.

III E: Requires IBC notification simultaneous with initiation of experiments

This group would include experiments involving the formation of rDNA molecules containing no more than $\frac{2}{3}$ of the genome of any eukaryotic virus; experiments involving rDNA-modified whole plants, and the generation of transgenic rodents- including the crossing of 2 previously-generated transgenic rodents.

III F: Exempt from NIH Guidelines

This group would include experiments in which the rDNA is not in an organism or virus; those that consist entirely of DNA segments from a single non-chromosomal or viral DNA source though one or more of the segments may be a synthetic equivalent; those that consist entirely of DNA from a prokaryotic host including its indigenous plasmids or viruses when propagated only in that host or when transferred to another host by well-established physiological means, those that consist entirely of DNA from a eukaryotic host when propagated only in that host; those that consist entirely of DNA segments from different species that exchange DNA by known physiological processes though one or more of the segments may be a synthetic equivalent, and those that do not present a significant risk to health or the environment as determined by the NIH Director and the RAC.

Responsibilities when using rDNA

Institutional Responsibilities

1. Establish and implement policies that provide for the safe conduct of rDNA research and ensure compliance with the NIH Guidelines.
2. Establish an Institutional Biosafety Committee (IBC).
3. Establish a biosafety officer (BSO) if the institution either conducts rDNA at BSL-3 or BSL-4; and/or engages in large scale (>10 liters) research.
4. Appoint at least 1 individual with expertise in plant, plant pathogen, or plant pest containment principles if it conducts rDNA research in plants.
5. Appoint at least 1 individual with expertise in animal containment principles if it conducts rDNA research in animals.
6. Ensure that when the institution participates in or sponsors rDNA research involving human subjects, it complies with all NIH Guidelines regarding human subject protection.
7. Assist and ensure compliance with NIH Guidelines by PIs conducting the research.
8. Ensure appropriate training for IBC members, PIs, and laboratory staff regarding laboratory safety and the implementation of the NIH Guidelines.
9. Determine the necessity for health surveillance of personnel working with rDNA.
10. Report any significant problem, violations of the NIH Guidelines, or significant research-related accidents to OBA.

IBC Responsibilities

1. Reviewing rDNA research for compliance with the NIH Guidelines.
2. Notifying the PI of results of IBC review.
3. Lowering containment levels for certain experiments as detailed in the NIH Guidelines.
4. Setting containment levels as specified by the NIH Guidelines.
5. Periodically reviewing rDNA research at the institution.
6. Adopting emergency plans covering accidental spills and personnel contamination resulting from rDNA work.
7. Reporting any significant problem, violations of the NIH Guidelines, or significant research-related accidents to OBA.
8. Not authorizing the initiation of experiments which are not explicitly covered by the NIH Guidelines until the NIH establishes the containment requirements.

BSO Responsibilities

1. Periodic inspections to ensure laboratory standards are vigorously followed.
2. Reporting to the IBC any significant problem, violations of the NIH Guidelines, or significant research-related accidents.
3. Developing emergency plans covering accidental spills and personnel contamination resulting from rDNA work.
4. Providing advice on laboratory security.
5. Providing technical advice to PI and IBC on research safety procedures.

PI Responsibilities

1. Do not initiate or modify any rDNA research with requires IBC approval prior to the initiation of such research until approval is received.
2. Report to the IBC any significant problem, violations of the NIH Guidelines, or significant research-related accidents.
3. Determine whether experiments are covered by Section III E and ensure that appropriate procedures are followed.
4. Report any new information bearing on the NIH Guidelines to the IBC.
5. Be adequately trained in good microbiological techniques.
6. Adhere to IBC emergency procedures.
7. Comply with shipping requirements for rDNA molecules.

Recombinant DNA Advisory Committee (RAC)

The RAC is a committee that is responsible for carrying out function specified in the [NIH Guidelines](#). It consists of not less than 15 voting members appointed under the procedures of the NIH and DHHS. A majority of the voting members must be knowledgeable in relevant fields (microbiology, molecular medicine, etc.) and at least 4 members must be knowledgeable in fields such as public health, lab safety, ethics, or law. This committee has numerous responsibilities, including:

1. Advises the NIH Director on adopting changes to the [NIH Guidelines](#), assigns containment levels, promulgates and amends list of classes of rDNA molecules to be exempt from the [NIH Guidelines](#), and certifies new host-vector systems.
2. Identifies novel human gene transfer experiments deserving of public discussion by the full RAC.
3. Transmits to NIH Director specific comments/recommendations about specific human gene transfer experiments or categories of human gene transfer experiments.
4. Public review of human gene transfer clinical trial data and relevant information evaluated and summarized by NIH/OBA.
5. Identifies broad scientific, safety, social, and ethical issues relevant to gene therapy research.
6. Identifies moral, social, and ethical issues relevant to specific human applications of gene transfer.

Office of Biological Activities (OBA)

OBA is the Office in the NIH that has oversight for all research utilizing recombinant DNA molecules. It has numerous responsibilities, including:

1. Monitoring scientific progress in human genetics research in order to anticipate future developments in basic and clinical research involving rDNA.
2. Managing the operation of, and providing analytical support to, the RAC, DHHS Secretary's Advisory Committee on Genetics, Health, and Society and the DHHS Secretary's Advisory Committee on Xenotransplantation.
3. Coordinating with the federal and non-federal national and international organizations concerned with rDNA.
4. Providing advice to the NIH Director, other federal agencies, and state regulatory organizations concerning rDNA research.
5. Responding to requests for information on highly technical matters and matters of public policy related to rDNA, human gene transfer, genetic technologies, and xenotransplantation.
6. Developing and implementing NIH policies and procedures for the safe conduct of rDNA activities and human gene transfer.
7. Developing registries of activities related to rDNA research and human gene transfer.
8. Reviewing and approving experiments involving the cloning of genes encoding for toxin molecules that are lethal for vertebrates at an LD50 of ≤ 100 ng/kg.

Frequently Asked Questions

I have two transgenic rodents that I want to breed. What category does this fall into?

The creation of a new transgenic rodent by breeding two strains that can be housed under BSL-1 conditions are covered under section III E of the [NIH Guidelines](#) and must be registered with the IBC at the time the experiment is initiated. The creation of a new transgenic rodent by breeding two strains that require BL-2, BL-3, or BL-4 containment are covered under Section III D of the [NIH Guidelines](#) and require IBC approval prior to initiation.

I am performing an experiment where cells previously transfected with rDNA are being adoptively transferred into rodents. What category does this fall into?

This type of experiment is covered under Section III D of the [NIH Guidelines](#) and requires IBC approval prior to initiation.

I am performing an experiment in which established mouse lymphoma cells carrying an expression plasmid expressing chicken ovalbumin are injected into mice. What category does this fall into?

This type of experiment is covered under Section III D of the [NIH Guidelines](#) and requires IBC approval prior to initiation.

I am performing an experiment in which cells are harvested from a transgenic rodent and transferred into an unlike rodent strain. What category does this fall into?

This type of experiment is covered under Section III D of the [NIH Guidelines](#) and requires IBC approval prior to initiation.

If you have questions you'd like to see answered in future issues, please send them to pohl@uchc.edu and we will do our best to answer as many questions as possible.

Upcoming Training, October 2006 – December 2006

New animal Users Initial Basic Core Training

Monday, October 23	9:00 am – 12:00 pm	Building 20 conference room
Monday, November 20	9:00 am – 12:00 pm	Building 20 conference room
Monday, December 18	9:00 am – 12:00 pm	Building 20 conference room

New Institutional, State, or Federal Regulations

Institutional

ACC Policy	7/27/06	Training New ACC Members. To view policy, go to: http://clacc.uchc.edu/ACC/Policies/TrainIACUC.htm
ACC Policy	7/27/06	Semi-Annual Program Review. To view policy, go to: http://clacc.uchc.edu/ACC/Policies/SemiAnnual.htm
ACC Policy	7/27/06	Animal Training Requirements. To view policy, go to: http://clacc.uchc.edu/ACC/Policies/AnimalTrainRequirements.htm
ACC Policy	7/27/06	Inter-Agency IACUC Reviews. To view policy, go to: http://clacc.uchc.edu/ACC/Policies/InteragencyIACUCReviews.htm

State

None

Federal

USDA Animal Care Policies #3 and #17 revisions, effective 8/18/06 and 8/25/06 respectively. To view new policies, go to: <http://www.aphis.usda.gov/ac/polmanpdf.html>.

The January 2007 edition of The ACC Connection will start as a bi-monthly publication rather than quarterly. We hope this will further help our animal research investigators at the Health Center.



Next Issue: Animal Rights Activists

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