Using recombinant or synthetic Nucleic Acids (r/s NA) or Hazardous Materials with Animals. 7/2017

The UCHC is required, as a condition of both institution-wide and individual PIs' funding, to comply with the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* (a.k.a. *NIH r/s NA Guidelines).* Use of r/s NA must be either registered with the UCONN Health Institutional Biosafety Committee (IBC) or judged exempt as specified in the *NIH r/s NA Guidelines.* The contact person for doing this is the IBC Coordinator, Dr. Ron Wallace (rwallace@uchc.edu, x3781), who can also tell you if your experiment is exempt or not. Sometimes people look at experiments and because they see they are safe (e.g., BSL-1 or materials are supplied in a commercial kit) they reason that they are exempt to the NIH r/s NA Guidelines. This is not always the case. Frequently enough, safe experiments are not exempt.

Your IACUC Protocol will be reviewed for human occupational health, safety and compliance issues by the IBC Coordinator, who is also the Biological Safety Officer (BSO) and a Chemical Safety Specialist who looks for chemical hazard issues. Those IACUC protocols that have human occupational health, safety and/or compliance issues must be approved by the safety reviewers before the IACUC will grant approval. These issues will mainly be for *in vivo* experiments, which are the purview of the IACUC. Occasionally, *in vivo* issues transfer into the lab for *in vitro* analysis. Those *in vitro* issues that originate *in vivo* will also be addressed by the safety reviewers. You will be notified by the IACUC after the Committee meeting if such issues exist in your IACUC protocol and asked to contact the safety reviewer with information, clarifications, to fill out an application for the IBC, or to fill out an IACUC Safety Protocol (IACUC SP). If you anticipate issues with hazardous materials and contact the BSO for biological issues or the Chemical Safety Specialist for chemical issues, it may facilitate the approval of your IACUC protocol. You do not need to wait to submit your IACUC protocol, IACUC SP or IBC registration based on prior submission of any of the other two submissions. They can all be reviewed and processed simultaneously. However, by policy, approval of the IACUC protocol waits for approval of the IACUC SP and/or IBC registration.

There is a section in the IACUC protocol application that requests information regarding experiments that involve r/s NA in animals. Please read this carefully and answer the questions. This will alert the BSO that an IBC registration will be needed, or not, and often supply information to organize the IBC registration application if one is needed. Filling out the registration within the IACUC protocol for recombinant animals created at UConn Health actually constitutes the IBC registration.

Please note that the IBC is a separate committee from the IACUC. It is possible that you will be asked to fill out both forms for the IACUC SP and for an IBC registration. There has been confusion, because the BSO collaborates with PIs or designees for both committees, that after the BSO was encountered once, all of the requirements had been met. You may need both an IACUC SP and an IBC registration. Please see that all of the requirements listed by the IACUC in their review are addressed by their respective committees. If you have questions, contact the BSO (rwallace@uchc.edu). As mentioned above, IBC approval for r/s NA issues in an IACUC protocol is required before the IACUC will approve the IACUC protocol.

Below are a *partial* list of experiments typical to IACUC protocols (and modifications) related to their exempt or non-exempt status in the *NIH r/s NA Guidelines* and another *partial* list of experiments that need an IACUC SP. Even if you know that your experiment is exempt, please document how this is true under the *NIH r/s NA Guidelines* in the recombinant section in your IACUC protocol. If the BSO agrees, the BSO will not need to contact you for verification and documentation.

Partial list of experiments typical to IACUC protocols (and modifications) related to their exempt or non-exempt status in the *NIH r/s NA Guidelines*

Description of Experiment or Procedure	***Needs IBC Regis-tration***	***Exempt to NIH r/s NA Guide-lines***	***Notes for IACUC Protocol; refers to fields in the IACUC Protocol Application***
Recombinant (Tg/GT) rodent(s) will be constructed for you in the GTTF at UCONN Health. OR You will construct your recombinant rodent in your lab at UCONN Health.	X		Fill out the table of all of your Tg/GT lines and indicate they were or will be constructed in the GTTF or your lab. Then fill out the form below the table in the IACUC protocol which is your IBC registration.
Tg/GT rodents will be acquired from a *domestic* institution or vendor.		X	Fill out the table of all of your Tg/GT lines and indicate where they were constructed and from where acquired.
Tg/GT rodents will be acquired from an institution or vendor *outside the USA.*	Depends	Depends	Fill out the table of all of your Tg/GT lines and indicate where they were constructed and from where acquired. If they were originally constructed in the US, they should be exempt. If they were constructed and acquired from outside the USA they need to be registered in the form below the table.
You will cross a Tg/GT rodent line with another Tg/GT line or a non-recombinant strain. With certain exceptions involving virus sequences, crosses are now exempt. If no viral sequences are present in the recombinant inserts of either parent, they are definitely exempt. However there are exceptions to the exemptions. See NIH r/s NA Guidelines, Appendix C-VIII for the conditions of exemption.	Depends	Depends	In the table of all your Tg/GT lines, make sure the parental lines and progeny lines are listed. Indicate whether or not they contain eukaryotic viral sequences.
You will transfer uninfected, untransfected, untransduced, non-Tg/GT, non-recombinant eukaryotic cells into animals. If cells are human, see table below.		X	Please state in your IACUC protocol that the transferred cells are *recombinant* or *not recombinant.* Indicate if they are *infected or human*.
You will introduce r/s NA into animals, either directly or using viral vectors	X		Please indicate this in the r/s NA section of your IACUC protocol.
You will transfer recombinant cells (containing r/s NA introduced by any means) or that come from a Tg/GT animal, into other animals.	X		Please indicate this in the r/s NA section of your IACUC protocol.
You will infect animals with recombinant infectious agents.	X		Please indicate this in the r/s NA section of your IACUC protocol and on the Hazard List
You will transfer, non-recombinant untransfected, untransduced hESC into animals (see table below)		X	Please indicate this in your IACUC protocol. SCRO approval is required.
You will transfer recombiant hESC (containing r/s NA introduced by any means) into animals. (see table below)	X		Please indicate this in the r/s NA section of your IACUC protocol. SCRO approval is required.
You will transfer iPSC (all considered recombinant unless shown to have lost reprogramming vector) into animals.	X		Please indicate this in the r/s NA section of your IACUC protocol. SCRO approval is required.

Exemptions for Tg/GT animals are in Section III-E-3 and Appendix C-VII and -VIII in the NIH r/s NA Guidelines. Most of the transfer of recombinant materials into animals experiments fall under Section III-D-4 of the NIH r/s NA Guidelines.

Partial list of experiments typical to IACUC protocols that need safety documentation: either a description in the IACUC protocol, or an IACUC SP (independent of an IBC registration).

Description of Experiment or Procedure	***Needs IACUC.SP***	***Notes for IACUC Protocol***
Use of paraformaldehyde or formalin (carcinogen, sensitizer) in perfusion or fixation,	No	Check 'yes' for aldehyde use in Section 10 of the IACUC protocol. Fill out the sections that generate after checking 'yes'.
Use of anesthetic gasses (e.g., isoflurane) with a chamber, or vaporizer	No	Check 'yes' for isoflurane use in Section 10 of the IACUC protocol. Fill out the sections that generate after checking 'yes'.
Use of toxicologically hazardous or uncharacterized chemicals in animals.	Often	Check 'yes' for hazardous chemicals in Section 10 of the IACUC protocol. Enter this chemical in the hazard list. Wait for or contact the chemical safety specialist to determine what risk this chemical poses and whether an IACUC-SP needs to be written
Use of ionizing and non-ionizing radiation producing instruments and/or radioactive materials (RAM).	Yes for RAM	These issues are listed in a series of questions in section 10. Check ' yes' by the appropriate box and fill out the sections that generate after checking 'yes'.
Use of human or non-human primate tissues, blood or body fluids, including cultured human cell lines (e.g., hESC, iPSC, HeLa, HEK, etc.) for transfer into animals or any other purpose.	Yes, a chemical or biological safety protocol	Human or non-human primate materials are risk group 2 and animals that receive them are housed in containment. Typically, if animals receive only human materials they are housed in ABSL-2 and require a biological safety protocol. If animals receive both human materials and hazardous chemicals the animals are housed in chemical isolation and require a chemical safety protocol that includes the human materials in the list of hazards.
Use in animals of organisms or viruses pathogenic for humans, animals or plants. This includes recombinant organisms and viruses and most viral vectors, even if replication incompetent	Yes	Please indicate the genus/species and strain(s) of the organism(s) or virus(es) and the time course of infection and clearing. You may also be required to register your lab with the CT Department of Public Health.
Use of disease carrying vectors (arthropods, etc.)	Yes	Please specify species/strain of vector and containment conditions.

A positive answer in both tables generally means that both requirements will need to be fulfilled. Two separate committees, the IBC and the IACUC are involved. The IBC meets monthly (http://research.uchc.edu/rcs/ehs/biosafety/ibc-meeting-dates/) and you may prepare the IBC registration in advance or in parallel with the IACUC protocol and IACUC Safety Protocol. Please contact the BSO for forms, details and answers to questions about this. In addition, if hESC or iPSC are involved, please allow time for consideration by the SCRO (committee).