Policy on Protocol and Amendment Submission and Review

1.0 Purpose

To detail the submission and review process for IBC protocol applications.

2.0 Submissions – General Information

The Virginia Tech IBC is responsible for evaluating all aspects of research and teaching involving Recombinant and Synthetic Nucleic Acids (rsNA) and biohazardous materials, agents, and toxins. The IBC is charged with reviewing and approving proposals that involve rsNA and biohazardous materials, agents, and/or toxins to ensure that the criteria established in the Virginia Tech Recombinant and Synthetic Nucleic Acid and Biohazard Research Policy (Policy 13030) and the federal regulations and guidelines [at Section III and Section IV-B-2-b-(1) of the *NIH Guidelines for Research Involving Recombinant and Synthetic Nucleic Acid Molecules (NIH Guidelines)*] are implemented. In its review of the applications, 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 application submissions, whether they are new IBC protocol submissions, modifications, or renewals, must be submitted to the IBC Program in Scholarly Integrity and Research Compliance for administrative review prior to full IBC review and approval. All applications are submitted using the IBC Protocol Management system. No research or teaching activities involving rsNA, biohazardous materials, agents, and/or toxins can be initiated until the Principal Investigator (PI) has received the approval of the IBC and other compliance committees as applicable (e.g., the IACUC when animals are utilized, or the IRB when human subjects are used). Although federal regulations allow exemptions for some types of rsNA used, the PI must submit an application for all projects using rsNA and biohazardous materials, agents, and toxins so that the IBC is aware of the activities and can verify that they are exempt.

In general, a PI is a tenured, tenure track, or research faculty with assigned research space. Post-doctoral researchers and other faculty will be considered as PIs on a case-by-case basis. Students cannot be PIs of record. The PI on an instructional protocol can be the designated instructor for the course(s), regardless of title. However, all instructional protocols in which the instructor is not designated as faculty are required to include the Department Head or Department Designee, as a responsible supervisor.

Researchers and their staff must complete all IBC-required training for the work being proposed. Application submissions will be reviewed by the IBC Program to ensure that all individuals listed on the protocol have completed the required training prior to approval.

2.1 Experiments Requiring IBC Review

Experiments that require Virginia Tech IBC review include, but are not limited to

- The deliberate transfer of a drug resistance trait into microorganisms that are not known to acquire the trait naturally.
- The deliberate transfer of rsNA, or DNA or RNA derived from rsNA, into human research participants (human gene transfer).
- The deliberate formation of rsNA containing genes for the biosynthesis of toxin molecules.
- The use of Risk Group-2 (RG-2) or Risk Group-3 (RG-3) agents.
- The use of human etiologic and animal viral etiologic agents.
- The cloning of nucleic acids into non-pathogenic prokaryotes or lower eukaryotic host-vector systems.
- The use of infectious or defective RG-2 or RG-3 agents, including viral vectors.
- Whole animals in which the animal's genome has been altered by stable introduction of nucleic acids (i.e. genetically modified animal, genetic engineering of animals).
- Viable rsNA modified microorganisms, cell lines, or other rsNA materials tested on whole animals.
- Genetically engineered plants created using rsNA methods, including gene editing.
- More than 10 liters of culture in a single vessel.
- The formation of rsNA molecules containing one-half or more of the genome of a eukaryotic virus or from the same virus family.
- Experiments requiring the use of BSL-2 or BSL-3 containment.
- Non-recombinant research using biohazardous materials, agents, or toxins.
- All research using biological toxins or bioactive derivatives or subunits of toxins.
- Research manipulating human or non-human primate cell lines, tissues, fluids, or other potentially infectious material.

2.2 New Submissions

The IBC application for work involving the use of biohazardous materials and/or recombinant/synthetic nucleic acid (rsNA) manipulation must be accurately completed and submitted using IBC Protocol Management.

The PI must submit an application for all projects using rsNA and biohazardous materials, infectious agents, and/or toxins. The IBC Program staff will work with each PI to ensure a complete submission. When all required forms are completed, the IBC Program will send the protocol to the BSO and to either the IBC Chair (if submitted as an exempt protocol), or an IBC Primary Reviewer for full committee applications. The entire IBC will also be responsible for reviewing all applications placed onto the agenda for an IBC meeting.

During the review of the applications, all reviewers will be responsible for the timely issuance of a brief summary reporting the suitability of procedures and containment practices described in the submitted application, any recommended training for lab personnel and PIs, and an evaluation of any risk assessments. The BSO will also provide the results of a recent (<3 years) lab inspection.

New applications are designated as either exempt or full committee. That designation is determined using the following definitions.

1. **Exempt**: applications involving rsNA, but where all such work is exempt from the *NIH Guidelines* under section III-F, and do NOT involve the use of RG-2 or RG-3 agents, and do NOT require BSL-2 or BSL-3 containment.

2. **Full** Committee: applications involving
   a. rsNA that are applicable to *NIH Guidelines* sections III-A, III-B, III-C, III-D, or III-E
   b. the use of RG-2 or RG-3 agents or those requiring BSL-2 or BSL-3 containment.
   c. Any work that the IBC Chair determines to need review by the full committee.

Submissions classified as "Exempt" will be approved with no full committee review needed. All application submissions which undergo "Full Committee" review will be reviewed by the full committee at a convened meeting.

As part of the review process, full committee submissions will be assigned to an IBC member with requisite subject matter expertise to serve as the Primary Reviewer. The Primary Reviewer will be responsible for reviewing the application in detail, and for leading the discussion of the application during the convened meeting. The application(s) will be made available to the primary reviewer(s) approximately 2

weeks prior to the meeting date. It may be necessary for the PI to submit additional information if required by the Primary Reviewer or other IBC members. The PI will be encouraged to attend the meeting during which the application is discussed to provide any necessary clarifications.

All applications being discussed at the next meeting will be made available to all IBC members 1 week prior to the meeting date.

Once applications have been approved, the final approval number can be used to reference the study with the Virginia Tech Office of Sponsored Programs for grant applications, the IACUC, and the IRB. The PI will be notified of the IBC's decision within 24 hours after the IBC meeting or completion of a review by the IBC Chair and other members, as needed.

2.3 Protocol Modification by Amendment

Changes or modifications to approved protocols (e.g., new procedures, genes, species, laboratories, or agents) must be reviewed and approved by the IBC prior to initiation. If the changes are extensive, or change the scope of the review, a new submission should be made.

Amendments are designated as either minor (exempt) or major (full committee). That designation is ultimately determined by the IBC Chair, but is generally determined using the following definitions.

1. **Minor**:
   a. applications involving rsNA, but where all such work is exempt from the *NIH Guidelines* under section III-F, or new genes added are within the same family of genes in the current approval (e.g. risks remain the same).
   b. editing current projects to include new species, agents, or procedures are within the same risk groups, and/or risk levels of the currently approved work, and there are no new applicable *NIH Guidelines* or risks associated with the amended information.
   c. These applications are approved by the Chair, but the BSO and another member with requisite subject matter expertise may also be asked to review the application.

2. **Full** Committee: applications involving
   a. change of PI
   b. addition of new project(s) to the protocol
   c. newly added species, agents, or procedures that are applicable to additional *NIH Guidelines* and/or present new risks that need to be evaluated

d. new genes for study are added that require a new risk assessment by the expertise of the IBC members

3.0 Annual / Continuing Review

PIs with approved protocols/registrations will be contacted annually, prior to the approval anniversary date, and asked to confirm if the research is still active, if the protocol needs to be closed (research is no longer being conducted), or if an amendment is required. If changes are indicated which have not been captured in previously submitted amendments, the PI will be asked to submit an amendment to provide an update of changes/modifications.

Randomly, a minimum of 10 protocols will be selected for an on-site or virtual annual review. The purpose of the review is the same, but the PI or a designated member of the lab will meet with the IBCP staff to review the protocol and to discuss any upcoming changes that are being considered to the research and to answer any questions that the PI has about the protocol and/or the IBC. The purpose of the on-site/virtual review is to establish direct communication between the researchers and the IBC Program, to make contact with the IBCP staff more personal, and to provide researchers with an opportunity to speak more freely to IBCP staff.

4.0 Triennial Renewals

Full-committee IBC protocols/registrations are approved for three years. IBC Protocol Management will notify the PI of a pending expiration at least four months prior to the expiration. The PI must submit a *renewal* protocol, reviewed in the same manner as new protocol submissions. Research cannot be continued if a protocol renewal is not submitted prior to the date established by the IBC. The IBC is required to periodically review all active protocols thoroughly as part of the *NIH Guidelines*. The triennial renewal meets this requirement.

If extenuating circumstances exist which will prohibit the submission or completion of the renewal protocol, the Principal Investigator may request an extension of the current expiration. The request must be submitted and reviewed prior to the current expiration date. A 1-month extension of the protocol can be approved by the IBC Chair. The PI will be notified of the Chair's decision as soon as the IBC Program Director receives his/her/their response.

If more than 1 month is requested by the PI, the IBC Chair will be notified of the request and the request will be added onto the agenda for the next IBC meeting. The IBC members will discuss the request and conduct a vote to determine if the extension of the protocol expiration will, or will not, be granted. If an extension will be granted, the IBC members will determine the extended timeframe. The PI will be notified of the results of the IBC vote within 24 hours following the IBC meeting.

If the Principal Investigator fails to provide a renewal protocol to the IBC by the expiration date, a letter will be sent to the Principal Investigator, and copied to the Chair/Dean of the department. All research activities pertaining to the research described in the expired protocol must cease. Expiration of the IBC protocol may require termination of any related IACUC or IRB protocols, and notification to OSP.

5.0 Protocol Termination / Closure

The Principal Investigator will close the IBC protocol when all research included in the protocol has been stopped, using IBC Protocol Management. The IBC Protocol Management will notify the IBC Program when the protocol is closed. The IBC Program Director shall contact the Principal Investigator if there are any questions or concerns regarding the closure.

As stated in Section 4 above, failure to renew a previously approved IBC protocol may result in automatic termination of the protocol(s).

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. The IBC, at a properly convened meeting, may determine that the incidents require protocol termination.

6.0 Relationships/Cross-linking Approval with IACUC, IRB, and RSC

IBC protocol submissions involving the use of live vertebrate animals will require Virginia Tech Institutional Animal Care and Use Committee (IACUC) review and approval prior to ordering the animals and the initiation of the research. IBC approval must be in place prior to receiving approval from the IACUC. When an IACUC application is submitted that involves the use of biohazardous agents, including transgenic animals, the IBCP Director will complete an IBC comparison. If IBC approval is not in place for the work included in the IACUC protocol, an IBC hold will be placed onto the IACUC protocol and the PI will be contacted to submit an IBC application. IACUC approval letters will not be released/sent until the IBC hold is released. The IBC hold will be released when the IBC application is approved. Communication between the IBCP staff and Animal Care and Use Program (ACUP) staff is done through the protocol management systems.

IBC protocol applications involving the administration of biohazardous agents or rsNA to humans, or those involving the collection of tissues or fluids from humans, require Virginia Tech Institutional Review Board (IRB) review and approval prior to initiation of the research.

IBC protocol submissions involving the use of radioactive material in research will require Virginia Tech Radiation Safety Committee review and approval prior to initiation of the research.

Current IACUC and IRB protocol numbers, when applicable, must be included on the IBC application. IBC Program staff will coordinate with the Human Research Protection Program and ACUP Directors regarding notification of IBC final approval, when applicable.