Standard Operating Procedures
Atlanta VAMC Institutional Biosafety Committee

INTRODUCTION

The *NIH Guidelines* outline procedures involving the use of recombinant DNA (rDNA) and describe the roles, responsibilities, and relationships among the principal investigator (PI), the Institutional Biosafety Committee (IBC), and the National Institutes of Health (NIH)/Office of Biotechnology Activities (OBA). It is the intention of the Atlanta VA Medical Center (AVAMC) to abide by these guidelines. The manner in which experiments are classified in the *Guidelines* determines the required review procedures. This document is a summary of the review procedures for those planning to initiate any type of rDNA research at the AVAMC, regardless of funding source.

In that the AVAMC does not have Biosafety Level (BSL)-3 or higher facilities, no research deemed to require greater than BSL-2 facilities, practices, and procedures will be approved.

No human gene transfer experiments will be approved.

No research involving plants will be approved.

I. ROLES AND RESPONSIBILITIES

A. Institution

The IBC and Research Office must submit through the Medical Center Director an annual report to the NIH including a roster of all members and their biographical sketches. The chair and contact person must be clearly indicated.

Any changes or significant new information regarding the guidelines or the functioning of the Committee will be communicated to all investigators via email.

B. The Research and Development Committee (R&DC)

The R&DC is responsible for the review and approval of all research at the AVAMC. Procedures for submission of projects and details of the approval process are outlined in MCM 151-1. The Subcommittee on Research Safety (SRS) ensures compliance with applicable biosafety requirements and has delegated the authority for review of research involving rDNA to the Atlanta IBC. If a project involves non-exempt rDNA experiments, it must be reviewed and approved by the Atlanta IBC prior to initiation.

C. The Atlanta IBC.

1. Membership

   a. The Atlanta IBC will have at least 5 voting members who collectively have experience and expertise in recombinant DNA technology and the capability to assess the safety of recombinant DNA research and to identify any potential risk to public health or the environment. At least 2 of these individuals must be non-affilliated with the institution.

   b Members will be appointed by the Medical Center Director for terms not to exceed 3 years. Consecutive terms are permitted.

   c. The Chairperson will be appointed by the Medical Center Director from among the voting members.

2. The IBC will review all rDNA research to be conducted at the Atlanta VAMC for compliance with *NIH Guidelines* and approve those research projects that are in conformity. However, no voting member may be involved in the review or approval of a project in which (s)he has been or expects to be engaged or has a direct financial interest. This review shall include:

a. An independent assessment of the containment levels required by the *Guidelines* for the proposed research.

b. An assessment of the facilities, procedures, practices, and training and expertise of personnel involved in rDNA research.

c. Ensuring compliance with all surveillance, data reporting, and adverse event reporting as required by the *Guidelines*.

3. All reviews shall take place at a convened meeting where a quorum (>50% of voting members) is present. Email exchanges cannot fulfill this expectation. Each member will be provided with all relevant information. If changes to a protocol are required based on a full committee review, the Chair and the primary reviewer may review these changes prior to granting final approval providing no member objects. If any member requests a secondary review, the protocol must be returned to the convened committee. If the approval requires specific conditions then the chair or designee must verify that those conditions have been met and this must be reported at the next convened meeting.

4 Other responsibilities include:

a. Report the results of committee reviews to the Biosafety/Biosecurity Committee in writing.

b. Set containment levels for certain specified experiments.

c. Review periodically rDNA research being conducted at the AVAMC to ensure compliance with the *Guidelines*.

d. Adopt emergency plans covering accidental spills and personnel contamination resulting from such research.

e. Report within 5 days to the Research Compliance Officer, to the NIH, and to ORO any significant problems with or violations of the *Guidelines* and any significant research-related accidents or illnesses.

f. Prohibit initiation of experiments not explicitly covered by the *Guidelines* until NIH establishes the required containment.

g. Perform such other functions as may be delegated to the committee by the *Guidelines*.

5. Minutes:

Minutes of the Atlanta IBC will be written and submitted to SRS Committee and to the R&DC for approval. Since minutes are a primary means of communication with upper management, they will be sufficiently detailed to provide a clear understanding of the operation of the committee. Minutes will be forwarded to VA Central Office upon request.

D. Principal investigators conducting rDNA research

Principal Investigators are responsible for full compliance of the *Guidelines.* These responsibilities are outlined in Section IV-B-7 of the *Guidelines*.

1. General requirements state that the investigator shall:
    a. Initiate or modify rDNA research subject to the *Guidelines* only after that research or the proposed modification thereof, has been fully approved and has met all other requirements of the *Guidelines*.
    b. Determine the classification of the experiment and follow appropriate procedures.

c. Report immediately to the Research Office all problems with and violations of the *Guidelines* and all research-related accidents and illnesses. Significant problems must be reported to the NIH and ORO within 5 days.

d. Report new information bearing on the *Guidelines* to the Research Office.

e. Be adequately trained in good microbiological techniques.

f. Adhere to approved emergency plans for dealing with accidental spills and personnel contamination.

g. Comply with shipping requirements for rDNA molecules (Appendix H of the *Guidelines*).

2. In submissions to the Atlanta IBC, the PI shall:
   a. Make an initial determination of the required levels of physical and biological containment in accordance with the *Guidelines*.
   b. Select appropriate microbiological practices and laboratory techniques to be used for the research.
   c. Submit the initial research protocol and any subsequent changes to the Committee for review and approval or disapproval.
   d. Remain in communication with the Committee throughout the conduct of the project.

3. Prior to initiating the research, the PI shall:
   a. Make available to all lab staff the protocols that describe the potential biohazards and the precautions to be taken.
   b. Instruct and train lab staff in:
      (1) Practices and techniques required to ensure safety, and
      (2) Procedures for dealing with accidents.
   c. Inform the lab staff of the reasons and provisions for any precautionary medical practices advised or requested (e.g., vaccinations or serum collection).

4. During the conduct of the research, the PI shall:
   a. Supervise the safety performance of the laboratory staff to ensure that the required safety practices and techniques are employed.
   b. Investigate and report any significant problems pertaining to the operation and implementation of containment practices and procedures in writing to the RCO, the Committee, and other appropriate authorities, if applicable.
   c. Correct work errors and conditions that may result in the release of rDNA materials.
   d. Ensure the integrity of the physical containment (biological safety cabinets) and the biological containment (purity, genotypic and phenotypic characteristics).

II. CONTAINMENT GUIDELINES

Experiments involving recombinant DNA are divided into six classes (Nomenclature based on guidelines). This committee will **not** approve protocols involving experiments classified under Section III-A, III-B or III-C of the *NIH Guidelines* or experiments involving Risk Group 3 or higher agents.

A. Section III-D Experiments

These experiments require approval and submission of an rDNA Registration Document prior to initiation. These experiments involve:

1. The introduction of rDNA into Risk Group 2 agents shall be conducted at Biosafety Level (BSL)-2 containment. Experiments with such agents shall be conducted with whole animals at BSL-2 or Animal BSL (ABSL)-2 containment.

2. Experiments in which DNA from Risk Group 2 agents is transferred into nonpathogenic prokaryotes or lower eukaryotes may be performed under BSL-2 containment. The Committee may approve the specific lowering of containment for particular experiments to BSL-1. Many experiments in this category are exempt from the *Guidelines* (see Section III-F). Experiments involving the formation of rDNA for certain genes coding for molecules toxic for vertebrates require NIH/OBA approval (see Section III-B-1 of the *Guidelines*) or shall be conducted under NIH specified conditions as described in Appendix F of the *Guidelines.*

3. The use of infectious DNA or RNA viruses or defective DNA or RNA viruses in the presence of helper virus in tissue culture systems.

a. Experiments involving the use of infectious or defective Risk Group 2 animal viruses in the presence of helper virus may be conducted at BSL-2.

b. Experiments involving the use of infectious or defective restricted poxviruses in the presence of helper virus shall be determined on a case-by-case basis following NIH/OBA review.

c. Experiments involving the use of infectious or defective viruses in the presence of helper virus which are not covered in Sections III-D-3-a through III-D-3-d may be conducted at BSL-1.

4. Whole animals.

a. Recombinant DNA, or DNA or RNA molecules derived therefrom, from any source except for greater than two-thirds of eukaryotic viral genome may be transferred to any non-human vertebrate or any invertebrate organism and propagated under conditions of physical containment comparable to BSL-1 or AABSL-1 and appropriate to the organism under study.

b. Animals that contain sequences from viral vectors, which do not lead to transmissible infection either directly or indirectly as a result of complementation or recombination in animals, may be propagated under conditions of physical containment comparable to BSL-1 or AABSL-1 and appropriate to the organism under study.

c. For experiments involving rDNA, or DNA or RNA derived therefrom, involving whole animals, including transgenic animals, and not covered by Sections III-D-1 or III-D-4-a, the appropriate containment shall be determined by the Committee

d. Exceptions under Section III-D-4, *Experiments Involving Whole Animals*

1) Experiments involving the generation of transgenic rodents that require BSL-1 containment are described under Section III-E-3.

2) The purchase or transfer of transgenic rodents is exempt from the *Guidelines* under Section III-F, *Exempt Experiments* (see Appendix C-VI, *The Purchase or Transfer of Transgenic Rodents*).

5. More than 10 liters of culture.

B. Section III-E Experiments

These experiments require Committee notification and submission of an rDNA Registration Document simultaneously with initiation. Those experiments not included under Classes A, B, C, D or F are considered in this class. For example, experiments in which all components are derived from non-pathogenic prokaryotes and non-pathogenic lower eukaryotes are included in this class and can be carried out at BSL-1 containment. Creation of transgenic and knockout animals, or other projects which involve modification of the genome, that may be housed at ABSL-1 containment, are also classified under III-E. Additional rDNA experiments include:

1. Experiments involving the formation of rDNA molecules containing no more than two-thirds of the genome of any eukaryotic virus (all viruses from a single Family being considered identical). These experiments may be propagated and maintained in cells in tissue culture using BSL-1 containment. For such experiments, it must be demonstrated that the cells lack helper virus for the specific Families of defective viruses being used. If helper virus is present, procedures specified under Section III-D-3 should be used. The DNA may contain fragments of the genome of viruses from more than one Family but each fragment shall be less than two-thirds of a genome.

2. Experiments involving the generation of rodents in which the animal's genome has been altered by stable introduction of rDNA, or DNA derived therefrom, into the germ-line (transgenic rodents). Breeding of rodents which results in modification of the genome is also covered under this section (crossing 2 transgenics or crossing onto another background). Only experiments that require BSL-1 containment are covered under this section; experiments that require BSL-2, BSL-3, or BSL-4 containment are covered under Section III-D-4.

C. Section III-F Experiments

These experiments are exempt from the *Guidelines* and no registration is required. These experiments include:

1. Those that are not in organisms or viruses.

2. 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.

3. Those that consist entirely of DNA from a prokaryotic host, including its indigenous plasmids or viruses, when propagated only in that host (or a closely related strain of the same species) or when transferred to another host by well-established physiological means.

4. Those that consist entirely of DNA from a eukaryotic host including its chloroplasts, mitochondria, or plasmids (but excluding viruses) when propagated only in that host (or a closely related strain of the same species).

5. 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.

6. Those that do not present a significant risk to health or the environment (see Section IV-C-1-b -(1)-(c)) as determined by the NIH Director, with the advice of the RAC, and following appropriate notice and opportunity for public comment. See also Appendix C of the *Guidelines*.

III.REVIEW PROCEDURES

1. All projects must be reviewed and approved by the R&DC and all applicable subcommittees before research commences. Refer to the ”Atlanta VAMC Investigator’s Handbook” for details.

2. For all rDNA experiments which are not exempted from the *Guidelines*, and are therefore defined as subject to the *Guidelines* (See Section III), PIs are required to submit an rDNA Registration Document to the Research Office along with the SRS project review form. The rDNA Registration Document must be reviewed and approved prior to the initiation of the research, except for Section III-E experiments which require submission that is concomitant with the initiation of the project.

3. PIs will receive formal notification when their rDNA Registration Document is approved.

IV. CONTENTS OF rDNA REGISTRATION DOCUMENT

A. Description.

This should include the name and department of the principal investigator and Co-investigator(s), when appropriate. Be succinct and explicit enough so that additional explanatory materials are not needed. Description will include:

1 A brief overview of the project

2 The hosts and vectors to be used

3 Experimental design

4 The expression of proteins or regulatory RNAs

5 Whether it will involve gene transfer to humans or animals

6 Whether it will involve the generation of transgenic or knockout animals

7 Whether other laboratories or core facilities will be involved in the project and whether materials will be shipped.

8 A risk assessment including section(s) of the NIH Guidelines which apply to the proposed research activities.

B. Assessment of containment.

The PI must make an assessment of the physical and biological containment procedures and practices needed to carry out the experiment. When proposed facilities are under construction or in renovation at the time the rDNA Registration Document is reviewed, the PI must include an assurance that rDNA experimentation will not occur until the Committee has surveyed the completed facility and found it to be in compliance with *Guidelines*.

C. Information on health surveillance

If applicable (see Section IV-B-1-i of the *Guidelines*), information on health surveillance of personnel and the nature of the program and procedures that will be initiated should be submitted with the application.

D. Training

The PI must provide information on the relevant experience he/she and all applicable personnel have in relation to the proposal (work with organisms, viruses, BSL-2 work, etc.) or, if applicable, describe the training the PI and/or personnel will receive.

E. Shipment

The PI will agree to comply with the shipment requirements for rDNA as indicated in Appendix H of the *Guidelines*.

F. Signature and Date

The PI must accept responsibility for compliance with the *Guidelines* as well as compliance with the items noted above and attest to the accuracy of the information submitted for review.

V. COMMITTEE FOLLOW-THROUGH MEASURES

A. The Committee will certify that the project has been reviewed and found to be in (non-) compliance with the *Guidelines* and other specific instructions. The date of the review will be specified.

B. The Committee will verify the PI's assessment of physical and biological containment levels.

C. The Committee will be responsible for annual review of the status of the research subject to the *Guidelines.*

VI. NOTIFICATION OF MAJOR CHANGES

The PI is responsible for notifying the Research Office of any significant changes in the rDNA component of all approved projects. Examples of such are: (a) a change in hosts or vectors; (b) a change in the donor species or nature of the DNA segments; (c) a change in the physical location of the experiments; and (d) a change of the responsible investigator. The changes should be submitted on a “Request for Modification” form. Modifications should not be initiated until approval is obtained.