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Section 3: Protocol/Modification Submission and Review

3.0 Submissions

The IBC is responsible for overseeing and evaluating all aspects of research involving recombinant or synthetic nucleic acid molecules and biohazardous materials, agents and toxins, and is charged with reviewing proposals that involve recombinant or synthetic nucleic acid molecules and biohazardous materials, agents and toxins to ensure that the criteria established in the IBC Policy and the federal regulations and guidelines are implemented. In its review of the proposals, the primary goal of the IBC is to facilitate research personnel compliance with applicable laws, regulations, guidelines and policies consistent with the performance of appropriate and productive scientific endeavors.

IBC protocol submissions, whether they are new IBC protocol submissions, modifications or renewals, must be submitted through the IRBNet system by the Principal Investigator for review and IBC approval. No research involving recombinant or synthetic nucleic acid molecules and biohazardous materials, agents and toxins can be initiated until the Principal Investigator has received the approval of the IBC.

Although federal regulations allow exemptions for some types of recombinant or synthetic nucleic acid molecules used, the Principal Investigator must submit an application for all projects using recombinant or synthetic nucleic acid molecules and biohazardous materials, agents and toxins so that the IBC is aware of the activities and can verify that they are exempt. For more information on exemptions visit: https://osp.od.nih.gov/biotechnology/faqs-about-experiments-that-are-exempt-from-the-nih-guidelines/

No one shall obtain or use recombinant or synthetic nucleic acid molecules and/or biohazardous materials, agents and toxins until the protocol has been approved by the IBC. Modifications to approved protocols shall not be implemented until approved by the IBC.

3.0.1 Who can be a Principal Investigator?

Principal Investigators (PIs) can submit applications to the IBC to work with recombinant or synthetic nucleic acid molecules and/or biohazardous materials, agents, and toxins. In general, a PI is a tenured, tenure track, or research faculty member with assigned

research space. Should a PI not have assigned space to conduct the research, the PI must submit the below statement from the person who is responsible for the research space. Exceptions to this policy will be considered by the IBC on a case-by-case basis.

Acknowledgement Statement
I, [insert name of person with assigned research space] am aware of the attached research of [insert name of PI without assigned space] that will be conducted in space assigned to me. I acknowledge my responsibility for ensuring that this research will be conducted in a safe manner and in accordance with institutional and federal regulations.

3.1 Experiments Requiring IBC Review
Experiments that require IBC review include, but are not limited to:

- Studies using recombinant or synthetic nucleic acid molecules that are exempt from the *NIH Guidelines*.
- The deliberate transfer of a drug resistance trait to micro-organisms that are not known to acquire the trait naturally.
- The deliberate transfer of recombinant or synthetic nucleic acid molecules or DNA or RNA derived from recombinant or synthetic nucleic acid molecules into human research participants (human gene transfer).
- The deliberate formation of recombinant or synthetic nucleic acid molecules containing genes or sequences for the biosynthesis of toxin molecules.
- The use of RG-2 or RG-3 agents as host-vector systems.
- The use of human etiologic and animal viral etiologic agents.
- The cloning of DNA from RG-2 or greater agents into non-pathogenic prokaryotes or lower eukaryotic host-vector systems.
- The use of infectious or defective RG-2 or greater agents.
- Whole animals in which the animal's genome has been altered by stable introduction of recombinant or synthetic nucleic acid molecules or DNA derived into the germ-line (transgenic animal).
- Viable micro-organisms or cell lines with modified recombinant or synthetic nucleic acid molecules - tested on whole animals.
- Genetically engineered plants by recombinant or synthetic nucleic acid molecules methods.
- More than 10 liters culture of organisms or cells containing recombinant or synthetic nucleic acid molecules in a single vessel.
- The formation of recombinant or synthetic nucleic acid molecules containing one-half or more of the genome of a eukaryotic virus or from the same virus family.
- Experiments using BSL-1 or BSL-2 containment.
- Non-recombinant research using biohazardous materials, agents or toxins.
- All research using biological toxins or bioactive derivatives or subunits of toxins.
- Research collecting or analyzing human or non-human primate cell lines, tissues, fluids or other potentially infectious material.

3.2 New Submissions
Protocol application forms for research, teaching, and testing activities involving recombinant or synthetic nucleic acid molecules and/or biohazardous materials, agents, or toxins must be accurately completed and submitted for review and IBC approval.

Requirements for Review and Approval:

- To facilitate the review of protocols, Principal Investigators submitting IBC protocols will have their labs inspected and they must have access to the DU Lab Biosafety Manual. This manual will be posted on the website – either EHS and IBC) The BSO as part of the annual lab inspection will verify access to the biosafety manual and document that labs were inspected. Upon submission, the IBC Administrator will review the protocol for completeness and it may be necessary for the Principal Investigator to submit additional information, to ensure a complete submission, if requested.
- Additional IBC protocols may be required based on the nature of the activities described in the protocol.
- The protocol will be assigned to designated reviewers (see Section 2.2) for review prior to a convened IBC meeting. It may be necessary for the Principal Investigator to submit additional information and/or clarifications if requested by the designated reviewers.
- Approval/Non-approval will be determined by the IBC, and the Principal Investigator will be notified of the decision.
- For submission deadlines and meeting dates visit: http://www.du.edu/orsp/research-compliance/biosafety/new-index.html
- The protocol application forms are available at: **http://www.irbnet.org**

Principal Investigators will need to register in the IRBNet electronic submission system before access to any IBC application forms are made available and a IRBNet protocol number is assigned. “How To” instructional guides are available in the IRBNet IBC “Forms and Templates” tab that provide step-by-step instructions on how to register and utilize the IRBNet system. Once a protocol number has been assigned, that can be used to reference the study with the Office of Research & Sponsored Projects (ORSP) for grant applications.

3.3 Periodic Assessments / Annual Post Approval Monitoring (PAM)

The Principal Investigator is required to meet annually with the IBC Administrator to conduct Post Approval Monitoring. The Principal Investigator will be notified of annual deadlines for scheduling the PAM meeting. The full committee reviews all PAM reports of protocols with significant changes. PAM reports without changes or with non-significant changes may be reviewed by designated reviewers and approved administratively (see Section 4.1.2). The IRBNet system will automatically notify the PI, via e-mail, of pending annual deadlines at 60 and 30-day intervals prior to the anniversary date of protocol approval. All PAM reports will be uploaded into IRBNet as a Board Document within a project package, and will be included in the agenda/minutes for review and discussion.

Listed below are the criteria that will be reviewed during the Annual PAM meetings:

1. Containment Breach Reporting
    a. Were there any accidental breaches of containment within the last year?
2. Proposed Changes
    a. Changes in biological materials?
    b. For experiments using recombinant or synthetic nucleic acid molecules, are there any changes in
        i. Host

   ii. Host Range
   iii. Natures of DNA
   iv. Vectors
   v. Physical Containment
   vi. Source of DNA
   vii. Deliberate attempts to express foreign genes
c. Changes in organisms, viruses, or toxins?
d. Changes to the specific aims of the project?
e. Changes in location of work or materials storage?
f. Personnel changes?
   i. List current personnel
   ii. Check personnel training and Occupational Health status

3.4 Failure to Schedule Annual PAM Meeting
If the Principal Investigator fails to schedule and complete their annual PAM meeting for their rDNA or biosafety protocol after two e-mail notifications have been issued and a phone call has been initiated directly to the PI by the IBC Administrator, the IBC Chair will contact the Principal Investigator. If the Principal Investigator does not complete an annual PAM meeting or communicate with the IBC within five business days after the protocol anniversary date, notification will be sent to the Institutional Official. Noncompliant issues will be added to the agenda for committee review.

3.5 Five Year Application (de novo) Submissions
IBC protocols are approved for a maximum of five years. All IBC teaching lab protocols are also approved for a maximum of five years. The IRBNet system will automatically notify the PI, via e-mail, of pending expiration 60 days and 30 days prior to the expiration of approval. The PI must submit a closure of the current application and submit a new application (de novo protocol). The de novo protocol will be reviewed in the same manner as new protocol submissions. Research cannot be continued if the de novo (new application) protocol is not submitted at least 3 – 4 weeks prior to the expiration date and approved by the IBC full committee during one of the designated quarterly meetings (March, June, September or December).

3.6 Failure to Submit New Application (de novo) to IBC
If the Principal Investigator fails to submit a new application (de novo) in IRBNet by the submission deadline to renew their rDNA or biosafety protocol before the expiration date, the IBC full committee may not be able to issue a renewal prior to the expiration date. In some circumstances (i.e. a protocol is approved during a non-meeting month) a 90 day extension may be granted to allow a PI to continue their work under the current protocol until the next scheduled quarterly meeting. If a protocol expires, all activities described in the expired protocol must cease. If a PI submits a new application after the submission deadline and it cannot be assigned to the next IBC agenda, the new application will be assigned to the next quarterly IBC meeting (March, June, September or December).

3.7 Modification to Protocol Process
Changes or modifications to approved protocols (i.e. change in or additional of research personnel, room changes, new procedures or agents) must be reviewed and approved by the IBC prior to initiation.

Significant changes are those that change the scope of the review or that are inconsistent with the focus of the approved protocol. For significant changes, the PI must submit an amendment for full committee review. Depending on the changes, the committee may require the closure of the current protocol and the submission of a new protocol application.

Significant changes are changes to approved protocols that are extensive and include but are not limited to the following: change in Principal Investigator, change of an infectious agent or toxin, a change of protocol components that are not exempt from the *NIH Guidelines*, and changes that affect the risk assessment of the protocol. Significant changes will be reviewed by a designated reviewer and require approval at a convened IBC meeting. Proposed significant changes require designated review and IBC approval prior to initiation.

Non-significant changes may be approved administratively, and do not require full IBC review may include but are not limited to the following: changes in research personnel other than Principal Investigator, protocol title, IACUC and IRB protocol numbers or ORSP grant number; changes of protocol components that are not recombinant and do not affect the risk assessment; and changes in BSL-1 agents, vectors, host and genes that are exempt from the *NIH Guidelines* and do not affect risk assessment. Non-significant changes may be approved by administrative approval outside a convened IBC meeting. Proposed non-significant changes require administrative review and approval. All administrative approvals will be included on IBC agendas.

3.8 Protocol Closure

The Principal Investigator shall submit a closure report through IRBNet when a protocol is completed, no longer active, or a new application (de novo) is required. The IBC Administrator shall contact the Principal Investigator if there are any questions or concerns regarding closure of a protocol due to a study closure or inactive study. All new applications (de novo) will be assigned to the next quarterly IBC meeting agenda (March, June, September or December). All closure approvals will be included on IBC agendas.

As stated in Section 3.4 failure to renew a previously approved IBC protocol may result in closure of the protocol. In addition, non-compliance with institutional and federal regulations, policies and guidelines or requirements of the IBC that are either serious or ongoing will be evaluated and the IBC may determine that the incidents require protocol closure.

3.9 Relationships to IACUC and IRB

IBC protocol submissions involving the use of live animals will require IACUC review and approval prior to initiation.

IBC protocol submissions involving the administration of recombinant or synthetic nucleic acid molecules or biohazardous materials, agents or toxins to humans, or involves the collection of tissues or fluids from humans, requires IRB review and approval prior to initiation.

Blood and fluid collection protocols require the completion of the IBC Blood Draw/Fluid Collection protocol form. This form must be completed and submitted in IRBNet to be reviewed and approved by a designated reviewer(s). Blood/fluid collection protocols do

not require approval at a convened IBC meeting, as they are exempt from the *NIH Guidelines*, but will be acknowledged at the next meeting following the designated reviewer's approval. The BSO and/or IBC Administrator must also inspect and approve the locations where blood/fluid are collected and stored. Please note that blood collection must be performed by certified phlebotomists and be insured for blood collection procedures (through DU's policy under Risk Management or through personal insurance)

Current IACUC and IRB IRBNet protocol numbers must be included on the IBC submission applications.