NIH GUIDELINES FOR RESEARCH INVOLVING RECOMBINANT DNA MOLECULES (NIH GUIDELINES)
May 2011

************************************************************
Visit the OBA Web site at:
For current information on Guidelines, protocols, Principal Investigators, meetings, and information about upcoming Gene Therapy Policy Conferences
************************************************************

DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health
Guidelines for Research Involving Recombinant DNA

About the Course
This training course was designed to inform principal investigators (PIs) about the requirements of the NIH Guidelines and to provide information regarding the roles and responsibilities of various personnel involved with recombinant DNA (rDNA) research. This course is a general overview of the NIH Guidelines and does not cover all information applicable to rDNA research. Please refer to the NIH Guidelines for all relevant provisions.

The NIH Guidelines defines rDNA as either (i) molecules that are constructed outside living cells by joining natural or synthetic DNA segments to DNA molecules that can replicate in a living cell or (ii) molecules that result from the replication of those described in (i) above.

Who Should Complete this Course?
As a condition for NIH funding, all rDNA research conducted at or sponsored by the institution, irrespective of the source of funding, shall comply with the NIH Guidelines.

Non-compliance may result in:
- suspension, limitation or termination of financial assistance for the noncompliant NIH-funded research project and of NIH funds for other rDNA research at the institution, or
- a requirement for prior NIH approval of any or all recombinant DNA projects at the institution.

Do NOT complete this course through the VAMC Staff Training Courses link if you have a Univ. of Iowa HawkID and password. Please access the course through the UI/UIHC ICON Training Courses link on EHS’s website and documentation of course completion will be downloaded into your “My Training” record in the Employee Self Service website.

Abbreviations
BSL: Biosafety Level
BSO: Biological Safety Officer
EHS: Environmental Health & Safety Office
FDA: Food and Drug Administration
IBC: Institutional Biosafety Committee
IND: Investigational New Drug Application
IRB: Institutional Review Board
NIH: National Institutes of Health
NSABB: National Science Advisory Board for Biosecurity
OBA: Office of Biotechnology Activities
PI: Principal Investigator
RAC: Recombinant DNA Advisory Committee, NIH
How Do I Receive Course Credit?

To receive course credit:
• Read the following material.
• Complete the online exam.

What Will This Course Cover?

This course will cover the following topics:
▪ Responsibilities
▪ Safety considerations
▪ Classification of experiments
▪ Procedures to obtain rDNA approval
▪ rDNA Research Registration
▪ Appendices of the *NIH Guidelines*

Introduction

The *NIH Guidelines* outline specific procedures for the construction and handling of rDNA molecules and organisms/viruses containing rDNA molecules.

The *NIH Guidelines* also outline the responsibilities and relationship between various governmental and University personnel.

The manner in which experiments are classified in the *NIH Guidelines* determines the required review procedures.

General Responsibilities of the Various Entities Involved in rDNA Experiments

**Governmental Responsibilities**

▪ It is the responsibility of the NIH Director to establish the *NIH Guidelines* and oversee their implementation and final interpretation.

▪ The responsibilities of the Office of Biotechnology Activities (OBA) include administrative duties as well as offering scientific and technical advice to the Institutional Biosafety Committee (IBC, rDNA Committee) or to Principal Investigators (PIs).

▪ The Recombinant DNA Advisory Committee (RAC) primarily offers scientific, technical and ethical advice to the NIH.

**University Responsibilities**

▪ It is the responsibility of the University to:
  • Ensure that all rDNA research conducted at or sponsored by the University complies with *NIH Guidelines*.
  • Establish procedures that the Institutional Biosafety Committee (IBC) must follow in the review and approval of applications, proposals and activities.
  • File an annual report to NIH that includes a list of the IBC members.
### Institutional Biosafety Committee (IBC)

- The IBC will review for compliance with the *NIH Guidelines* all rDNA research at the University and approve those projects in conformity with the *NIH Guidelines*.

- The IBC is comprised of at least 5 members with a collective expertise in rDNA technology, biological safety and physical containment.
  - At least 2 members are not affiliated with the University.
  - At least 1 member has expertise in animal or plant containment principles when research involves animals or plants, respectively.
  - The Biological Safety Officer (BSO) will be a member when research involves BSL3 containment or large scale production.

### IBC Responsibilities

- Responsibilities of the IBC include:
  - Reporting within 30 days to the Institutional Official in the Office of the Vice President for Research and to the NIH all significant problems with and violations of the *NIH Guidelines* and all significant research-related accidents and illnesses.
  - Prohibiting the initiation of experiments not explicitly covered by the *NIH Guidelines* until NIH establishes the containment required.
  - Adopting emergency plans covering spills and personnel contamination resulting from rDNA research.

### General Responsibilities of the PI

- In order to insure safety in research activities, ultimate responsibility rests with the PI, which includes:
  - Initiating or modifying rDNA research subject to the *NIH Guidelines* only after that research or the modification has been approved by the IBC.
  - Following appropriate procedures regarding the classification of the experiment.
  - Reporting within 30 days to the BSO, IBC and NIH/OBA all significant problems with and violations of the *NIH Guidelines* and all significant research-related accidents and illnesses.
  - Being adequately trained in good microbiological techniques.

### Responsibilities of the PI to NIH

- Submit information to NIH/OBA for certification of new host-vector systems.

- Petition NIH/OBA and the IBC, for proposed exemptions to the *NIH Guidelines* and for approval to conduct experiments specified in Sections III-A-I and III-B-I.

- Petition NIH/OBA for determination of containment for experiments requiring a case-by-case review and for experiments not covered by the *NIH Guidelines*.

- Reporting new information bearing on the *NIH Guidelines* to the NIH/OBA and IBC.

### Responsibilities of the PI to the IBC

- Register all non-exempt rDNA research with the IBC.

- Submit any subsequent changes to the research protocol to the IBC for review and approval or disapproval.

- Remain in communication with the IBC throughout the conduct of the project.

### Responsibilities of the PI to their staff

- Make protocols available that describe the potential biohazards and precautions to be taken.

- Inform their staff of the reasons and provisions for any precautionary medical practices.
- Supervise the safety performance of their staff and correct work errors and conditions that may result in the release of rDNA materials.

- Instruct and train laboratory staff in:
  - Practices and techniques required to ensure safety.
  - Protocols for dealing with accidents.
    - Note: Lab staff needs to complete the Basic Biosafety training course available on EHS’s web site.

### Safety Considerations: Risk Assessment and Containment

#### Safety Considerations

During rDNA registration with the IBC, the PI will be asked to determine the containment level appropriate for the proposal.

**Note:**
In the following information, “Section” and “Appendix” refers to the *NIH Guidelines*. A brief explanation of the appendices follows later in this course.

#### Risk Assessment

- It is the responsibility of the PI to determine a comprehensive risk assessment of the agent(s) being manipulated (Section II-A).
  - Factors to consider include:
    - Risk Group (see Appendix B)
    - Virulence
    - Pathogenicity
    - Communicability
    - Environmental stability
    - Quantity
    - Toxicity
    - Type of manipulations proposed (e.g., animal inoculation or transmission experiments)

#### Containment

- The appropriate containment levels for experimentation are based on the final risk assessment (Section II-B).
  - Appendices to refer to include:
    - G, Physical containment
    - I, Biological containment
    - P, rDNA research involving plants
    - Q, rDNA research involving large animals

- The IBC will review the containment levels set by the PI for rDNA experiments during review of the rDNA Registration Document and change, if necessary.

- In order to ensure proper containment of rDNA, all wastes involved with recombinant experiments are considered biohazardous and should be properly discarded in biohazardous waste tubs. Additionally, any animals used in rDNA research projects are also considered biohazardous wastes and should be discarded according to Office of Animal Resources guidelines.

### Classification of Experiments Involving rDNA

#### Classification
During rDNA registration with the IBC, the PI will also be asked to classify the research experiments. The *NIH Guidelines* list 6 Classifications (A through F). Following is a description of each Class, including the specific committees required to approve such work.

**IMPORTANT:**
A PI does not need to be directly involved in the creation of a recombinant organism to be covered by the *NIH Guidelines*. For example, a PI receiving recombinant bacteria from another investigator must submit an rDNA Registration Document (rDNARD) to the IBC in order to work with the bacteria.

### Class III-A
- Experiments that involve the deliberate transfer of a drug resistance trait to microorganisms not known to acquire the trait naturally.
  - Such a trait would compromise the use of drugs to control disease in humans, animals or plants.
- Requires IBC, RAC review and NIH Director approval prior to initiation.

### Class III-B
- Experiments that involve the deliberate formation of rDNA containing genes for the biosynthesis of toxic molecules.
  - Toxins in this classification are lethal for vertebrates at an LD₅₀ of less than 100ng per kg of body weight.
- Requires IBC and NIH/OBA approval prior to initiation.

### Class III-C
- Experiments that involve the deliberate transfer of rDNA, or DNA or RNA derived from rDNA, into human research subjects.
- IBC approval must be obtained from each institution at which rDNA will be administered to human subjects.
- Requires IBC and IRB approvals, RAC review and any other applicable regulatory authorization(s) prior to research participant enrollment.

### Class III-D
- Experiments that involve:
  - Human or animal pathogens (Risk group 2 or greater; could include microorganisms classified as select agents and toxins by the CDC and USDA*) as host-vector systems (see Appendix B).
  - DNA from human or animal pathogens (Risk group 2 or greater; including select agents and toxins) is cloned into nonpathogenic prokaryotic or lower eukaryotic host-vector systems.
  - Using infectious viruses (including replication defective) or helper virus systems.
  - Whole animals.
  - Whole plants.
  - Large scale culture preparations (> 10 liters) (see Appendix K).
  - Influenza viruses.
- Requires IBC approval prior to initiation.

* See CDC’s Select agent web page at: [http://www.selectagents.gov/](http://www.selectagents.gov/) or contact Carol McGhan or Haley Sinn at 5-8501.
Class III-E

- Experiments include those not listed under Class A-D or F. For example:
  - All rDNA components derived from non-pathogenic prokaryotes and non-pathogenic lower eukaryotes.
  - rDNA molecules that contain no more than two-thirds of the genome of any eukaryotic virus (without helper virus).
  - Creation of transgenic/knockout animals (requiring ABSL1 containment only).
    - On January 19, 2011 the NIH Guidelines were revised to exempt the breeding of transgenic/knockout rodents with the exception of:
      - Breeding experiments involving transgenic rodents that contain more than 50 percent of the genome of an exogenous eukaryotic virus from a single family, in order to prevent inadvertent reconstitution of an exogenous virus in the resultant transgenic rodent; and
      - Breeding experiments in which the transgenic rodent's transgene is under the control of a gammaretroviral long terminal repeat (LTR), in order to address the small risk of recombination with endogenous retroviruses which could potentially result in mobilization of the transgene via a replication-competent mouse retrovirus.
    - The above two types of experiments must still be registered with, and eventually approved by, the IBC. Please be aware that this exemption only applies to breeding; the initial production of transgenic/knockout rodents requires registration with and approval from the IBC.
  - rDNA modified whole plants and associated modified organisms.
  - Experiments using Baculovirus as the vector.

- Requires IBC notification simultaneously with initiation.

Class III-F

- rDNA molecules are exempt from the NIH Guidelines if they:
  - Are not in organisms or viruses.
  - Do not present a significant risk to health or to the environment, as specifically determined by the NIH Director (see Appendix C).
  - Consist entirely of a DNA segment from:
    - A single non-chromosomal or viral DNA source.
    - A prokaryotic host when propagated in that host.
    - A eukaryotic host when propagated in that host.
    - Different species that exchange DNA naturally (see Appendix A).

- Research involving rDNA molecules which are exempt, does not need to be registered with the IBC/BSO.

Procedures to Obtain Approval for rDNA Research

Initial Procedures for Protocols Not Involving Human Subjects

- A completed rDNA Registration Document must be submitted to the Environmental Health & Safety’s Biosafety Office for all rDNA experiments subject to the NIH Guidelines.
  Note: Throughout the rest of this document, “Biosafety Office” refers to the Environmental Health & Safety’s Biosafety Office.

- The online rDNA Registration Document is available through UIRIS (https://login.uiowa.edu/uip/login.page?service=https://uiris.research.uiowa.edu/index.php). Instructions for completing the form are located within the online process or are also available through EHS’s website at https://research.uiowa.edu/ehs/files/documents/biosafety/recom.pdf.
**IMPORTANT:**

Experiments in Classes III-A through III-D may **not** proceed until the rDNA Registration Document is approved by the IBC.
- The primary contact person for rDNA registration is Debbie Kratz, 3-5678. You may also direct questions to: rdna@uiowa.edu.

---

### Procedures for Annual Review

- Near the end of the first and second year of registration, an Annual Review letter will be mailed to the PI from EHS to determine if:
  - The protocol is active.
  - Any changes have been made to the protocol (includes changes in the host, insert or vector).
  - The project no longer involves rDNA.
  - The protocol is inactive and no longer valid.

- The PI should mark the appropriate response and note any changes before mailing the letter back to EHS.

---

### Procedures for Document Renewal

- The IBC approves rDNA protocols for 3 years.
- Near the end of the third year of registration, a letter will be mailed to the PI from EHS to determine if a new document will be submitted, as the current rDNA Registration Document will soon expire.
- The PI should mark the appropriate response, mail the letter back to EHS and submit a new rDNA Registration Document, if appropriate.

---

### Procedures for Amendment Requests

- Minor changes to rDNA protocols can be approved as amendments by the IBC Chair without full committee review.
  - Changes that would increase the biosafety level of what is already approved, adding animals to a protocol not approved for animal work, or adding a viral vector to a protocol only approved for bacterial plasmids would be considered a major change and would require submission of a new protocol.

- In order to initiate the process of amending an approved protocol, the PI must send an email to the Biosafety Officer at rdna@uiowa.edu indicating the rDNA protocol that is to be amended and detailing the proposed change(s). To facilitate review and record keeping, it is requested that, if appropriate, the PI insert the changes in highlighted form within the protocol or within the table associated with the protocol.

- The Biosafety Officer will review the request and forward the email to the IBC Chair. If the IBC chair agrees that the changes are appropriate for an amendment and approves them as such, he/she will communicate this by return email. The Biosafety Officer then will forward the email indicating approval to the PI.

---

### Initial Procedures for Protocols Involving Human Subjects

- For protocols involving human research participants:
  - PIs must submit documentation described in Appendix M to the NIH and forward a copy to the Biosafety Office (100 EHS).
  - Following RAC review, submit that correspondence, any response by the PI to the RAC recommendations and a complete protocol to the Biosafety Office for IBC review. An rDNA Registration Document will need to be completed through the online submission program and also submitted to EHS.
• IRB review will also occur after RAC and IBC review. All documents must be submitted to the Human Subjects Office using the web-based IRB application and review system, called HawkIRB. It can be found on the Human Subjects Office site at: http://www.research.uiowa.edu/hsoc/get=hawkirb

- PIs will be notified through email when the rDNA Registration Document is approved.
  - The approved rDNA Registration Document bearing the IBC Chair’s electronic signature is available through the online EHS rDNA Research Registration link on UIRIS.
  - A letter of approval will also be sent to the Human Subjects Office.

rDNA Review - IBC

- Criteria used to review submitted rDNA Registration Documents include assessment of:
  - Compliance with NIH Guidelines
  - Containment levels: physical and biological
  - Facilities
  - Procedures
  - Practices, training and expertise of personnel

- PIs will be notified by an email generated through UIRIS when their research protocol has been reviewed and approved by the committee.

- The IBC meets bi-monthly to review and approve submitted rDNA Registration Documents.

- Correspondence regarding the document will take place through the Biosafety Office at EHS.

rDNA Registration Document

Completing the Registration Document

- General information that is required on the rDNA Registration Document includes:
  - **Project Title:** This is the title of your research project.
  - **Funding Agency:** List the agencies that will fund this research.
  - **Name of PI:** In order to be considered a PI, a person must be a Professor (including Assistant, Associate, Emeritis, or Full). Research Scientists and Assistant Research Scientists may be listed as the PI if they have their own funding.
  - **Co-Investigator:** Co-investigators should include faculty members or research scientists who will also be creating, manipulating or otherwise utilizing the recombinant DNA or resulting recombinant organism.
  - **Overall goals:** Briefly (1-5 sentences) describe the overall goal or purpose of this project.

- Lab location and training information is required, including:
  - **Lab location:** all locations in which the rDNA will be utilized, including the PI and Co-PI’s laboratories.
  - **Other laboratory involvement:** State whether any other labs/core facilities will be involved with this rDNA work (e.g., vector construction, propagation, creation of transgenics, etc.). Check the appropriate box identifying which labs will be involved with the proposal and subsequently describe the work that will be carried out by this lab/facility.
  - If **employee health surveillance** is recommended, a description of the surveillance program is required. A statement regarding laboratory staff being offered any applicable immunizations should be included here. Depending on the research proposed some other examples include:
    - No immunocompromised or pregnant individuals will be allowed to work in the laboratory with vaccinia strains.
    - Baseline serum will be collected from all individuals working in the BSL3 laboratory.
    - Individuals working with TB will undergo PPD testing twice a year.
  - **Training:** For all laboratory staff involved in the project, please identify if they have completed the following basic courses listed in the question; this includes the PI and associated staff.
• **Experience:** During review of the rDNA Registration Document, the IBC is required to take into consideration the relevant experience of all personnel involved in the project. Provide information on relevant experience the PI and applicable personnel have in relation to the proposal. Any listed Co-PIs and associated staff will be asked to identify their laboratory experience in a separate email.
  - If personnel do not have experience, please explain who will train personnel, the associated qualifications of the trainer, and how lab staff will be trained.

• Insert, vector and host information is required, including:
  - **Insert/Vector/Host/BSL Table:**
    - By clicking on the button you will be shown the following 6 fields as described below:
      - **Insert:** List the genes/rDNA used in the proposal.
      - **Source of insert:** List the species from which the rDNA originates.
      - **Function:** List the function of the protein or the gene in which you are targeting.
      - **Vector:** Include a list of all possible vectors that will be used in the experiments; you may use broad categories by specifying a parental vector and its derivatives, e.g., “cloning vectors such as pBluescript and its derivatives” or “Saccharomyces expression vectors such as pESC and its derivatives.”
      - **Host:** Include an exhaustive list of all possible hosts that will be used in the experiments; you may use broad species categories, e.g., “human and mouse cell lines” or “InvSc1 and similar strains.”
      - **BSL/ABSL:** Assess the biosafety level of the work to be done; add animal (ABSL) if appropriate, see Risk Assessment and Containment.
        - If the facilities are under construction the PI must include an assurance that no rDNA work will occur until the Biosafety Office staff has surveyed the completed laboratory facility.
  - **Replication status of the vector:** explain the molecular basis for the designation of each vector as replication defective, e.g., adenovirus: E1, E3 deleted; FIV: gag, pol deleted, if appropriate.

• Details of the project are required, including:
  - **Antibiotic resistance:** Include all antibiotic resistance genes that will be expressed in bacteria or cell culture; this includes genes that are already present in a commercially available vector. If the transfer of these antibiotic genes is clinically relevant, NIH/OBA must approve this research prior to IBC review; please contact the Biosafety Office at EHS (5-8501) for further guidance.
  - **Expression of proteins and regulatory RNAs:** Include all proteins and/or regulatory RNAs that will be expressed from the inserted DNA.
  - **Function of the expressed proteins/RNAs:** Describe the function of the proteins and/or regulatory RNAs that will be expressed from the inserted DNA.
  - **Will this research involve:**
    - **Human subjects:** check the appropriate box and list the IRB protocol number (which must be current) if appropriate. Describe the rDNA and/or recombinant organisms that will be administered to the subjects and the route of administration.
    - **Animal subjects:** check the appropriate box.
    - **Transgenic/knockout animals:** check the appropriate box.
      - Where appropriate, state the species of the animal involved in the proposal, include the ACURF approval number (must be current), and describe the rDNA or recombinant organisms that will be administered to the animals and how it will be administered.
      - For transgenics/knockouts, describe the genetic alterations that will be made to the animal, either through the creation of the transgenic/knockout or through cross breeding.

• An assessment of the classification is required:
  - **Classification:** select the appropriate classification for your project from the drop down list provided (see Classification of Experiments).
When you have completed all requested fields and submit the document to EHS, instructions will direct you to the attestation statement. Carefully read the attestation statement that appears; by clicking on the “Submit Application” button you indicate your acceptance of all statements and your electronic signature will be applied to the document. Biosafety staff at EHS will be alerted to the submission of your document.

Major Changes

- The PI is responsible for notifying the IBC of any changes to the rDNA Registration Document, including changes in the:
  - Host or vector.
  - Donor species or nature of the DNA insert.
  - Physical location of the experiments.
  - Responsible investigator.

Appendices of the NIH Guidelines

Appendix A

- Appendix A of the NIH Guidelines:
  - Includes exemptions under Section III-F-5: Natural Exchangers.
  - Exempt experiments include rDNA molecules that are: (i) composed entirely of DNA segments from one or more of the organisms within a sublist, and (ii) to be propagated in any of the organisms within a sublist.
  - Sublists of natural exchangers are listed in this appendix.

Appendix B

- Appendix B of the NIH Guidelines:
  - Describes the classification of biological agents based on their potential effect on a healthy human adult.
    - **Risk Group 1**: not associated with disease (e.g. adeno- associated virus type 1- 4, Baculovirus).
    - **Risk Group 2**: associated with disease that is rarely serious and interventions are often available (Adenovirus, Listeria).
    - **Risk Group 3**: associated with disease that is serious or lethal and interventions may be available (Brucella).
    - **Risk Group 4**: associated with disease that is serious or lethal and interventions are not usually available (Ebola virus).
  - Commonly encountered agents are listed according to their associated risk group.
  - For questions regarding the rDNA Registration Document and biosafety level assessment please refer to Appendix B or contact EHS Biosafety personnel via email: rdna@uiowa.edu, or call 5-8501.

Appendix C

- Appendix C of the NIH Guidelines:
  - Includes those exemptions under Section III-F-6: rDNA molecules that “do not present a significant risk to health or the environment as determined by the NIH Director.”
  - The following experiments are exempt:
    - rDNA containing < one-half of any eukaryotic viral genome propagated and maintained in cells in tissue culture.
    - *E. coli* K-12, *Saccharomyces*, *B. subtilis* or *B. licheniformis* host-vector systems.
    - Extrachromosomal elements of gram positive organisms.
    - Purchase or transfer of transgenic rodents.
  - **Exemptions for each group** are also listed in this appendix.
Appendix D
- Appendix D of the NIH Guidelines:
  - Includes a listing of the major actions taken under the NIH Guidelines after the issues have been considered by the RAC.

Appendix E
- Appendix E of the NIH Guidelines:
  - Includes a listing of the certified Host-Vector systems. These are exempt from the NIH Guidelines.
  - These host-vector systems were previously classified as Host-Vector systems 1 or 2.
    - Specific listed systems include:
      - *Bacillus subtilis*
      - *Saccharomyces cerevisiae*
      - *Escherichia coli*
      - *Bacteriophage systems*
      - *Neurospora crassa*
      - *Streptomyces*
      - *Pseudomonas putida*

Appendix F
- Appendix F of the NIH Guidelines:
  - Specifies the containment conditions for the cloning of genes coding for the biosynthesis of toxic molecules for vertebrates.

Appendix G
- Appendix G of the NIH Guidelines:
  - Specifies the physical containment for standard lab experiments and defines Biosafety levels (BSL) 1 - 4.
  - Standard Practices and Training includes:
    - Training personnel in microbiological techniques.
    - Adopting emergency plans for work with biohazards.
    - Making vaccines available, when appropriate.
  - Physical Containment includes:
    - Primary containment: lab practices and containment equipment.
    - Secondary containment: special lab design.

- BSL-1: Appendix G-II-A:
  - **Standard Microbiological Practices**
    - Wastes are decontaminated before disposal.
    - Work surfaces are decontaminated daily and after spills.
    - Eating and drinking are not permitted in the lab.
    - Personnel wash their hands after handling rDNA organisms and before leaving the lab.
    - All procedures are performed carefully to minimize the creation of aerosols.
    - Hand washing sink, shower, changing room and protective clothing are provided if appropriate.
  - **Special Practices**
    - Contaminated material that is to be decontaminated at a site away from the lab is transported in a closed, durable leak-proof container.

- **Containment Equipment**
  - NONE

- **Laboratory Facilities**
  - The laboratory is easily cleaned.
Bench tops are impervious to water and resistant to acids, alkalis, organic solvents and moderate heat.
Each lab contains a sink for hand-washing.
Fly screens are present on all windows that open.
Furniture is sturdy and spaces between benches, equipment and cabinets are accessible for cleaning.

**BSL2:** Appendix G-II-B:
These practices are in addition to those described for BSL1 containment.
- **Standard Microbiological Practices**
  - Access is restricted by the supervisor when work with biohazardous agents is in progress.
- **Special Practices**
  - Hazard warning signs are posted identifying the agents.
  - Protective laboratory clothing is worn in the lab and removed before exiting the lab to non-lab areas.
  - Gloves are worn when handling animals or agents.
  - Spills and accidents resulting in exposure are immediately reported to the IBC and NIH/OBA.
  - Needles and syringes are placed in puncture resistant containers.
  - Baseline serum samples for lab personnel are obtained when appropriate.
- **Containment Equipment**
  - Biological safety cabinets are used when:
    - procedures with a high potential for generating aerosols are performed or
    - high concentrations or large volumes of organisms containing rDNA are used.
- **Laboratory Facilities**
  - An autoclave is available for decontaminating wastes.

**BSL3:** Appendix G-II-C:
These practices are in addition to those described for BSL1 and BSL2 containment.
- **Standard Microbiological Practices**
  - Persons under 16 are not allowed in the laboratory.
  - If other experiments are being conducted in the lab at the same time as those requiring BSL3 containment, they will be conducted in accordance with BSL3 level practices.
- **Special Practices**
  - The PI restricts access to the lab to those personnel required for support or program purposes.
  - All activities are conducted in a biological safety cabinet.
  - All work surfaces are decontaminated when work with rDNA organisms is finished.
  - Laboratory clothing is decontaminated prior to laundering.
  - Surgical masks or respirators are worn when handling animals.
  - A biosafety manual is prepared.
- **Containment Equipment**
  - Biological safety cabinets are used for all activities.
- **Laboratory Facilities**
  - A ducted exhaust air ventilation system provides directional airflow that draws air into the laboratory.
  - High efficiency particulate air (HEPA) filtered exhaust from biological safety cabinets is discharged through the building exhaust system.
- **Enhancements for Research Involving Risk Group 3 Influenza Viruses**
  - Additional personal protective equipment and procedural requirements.
  - Animal containment enhancements.
  - Occupational health plan requirements.

**Appendix H through J**
- Appendix H of the *NIH Guidelines:*
• Is applicable to the shipping of rDNA modified organisms or viruses.
  ▪ Online training for shipping infectious substances/diagnostic specimens and shipping with dry ice can be found at: http://www.uiowa.edu/~hpo/biosafety/biosafety.htm.

  ▪ Appendix I of the NIH Guidelines:
    • Describes levels of biological containment with regard to the prokaryotic host-vector system.

  ▪ Appendix J of the NIH Guidelines
    • Describes the responsibilities of the Biotechnology Research Subcommittee.

Appendix K

  ▪ Appendix K of the NIH Guidelines:
    • Describes the physical containment for research or production of viable organisms containing rDNA at a large scale (>10 Liters).

Appendix M

  ▪ Appendix M of the NIH Guidelines applies to research involving human participants.
    • No confidential commercial information or trade secrets should be provided in response to Appendix M, enabling all aspects of RAC review to be open to the public.
    • It is the responsibility of the PI to ensure all aspects of Appendix M have been addressed prior to submission of a human gene transfer experiment to NIH/OBA.
      ▪ The PI may delegate the reporting responsibilities to another party with written notification of the delegation to NIH/OBA.

  ▪ Protocol Submission
    • The following must be submitted to NIH/OBA:
      ▪ Cover letter stating all documents comply with Appendix M-I-A;
      ▪ Scientific abstract;
      ▪ Non-technical abstract;
      ▪ Proposed clinical protocol;
      ▪ Proposed informed consent document;
      ▪ CV of the PI(s); and
      ▪ Responses to Appendices M-II through M-V.
        ▪ A description of the proposal, informed consent document, and privacy and special issues.

  ▪ Initially, the RAC will determine if the protocol warrants public RAC review through consideration of:
    ▪ The scientific content and scientific rational.
    ▪ Appropriate and sufficient preliminary safety data.
    ▪ The presence of any social and ethical issues.
    ▪ The introduction of a novel vector/gene delivery system.
    ▪ Any new clinical applications.
    ▪ Any unique gene transfer applications.
    • Following revision, NIH/OBA will send a letter within 10 days to the NIH director, PI, the University, and any other DHHS components summarizing RAC recommendations.

  ▪ The Institutional Review Board (IRB) reviews submitted human gene transfer rDNA documents to assure all ethical issues have been addressed in order to protect the human subjects who volunteer in the research studies.

  ▪ The IRB also reviews protocols to:
    • Assess potential benefits against possible risks.
    • Assure appropriate recruitment and consent procedures are used.
    • Assure compliance with federal, state, and University policies.

  ▪ Initiation of the Clinical Investigation
• No later than 20 days after the first research participant has been enrolled, the PI must submit copies of the following to NIH/OBA:
  - IRB approved informed consent document.
  - IBC and IRB approved protocol.
  - Final IBC approval from the clinical trial site.
  - Final IRB approval.
  - Written report including how the PI responded to any RAC recommendations and any modification to the protocol as required by the FDA.
  - Applicable NIH grant numbers.
  - FDA Investigational New Drug Application number.
  - Date of the initiation of the trial.

• For clinical sites added after RAC review, no participant will be enrolled in the project until the following documentation is submitted to NIH/OBA:
  - IBC approval (from the clinical site);
  - IRB approval;
  - IRB-approved informed consent document;
  - CV of the PI(s); and
  - NIH grant number(s), if applicable.

• Annual data reports will be sent to the NIH/OBA by the PI and should include clinical trial information, a progress report, data analysis and a copy of the updated clinical protocol (including a technical and non-technical abstract).
  - Information submitted in these reports will be evaluated by NIH/OBA and the RAC and possibly considered at a future RAC meeting.
    - Send a copy of the report to Carol McGhan, Environmental Health & Safety.

• PIs must immediately report to the IRB, IBC and NIH/OBA:
  - Any serious adverse event that is unexpected and associated with the use of the gene transfer product.
  - Any finding from laboratory animal tests that suggests a significant risk for human research participants.
    1. A written report must be filed with each group above. NIH Guidelines for reporting are listed in Appendix M-I-C-4-a and forms are at http://oba.od.nih.gov/rdna/adverse_event_oba.html.

**Appendix P and Q**

• Appendix P of the *NIH Guidelines*:
  - Describes the physical and biological containment for rDNA involving plants (BSL-P).

• Appendix Q of the *NIH Guidelines*:
  - Describes containment and confinement practices for research involving large animals (BSL-N).

**Course Exam**

Please complete the course exam; to receive credit for this online training course, you must receive a score of 80% or greater. This exam will serve as a record that you have fulfilled *NIH Guidelines* training.

• Click [HERE](#) to go to the exam.