UTHealth Houston

Biosafety Basics

Module 2: Regulations and Committees

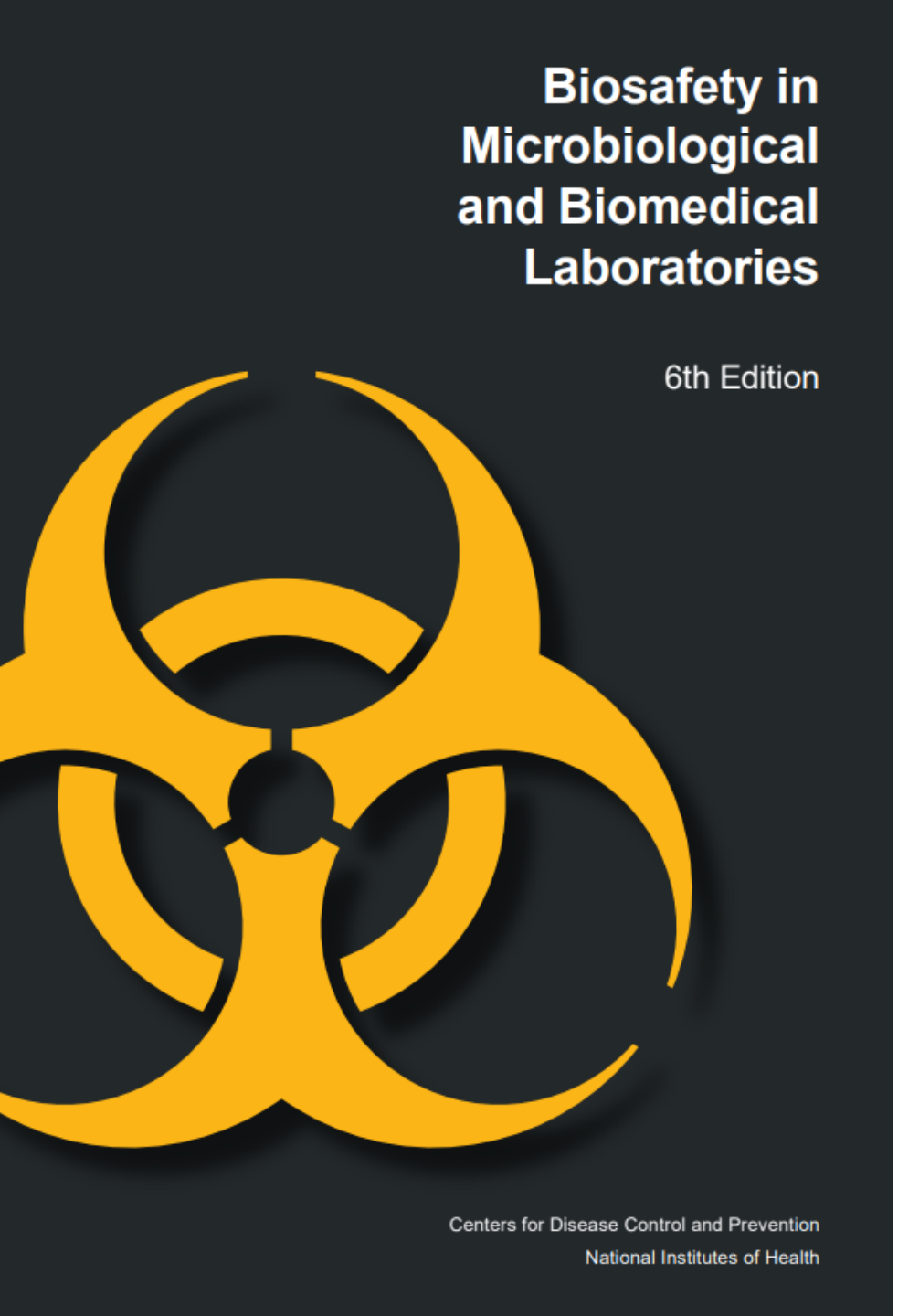
Topics Covered

- *Biosafety in Microbiological and Biomedical Laboratories* (BMBL)
- *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*
- OSHA Bloodborne Pathogens Standard
- Respiratory Protection, including Tuberculosis
- IATA Dangerous Goods Regulations
- Select Agents and Toxins Regulations
- UTHealth Houston Institutional Biosafety Committee (IBC)
  - Work that requires an IBC protocol, IBC protocol submission, and review process

Biosafety in Microbiological and Biomedical Laboratories (BMBL)

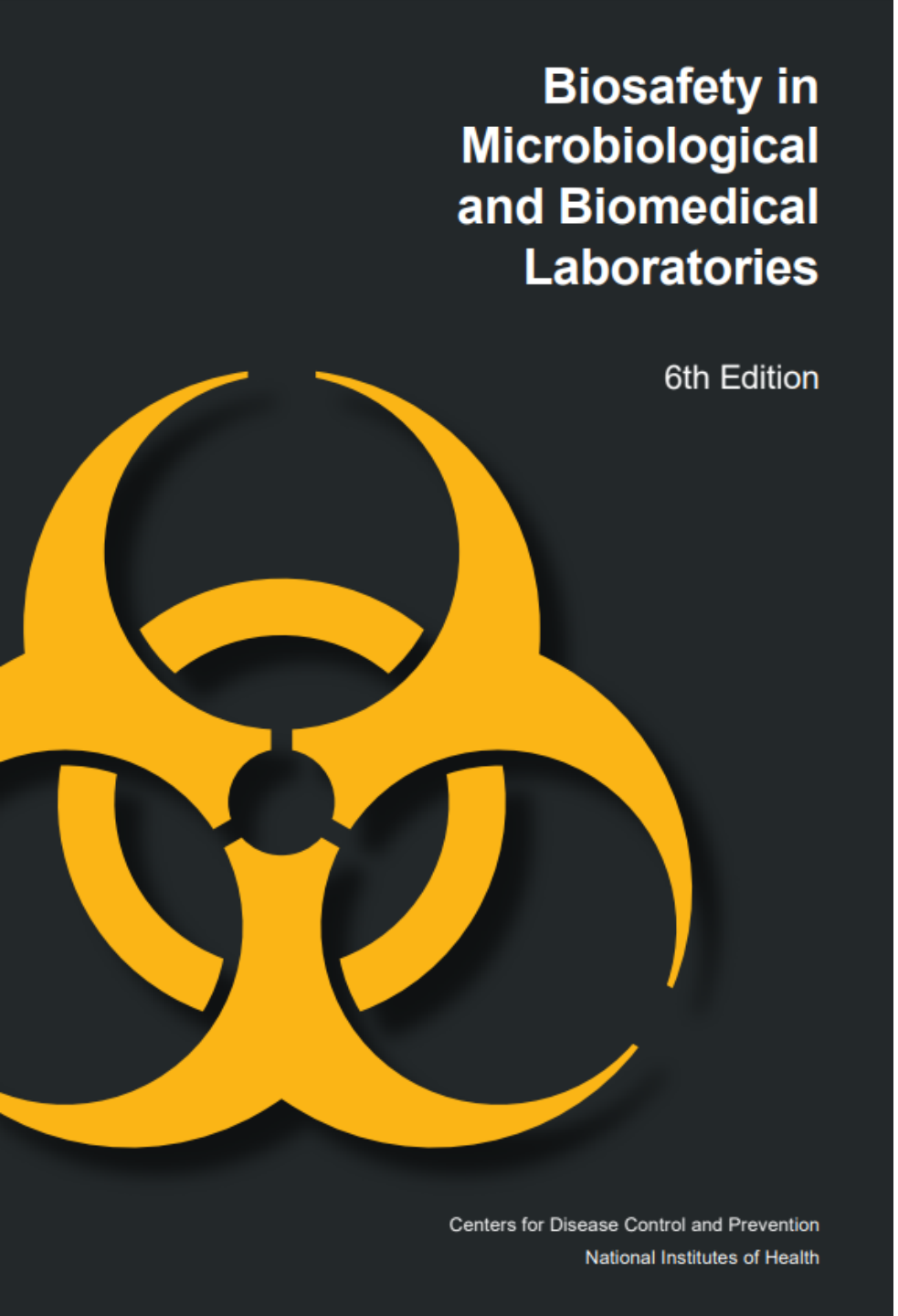
- Joint publication by CDC and NIH
- Originally released in 1984
- Most recent version (6th Edition) released 2020
- Evolution of NIH Guidelines set foundation for BMBL development
- Sets code of practice for biosafety in microbiological and biomedical laboratories

Link to BMBL 6th Edition



BMBL – Key Sections

I. Biological Risk Assessment
II. Principles of Biosafety
III. Laboratory Biosafety Level Criteria
IV. Vertebrate Animal Biosafety Level Criteria
V. Principles of Biosecurity
VI. Occupational Health & Immunoprophylaxis
VII. Biological Agent Summary Statements



BMBL – Key Appendices

Appendix A – Primary Containment for Biohazards (Biosafety Cabinets)

Appendix B – Decontamination and Disinfection

Appendix C – Transportation of Infectious Substances

Appendix D – Agriculture Pathogen Biosafety

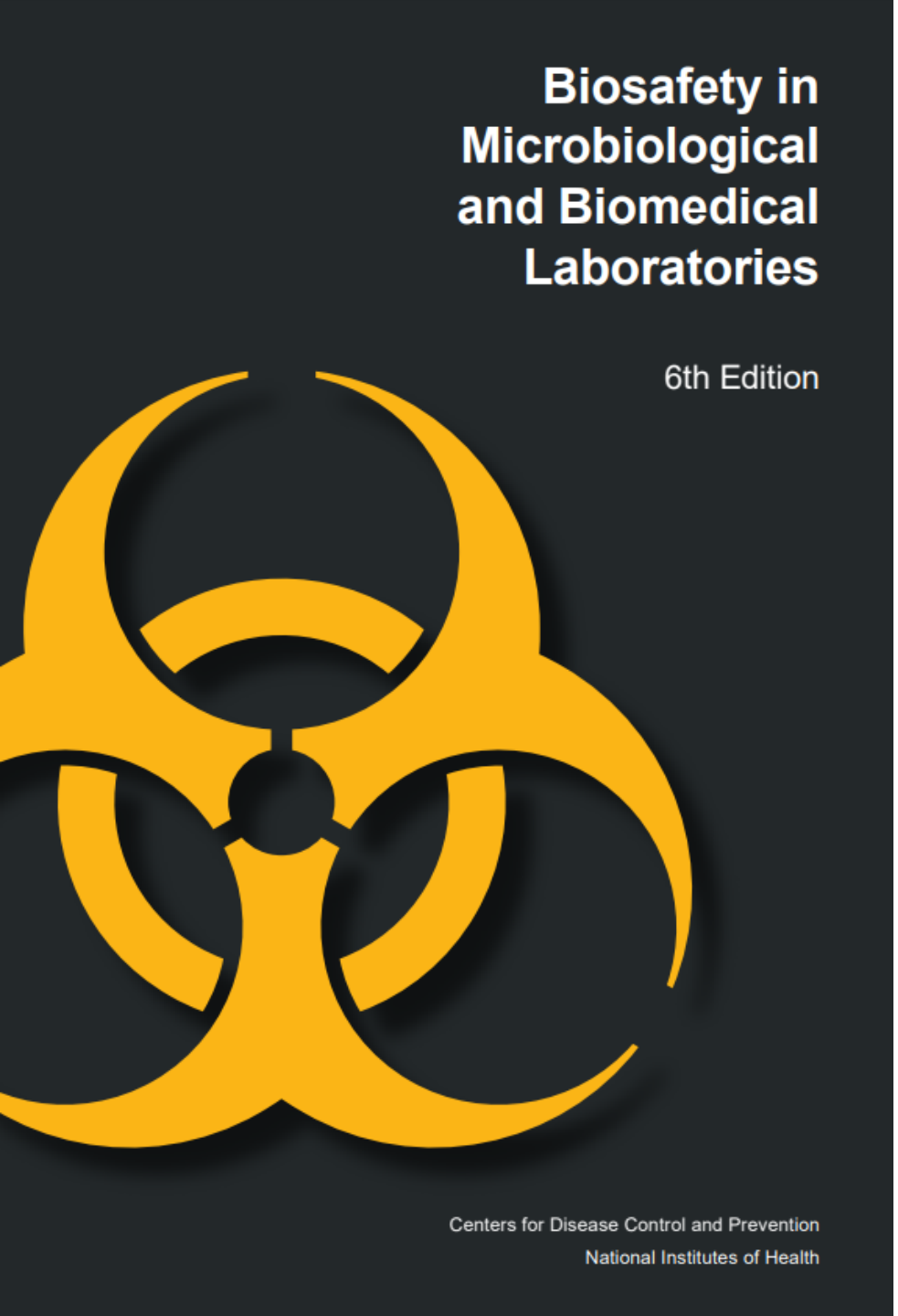
Appendix E – Arthropod Containment Guidelines

Appendix F – Select Agents and Toxins

Appendix G – Integrated Pest Management

Appendix H – Human, Non-Human Primate (NHP) and Mammalian Cells and Tissue

"*Recommended Practices*. Human and other primate cells should be handled using Biosafety Level 2 practices and containment."



BMBL – Key Appendices

Appendix I – Toxins of Biological Origin

Appendix J – NIH Oversight of Research Involving Recombinant Biosafety Issues

Appendix K – Inactivation and Verification

Appendix L – Sustainability

Appendix M – Large-Scale Biosafety

Appendix N – Clinical Laboratories

Appendix O - Acronyms

NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules

- The *NIH Guidelines* were implemented in response to public and scientific concern over the emerging science of rDNA technologies in the early 1970's
- Most recent revision released April 2024

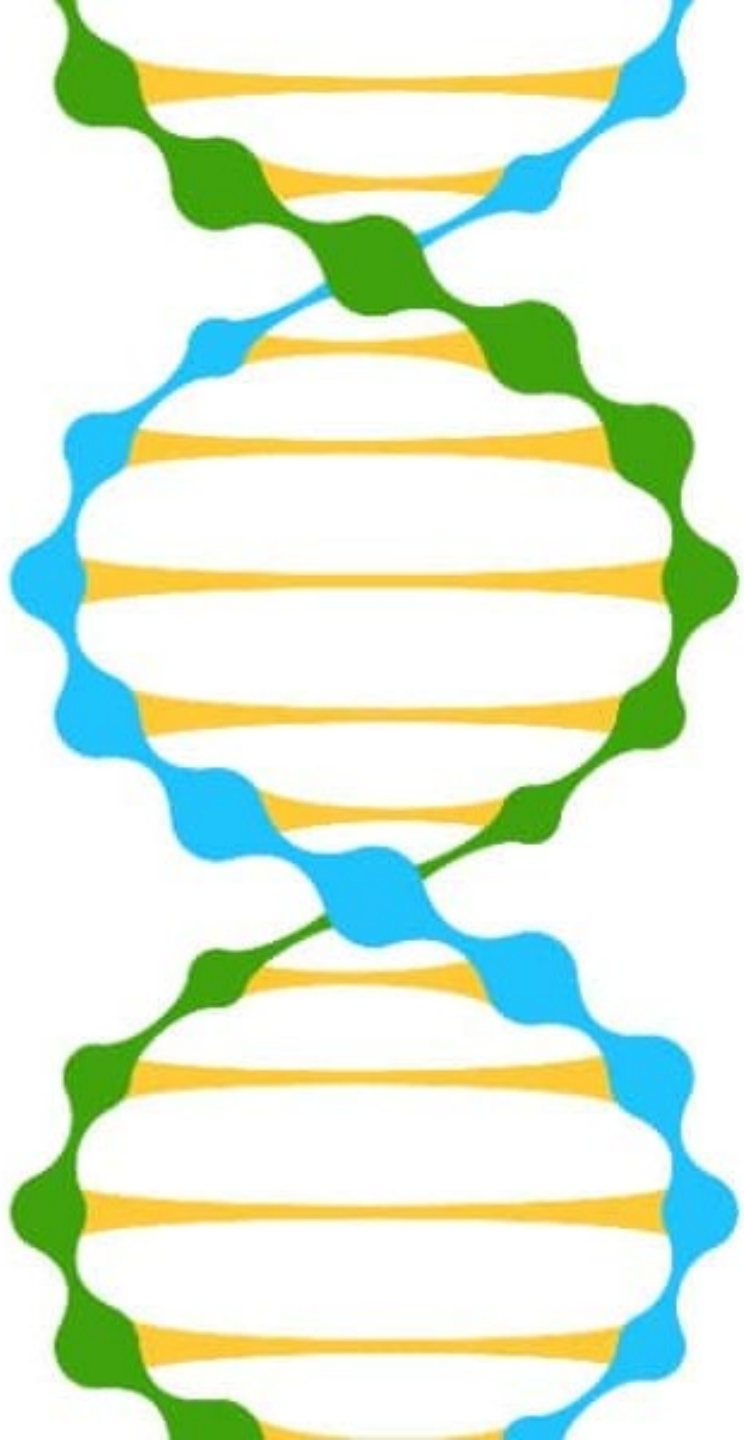
Purpose of Guidelines: Specify the practices for constructing and handling:

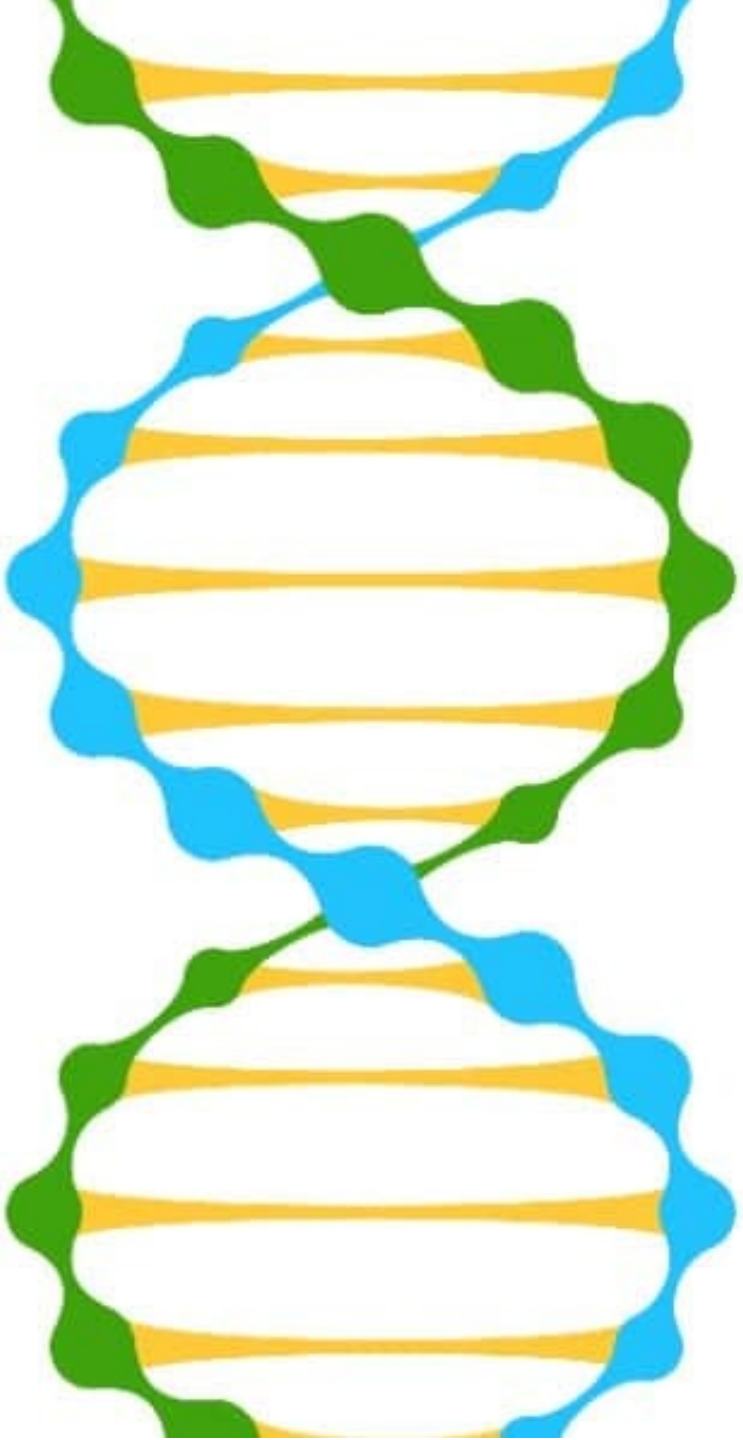
(i) recombinant nucleic acid molecules (rDNA),

(ii) synthetic nucleic acid molecules (sNA), including those that are chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules,

(iii) cells, organisms, and viruses containing such molecules

Link to NIH Guidelines





NIH Guidelines

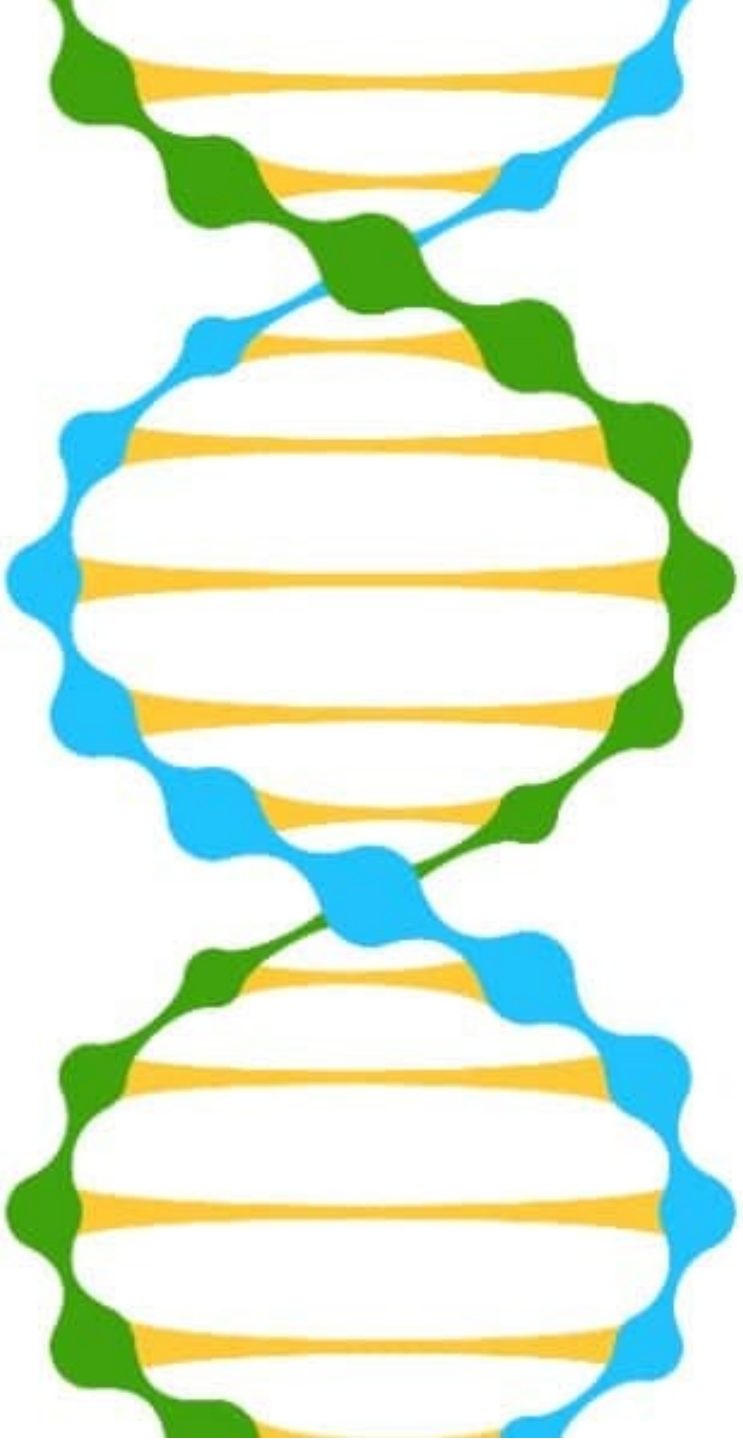
Section I: Scope and Applicability

If your institution receives Federal funding, then it must comply with the *NIH Guidelines* for recombinant DNA research.

Even if a project is privately sponsored, that research experiment must still be conducted in accordance with the NIH Guidelines.

Section II: Safety Considerations:

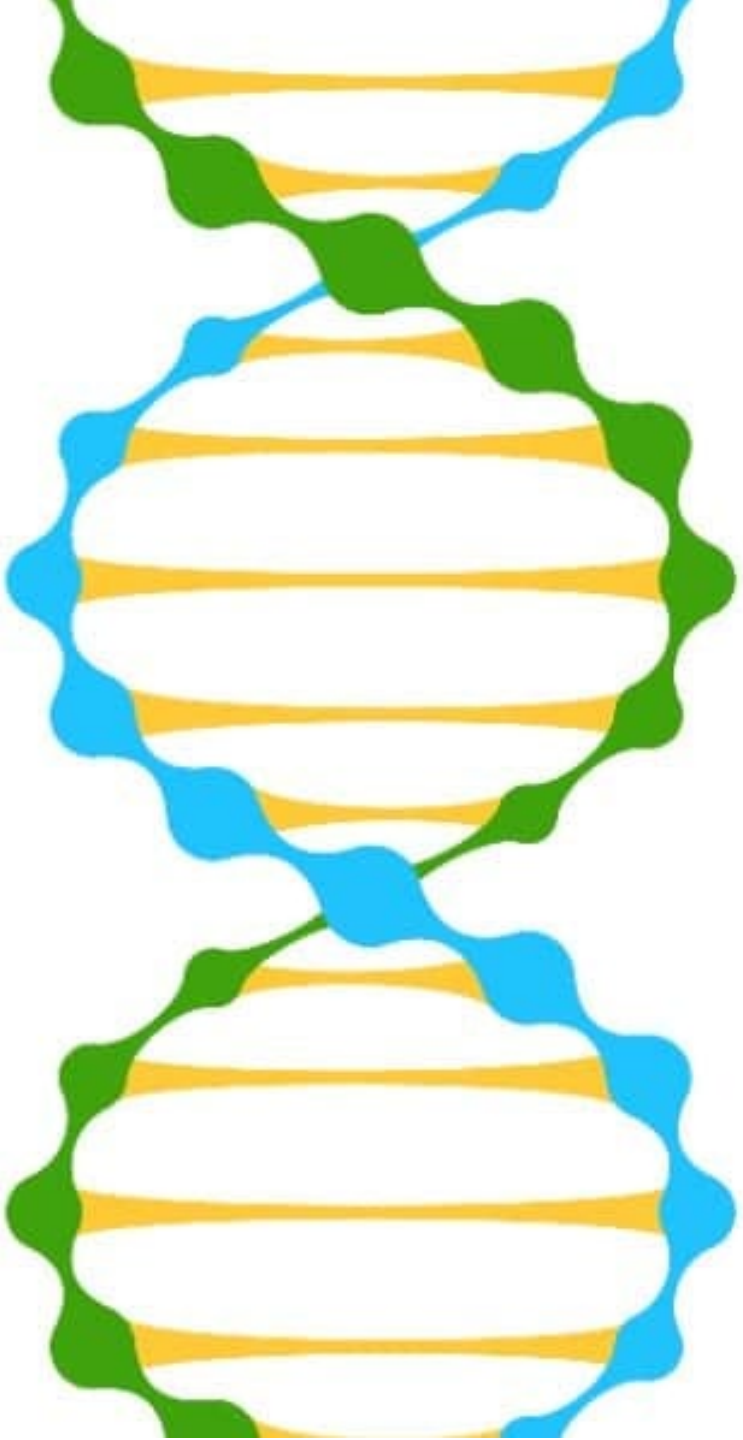
Risk Group and Risk Assessment



NIH Guidelines

Section III: Experiments Covered by the *NIH Guidelines*

Section	Level of Review	Research Example
III-A	IBC and NIH Director review and approval prior to initiation of work	Transfer of drug resistance (e.g. Cipro resistant *Bacillus anthracis*)
III-B	IBC approval and NIH OSP review for containment determination prior to initiation of work	Cloning of lethal toxins (e.g. cloning botulinum toxin expression into adenovirus)
III-C	IBC and IRB review and approval before participant enrollment	Human Gene Transfer
III-D	IBC approval before initiation of work	Infectious agents as vectors and transgenic animals (e.g. expression of non-native protein in *Staphylococcus aureus*) Gene drives
III-E	IBC notification at initiation of work	Transgenic rodents (e.g. germline alteration of animals that can be housed at ABSL-1)
III-F	Exempt work	Exempt work/BSL-1 (e.g. purchase of transgenic rodents)



NIH Guidelines

Section IV: Roles & Responsibilities

Ensure compliance with *NIH Guidelines*

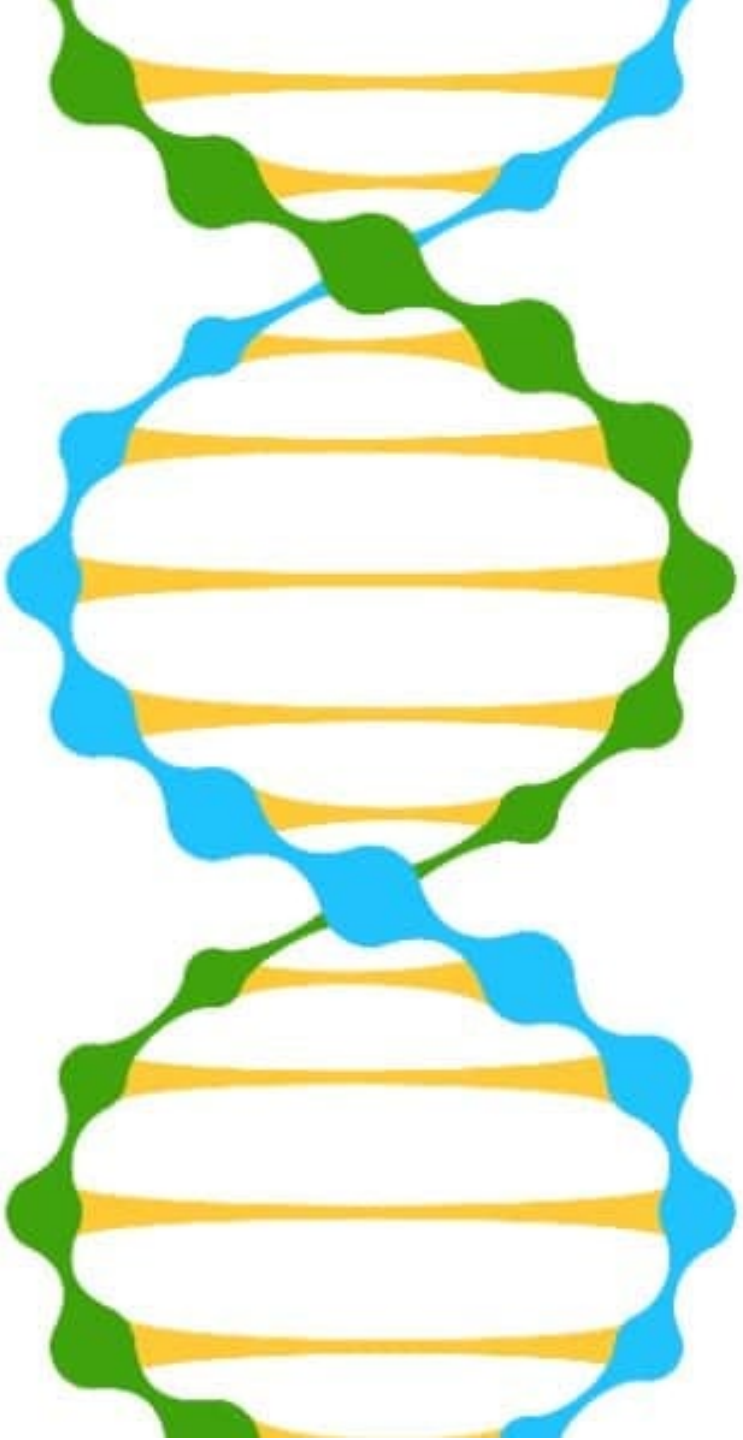
Establish IBC

Appoint a Biosafety Officer, if conducting BSL-3, BSL-4, or large-scale work

Ensure IBC has expertise in the research that is reviewed

Establish a medical surveillance program as needed

Report all incidents to the NIH-Office of Science Policy



NIH Guidelines

Section IV: Roles & Responsibilities

Responsibilities of the IBC:

Review rDNA research and approve those research projects that are found to conform with the *NIH Guidelines*.

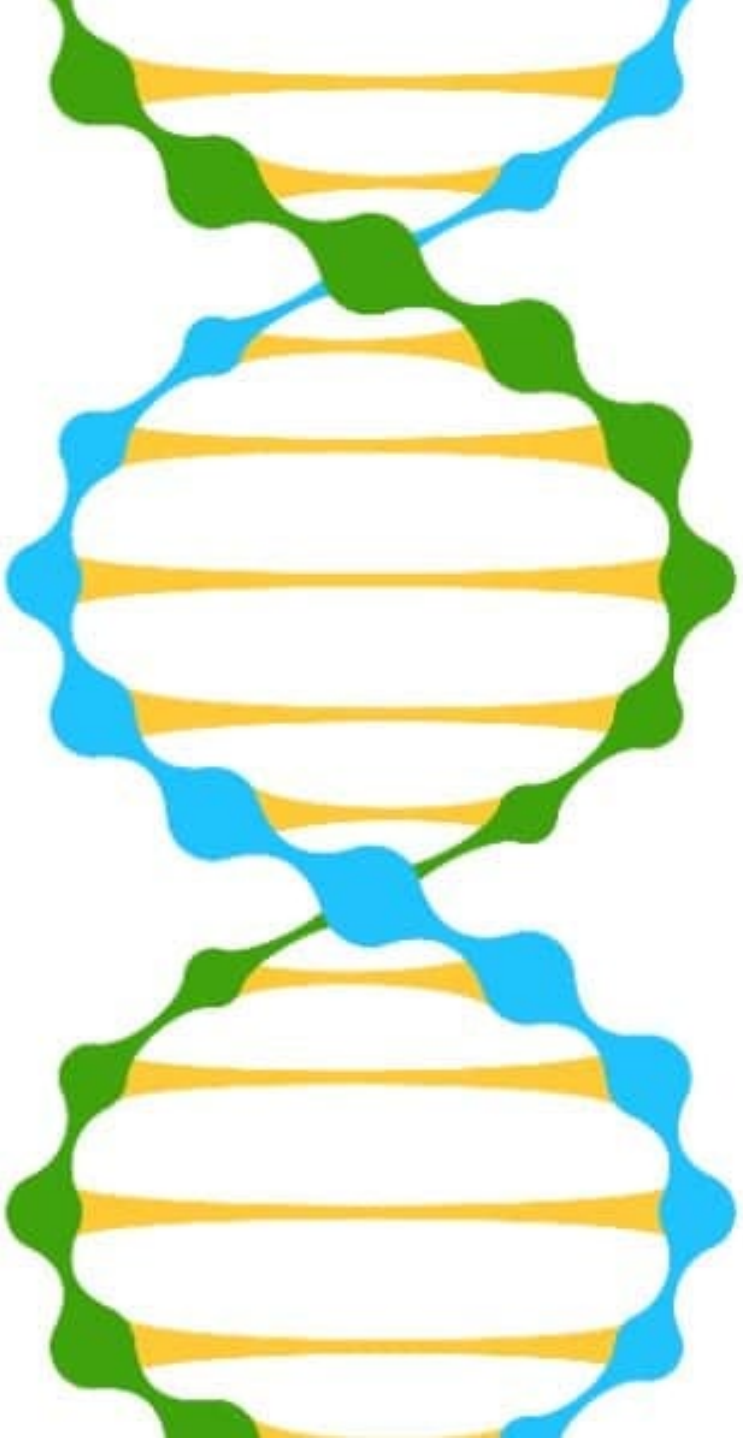
This review shall include:

1) independent assessment of the containment levels required by the *NIH Guidelines* for the proposed research;

2) assessment of the facilities, procedures, practices, training, and expertise of personnel involved in rDNA research;

3) ensuring that the PI has appropriately addressed all aspects of Appendix M and

4) ensure compliance with all surveillance, data reporting, and adverse event reporting requirements set forth in the *NIH Guidelines*.



NIH Guidelines

Section IV: Roles & Responsibilities

Responsibilities of the IBC:

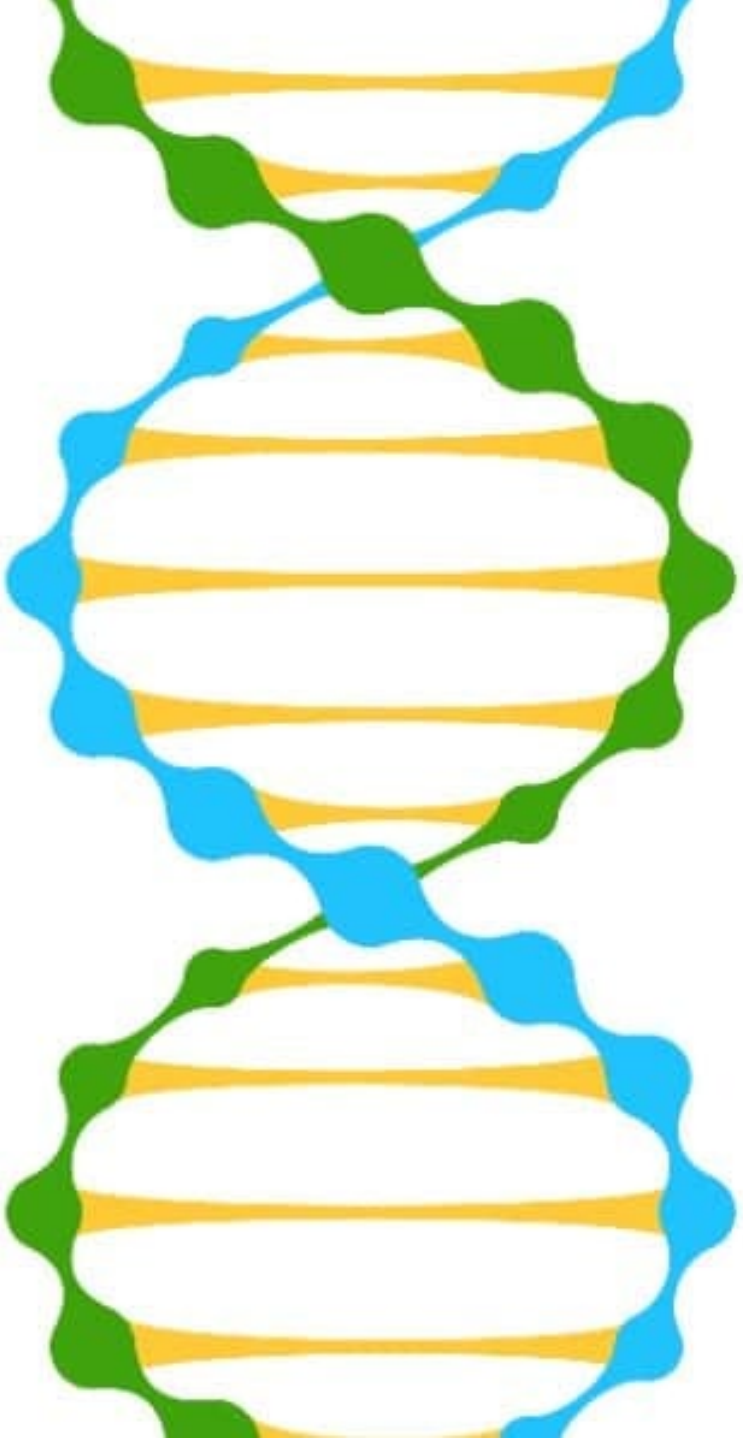
Notify the PI of the results of the IBC's review and approval.

Lower containment levels for certain experiments as specified in Section III-D-2-a, Experiments in which DNA from Risk Group 2, Risk Group 3, Risk Group 4, or Restricted Agents is Cloned into Non-pathogenic Prokaryotic or Lower Eukaryotic Host-Vector Systems.

Set containment levels as specified in Sections III-D-4-b, Experiments Involving Whole Animals.

Periodically review rDNA research conducted at the institution to ensure compliance with the *NIH Guidelines*.

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



NIH Guidelines

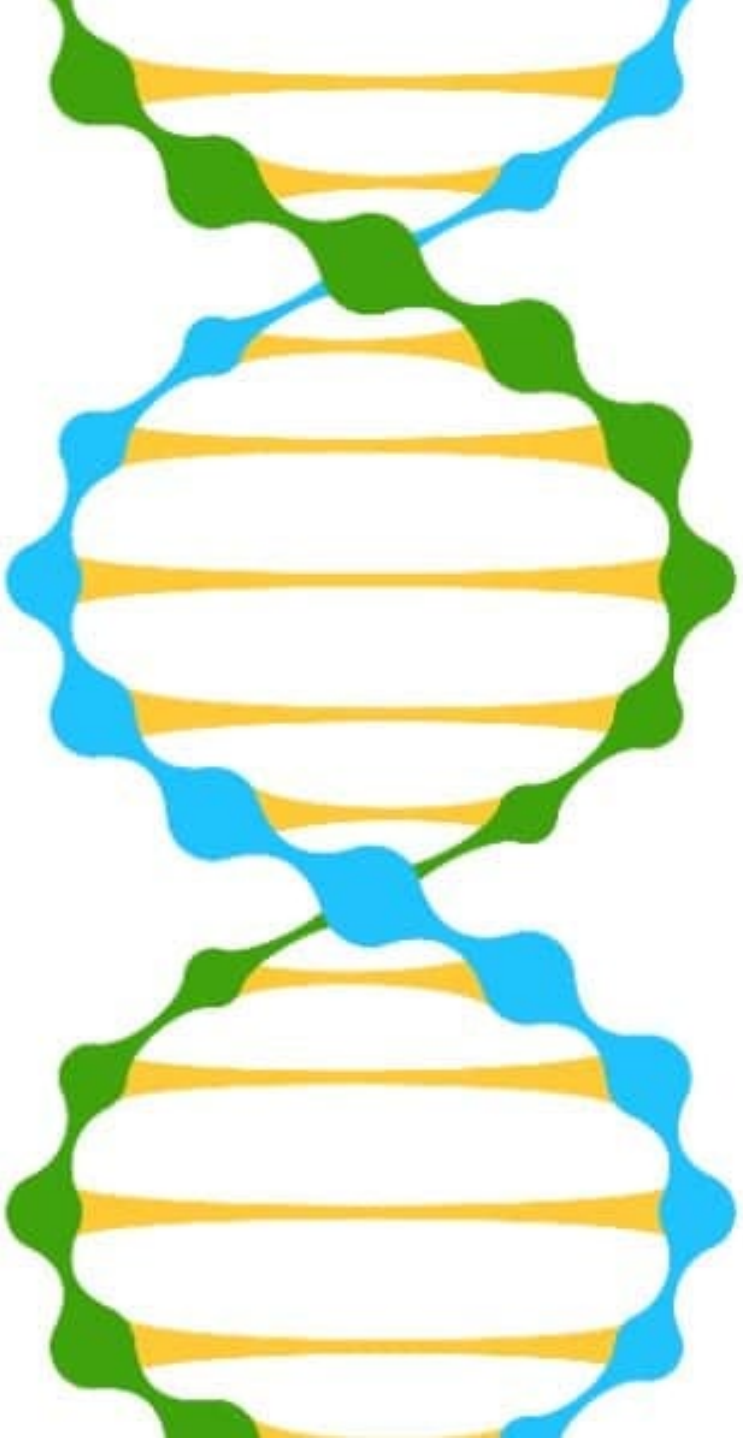
Section IV: Roles & Responsibilities

Responsibilities of the IBC:

Report any significant problems with or violations of the *NIH Guidelines* and any significant research-related accidents or illnesses to the appropriate institutional official and NIH/OSP within 30 days.

The IBC may not authorize the initiation of experiments that are not explicitly covered by the *NIH Guidelines* until NIH establishes the containment requirement.

Perform such other functions as may be delegated to the IBC.



NIH Guidelines

Section IV: Roles & Responsibilities

Responsibilities of the Principal Investigator:

Initiate or modify no recombinant DNA research which requires IBC approval prior to initiation until that research or the proposed modification thereof has been approved by the IBC and has met all other requirements of the *NIH Guidelines*;

Determine whether experiments are covered by Section III-E, and ensure that the appropriate procedures are followed;

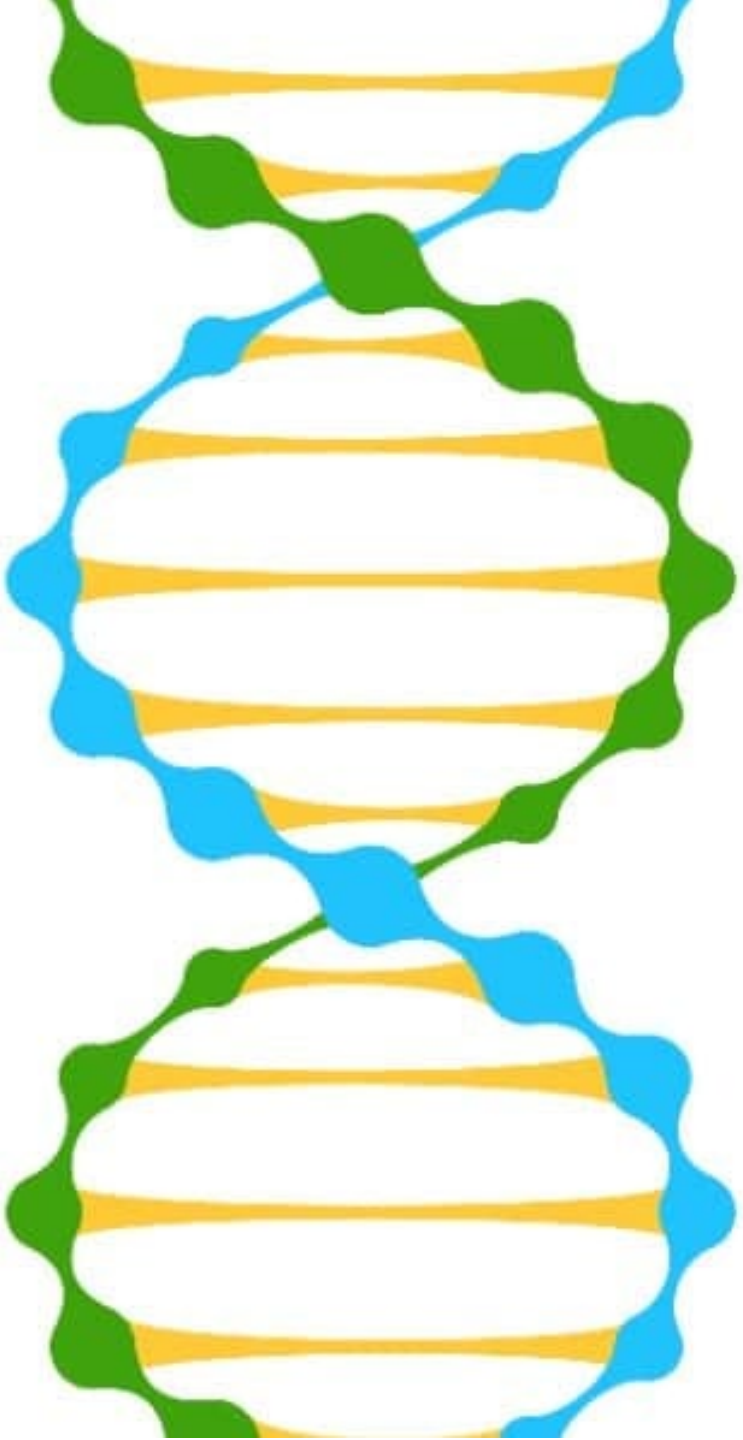
Report any significant problems, violations of the *NIH Guidelines*, or any significant research-related accidents and illnesses to the BSO, Animal Facility Director (where applicable), IBC, NIH OSP, and other appropriate authorities (if applicable) within 30 days;

Report any new information bearing on the *NIH Guidelines* to the Institutional Biosafety Committee and to NIH OSP

Be adequately trained in good microbiological techniques;

Adhere to IBC-approved emergency plans for handling accidental spills and personnel contamination;

Comply with shipping requirements for rDNA molecules.



NIH Guidelines

Section IV: Roles & Responsibilities

Responsibilities of the Principal Investigator:

Responsible for full compliance with the *NIH Guidelines* in the conduct of rDNA research.

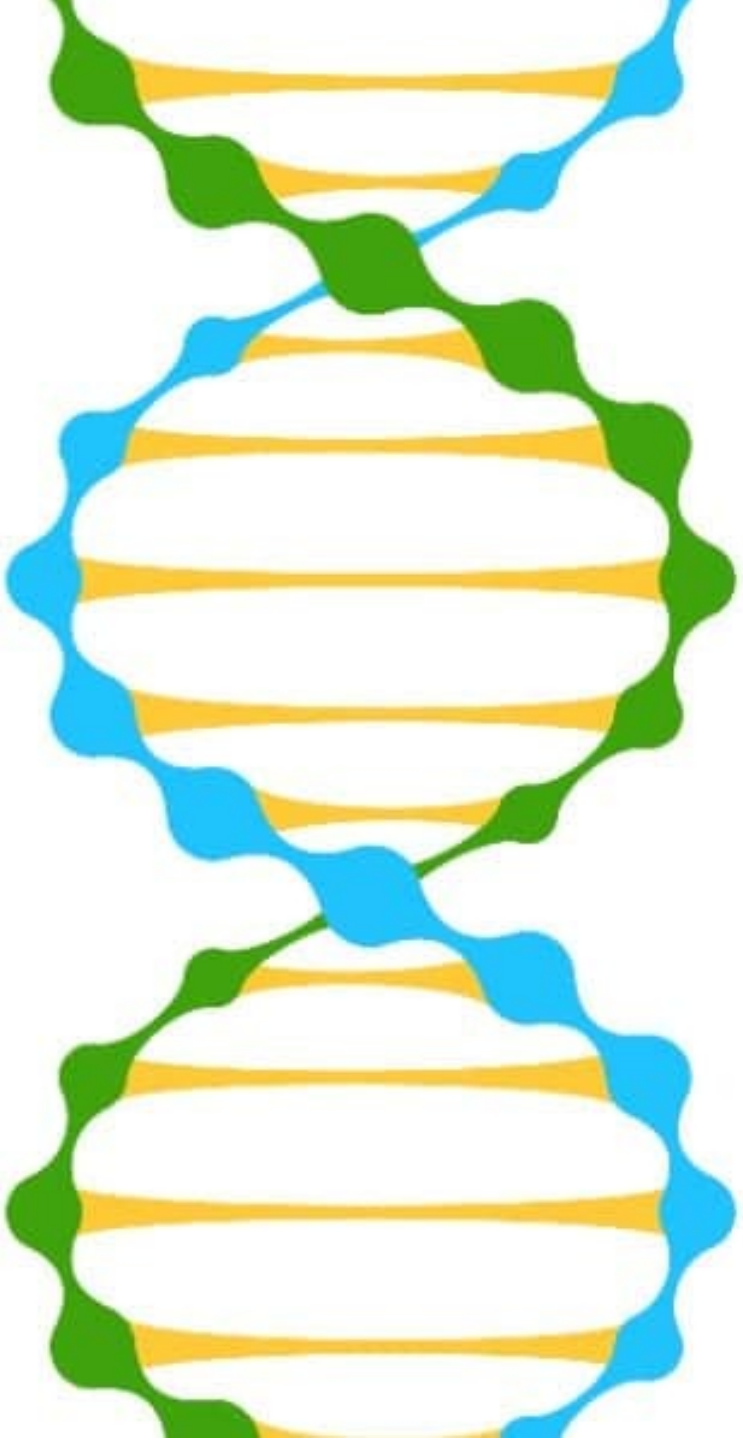
Responsible for ensuring that the reporting requirements are fulfilled and will be held accountable for any reporting lapses.

Prior to initiating research:

1) Make available to all laboratory staff the protocols that describe the potential biohazards and the precautions to be taken;

2) Instruct and train laboratory staff in: (i) the practices and techniques required to ensure safety, and (ii) the procedures for dealing with accidents; and

3) Inform the laboratory staff of the reasons and provisions for any precautionary medical practices advised or requested (e.g., vaccinations).



NIH Guidelines

Section IV: Roles & Responsibilities

Responsibilities of the Principal Investigator:

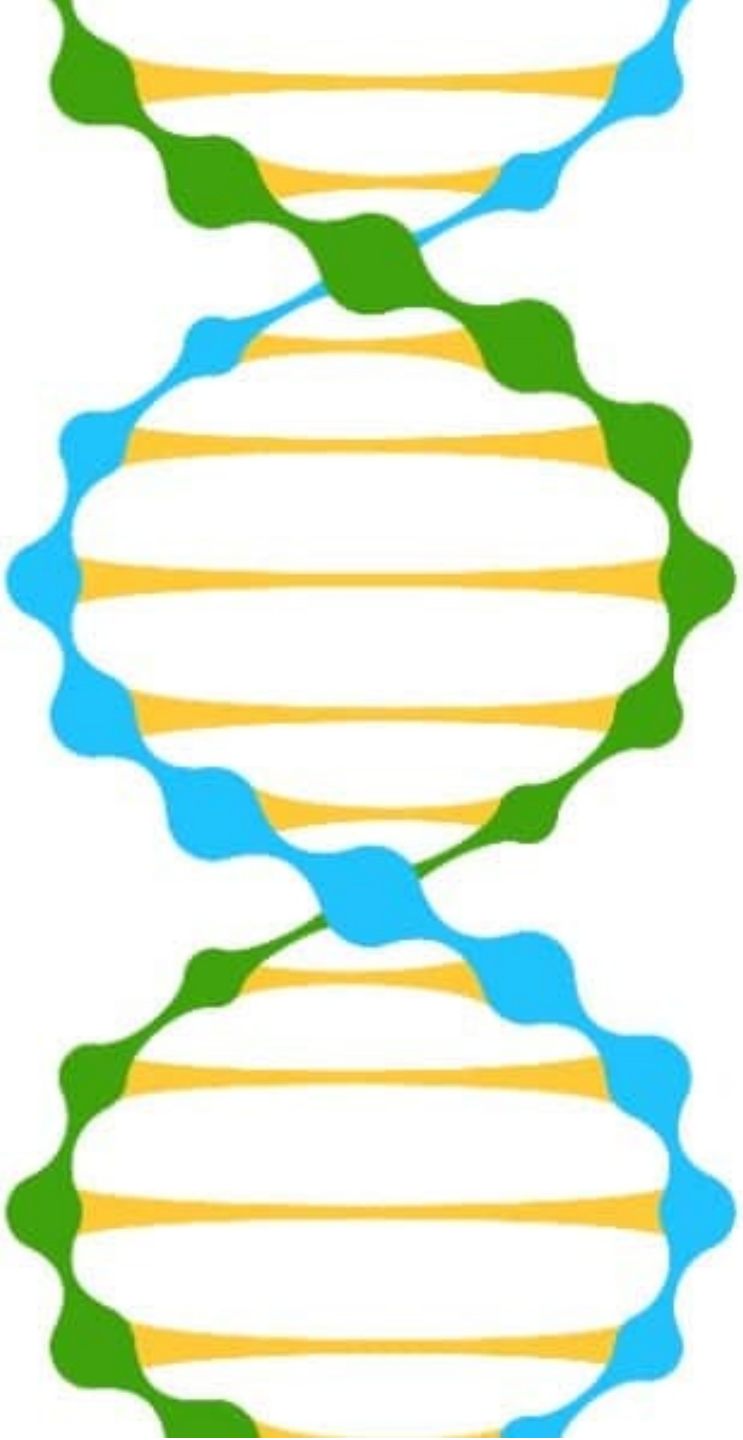
During conduct of research:

1) Supervise the safety performance of the laboratory staff to ensure that the required safety practices and techniques are employed;

2) Investigate and report any significant problems pertaining to the operation and implementation of containment practices and procedures in writing to the BSO, Animal Facility Director (where applicable), IBC, NIH OSP, and other appropriate authorities (if applicable)

3) Correct work errors and conditions that may result in the release of rDNA materials; and

4) Ensure the integrity of the physical containment (e.g., biological safety cabinets) and the biological containment (e.g., purity and genotypic and phenotypic characteristics).



NIH Reporting Requirements

Any significant problems, violations of the *NIH Guidelines*, or any significant research-related accidents and illnesses must be reported to NIH within 30 days.

Spills or accidents in BL2 laboratories resulting in an overt exposure must be immediately reported to NIH.

Spills or accidents occurring in high containment (BL3 or BL4) laboratories resulting in an overt or potential exposure must be immediately reported to NIH.

Relevant incidents would include spills and accidents which result in overt exposures to organisms containing recombinant or synthetic nucleic acid molecules in the laboratory

OSHA Bloodborne Pathogens Standard 29 CFR 1910.1030

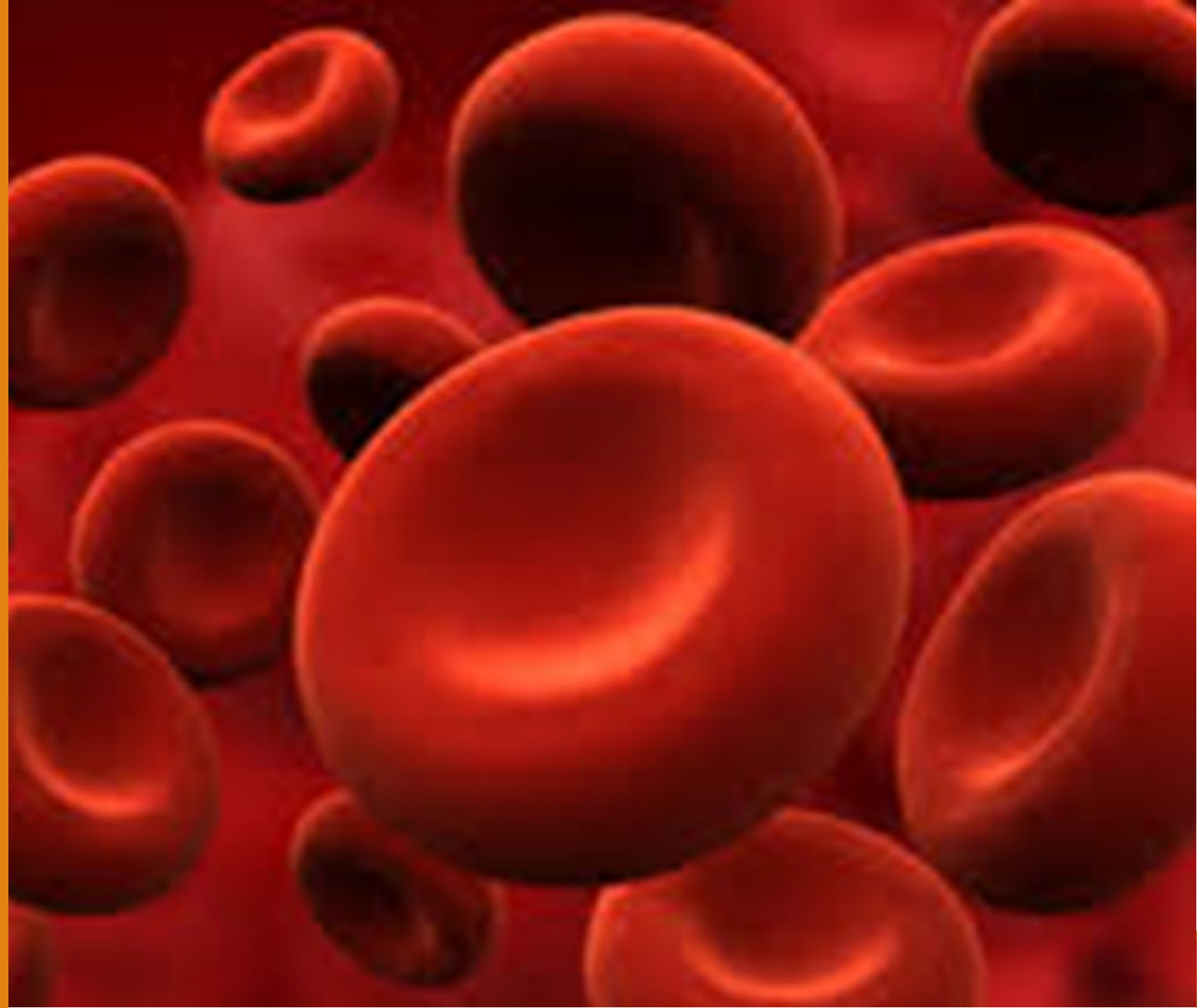
Covered in Initial and Annual Refresher Laboratory Safety Training

Define bloodborne pathogens and the risks associated with occupational exposure

Identify employer responsibilities related to compliance with the Standard

Needlestick Reduction Act (added in 2001)

Texas Department of State Health Services, Bloodborne Pathogens Control



Respiratory Protection including Tuberculosis 29 CFR 1910.134 (independent standard 1910.139 repealed)

The goal of the respiratory protection program is to protect individuals at UTHealth Houston from breathing in harmful airborne contaminants or infectious aerosols while they work or learn. This is accomplished through implementation of procedures to ensure the proper use of respiratory protection and adherence to the guidelines from Occupational Safety and Health Administration (OSHA) Respiratory Protection Standard (29 CFR 1910.134).

Respiratory Protection Program

IATA Dangerous Goods Regulations, DOT 49 CFR 171-185, & USPS 39 CFR Part 111

Needed for shipment or transport of any infectious substance or biological material

Separate Training Module Required

Transportation & Shipment of Biological Materials

Select Agents and Toxins Regulations

7 CFR Part 331 and 9 CFR Part 121 (USDA, APHIS)

42 CFR Part 73 (CDC)

Notify the Biosafety Program immediately of any planned work

The program currently regulates **68 select agents and toxins**. The list is reviewed at least every two years to determine if agents or toxins need to be added to or deleted from the list.

Common Examples of Select Agents and Toxins Include:

- ***Bacillus anthracis*** **(causative agent of anthrax)**
- **Variola major virus (causative agent of smallpox)**
- **Foot-and-mouth disease virus**
- ***Ralstonia solanacearum***
- **Ricin**

UTHealth Houston's Institutional Biosafety Committee (IBC)

Reviews work with biological agents and Recombinant or Synthetic DNA Molecules

Full Members

Serve staggered two-year terms

3+ faculty members with rDNA experience and/or biological safety and containment

2 community members

Director, Environmental Health & Safety (BSO)

At least 1 member from each school

At least 1 member with animal containment expertise

At least 1 with infectious disease expertise

1 student member

***Ex-Officio* Members**

Representative from Legal Affairs

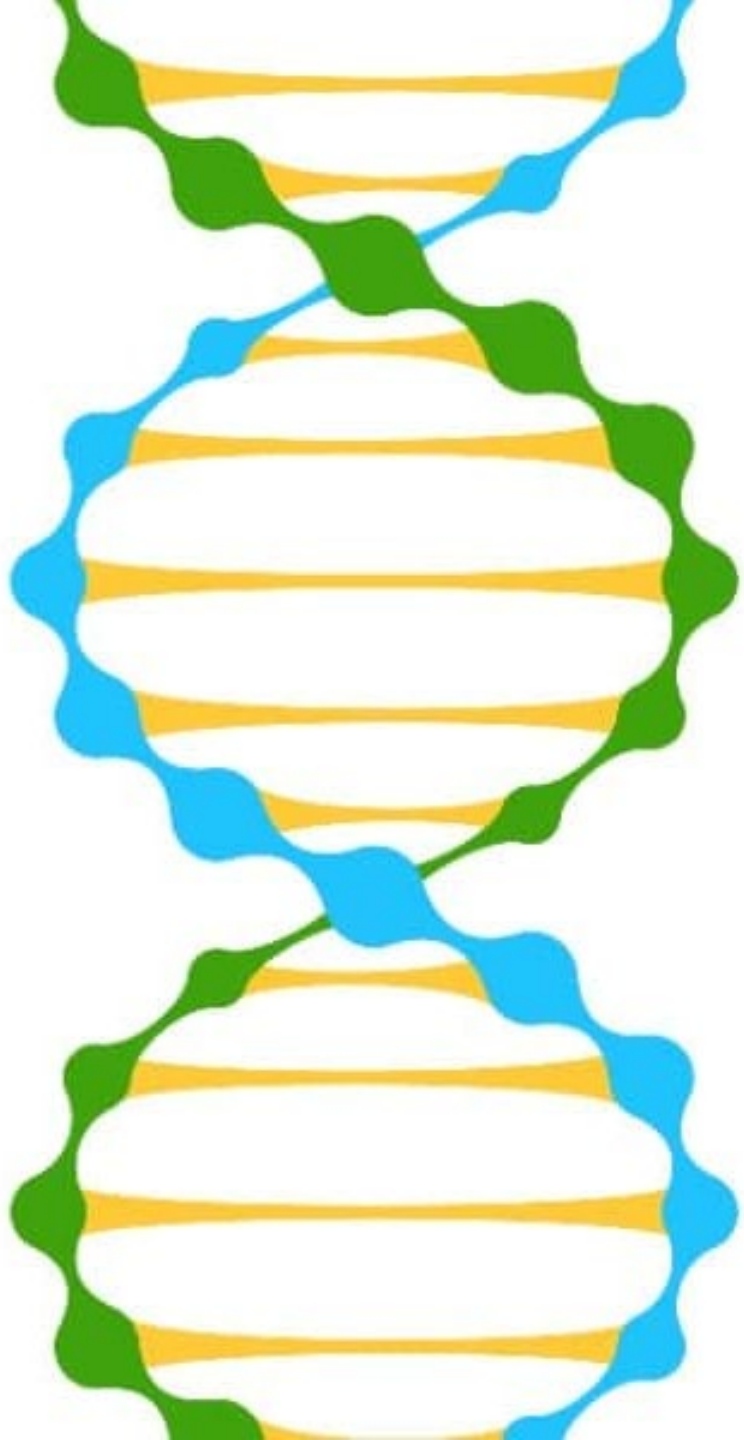
Safety Manager, Biological Safety Program

Safety Manager, Environmental Protection Program

Executive Vice President and Chief Academic Officer

Center for Laboratory Animal Medicine and Care

Representative from Employee Health Services



What work requires an IBC Protocol?

All Work with Recombinant and Synthetic Nucleic Acid Molecules

In vitro and *In vivo*
Human and animal studies

Plasmids
Viral vectors
Recombinant vaccines
Transgenic animals
Gene editing tools
Gene drives
siRNA
shRNA
miRNA
dsRNA

REQUIRES IBC APPROVAL

What work requires an IBC Protocol?

Cultures or Materials that is Risk Group 2 or higher

Human cell lines
Human samples

Refer to Module 1: Risk Group Resources

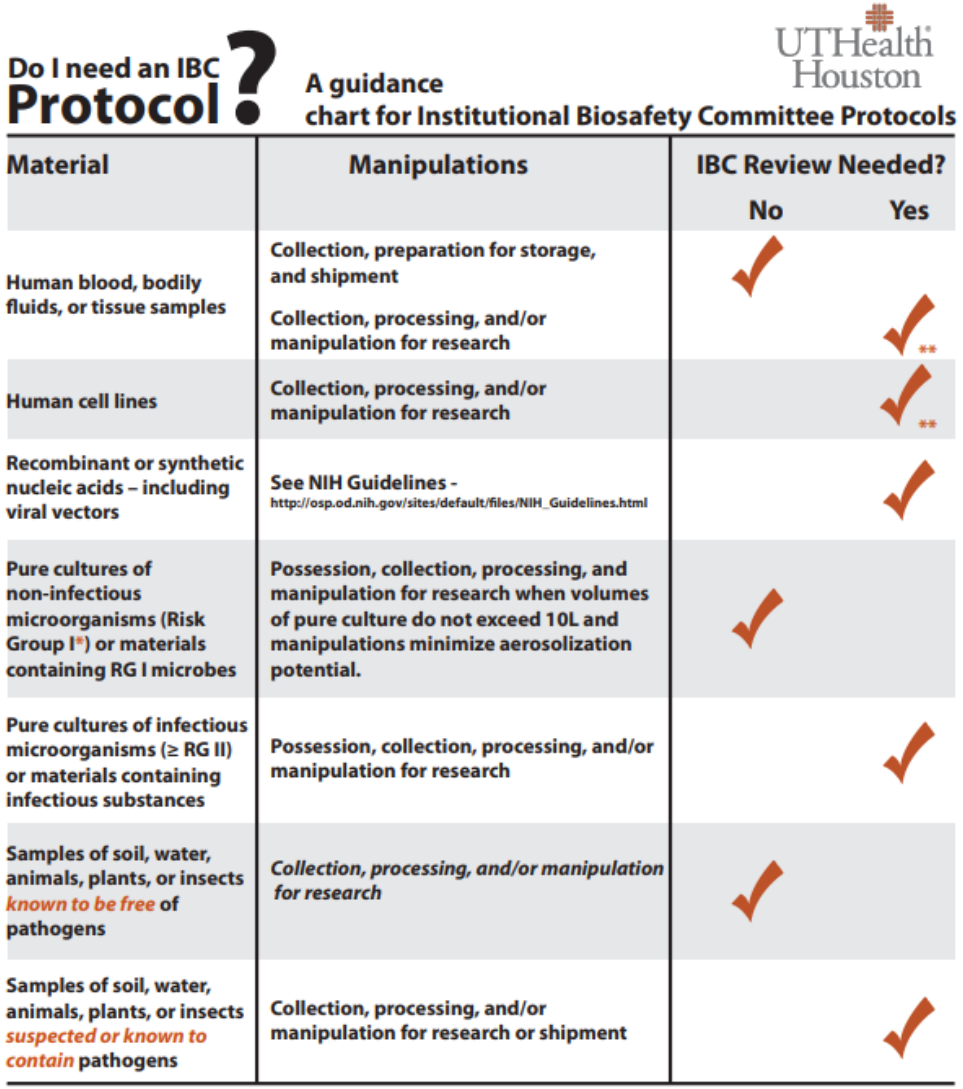
Risk Group	Agent Risk Description	Examples
RG-1	Agents not associated with disease in healthy adult humans (no or low individual risk).	*Bacillus subtilis, Escherichia coli* K12, adeno-associated virus
RG-2	Agents associated with human disease which is rarely serious & for which preventive or therapeutic interventions are *often* available (moderate individual risk).	*Staphylococcus aureus, Salmonella* sp., Herpes simplex virus (HSV), Adenovirus
RG-3	Agents associated with serious or lethal human disease for which preventive or therapeutic interventions *may be* available (high individual risk).	*Mycobacterium tuberculosis, Bacillus anthracis*, HIV
RG-4	Agents likely to cause serious or lethal human disease for which preventive or therapeutic interventions are *not usually* available (high individual & community risk).	Ebola virus, Marburg virus, Lassa virus

REQUIRES IBC APPROVAL

Samples of soil, water, animals, plants or insects suspected or known to contain pathogens

REQUIRES IBC APPROVAL

What work requires an IBC Protocol?



Do I need an IBC Protocol?

A guidance chart for Institutional Biosafety Committee Protocols

UTHealth Houston

Material	Manipulations	IBC Review Needed? No	IBC Review Needed? Yes
Human blood, bodily fluids, or tissue samples	Collection, preparation for storage, and shipment	✓	
	Collection, processing, and/or manipulation for research		✓**
Human cell lines	Collection, processing, and/or manipulation for research		✓**
Recombinant or synthetic nucleic acids – including viral vectors	See NIH Guidelines - http://osp.od.nih.gov/sites/default/files/NIH_Guidelines.html		✓
Pure cultures of non-infectious microorganisms (Risk Group I*) or materials containing RG I microbes	Possession, collection, processing, and manipulation for research when volumes of pure culture do not exceed 10L and manipulations minimize aerosolization potential.	✓	
Pure cultures of infectious microorganisms (≥ RG II) or materials containing infectious substances	Possession, collection, processing, and/or manipulation for research		✓
Samples of soil, water, animals, plants, or insects *known to be free* of pathogens	*Collection, processing, and/or manipulation for research*	✓	
Samples of soil, water, animals, plants, or insects *suspected or known to contain* pathogens	Collection, processing, and/or manipulation for research or shipment		✓

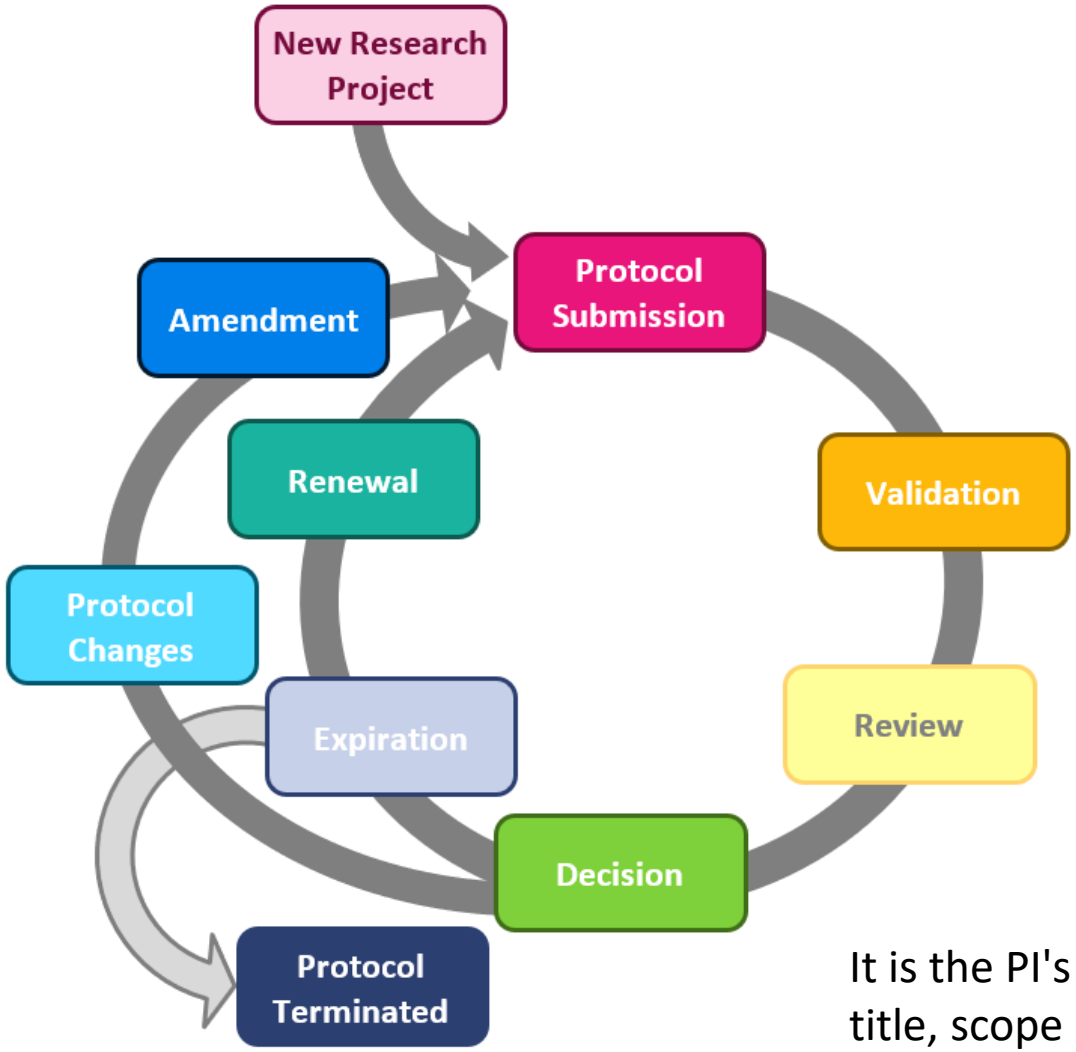
*Risk Group I organisms are not known to cause disease in healthy human adults. Risk Group II organisms are known to cause limited or treatable disease in healthy human adults. Risk Group III organisms are known to cause serious or lethal human disease with limited treatments available. Risk Group IV organisms are known to cause serious or lethal human disease and have no available treatments.[1] UTHealth does not perform work with RGIV organisms.

[1]A partial list RGI & II organisms is available here and here. These resources also include all known RG III & IV organisms.

** May meet Condionally Exempt Criteria.

1: Chosewood, L. Casey, and Deborah E. Wilson. Biosafety in microbiological and biomedical laboratories. Diane Publishing, 2007.

What work requires an IBC Protocol?



Online Protocol Submission Interface

Additional resources available at:
Biological Safety Program

It is the PI's responsibility to keep the IBC up to date with changes to title, scope of work, biological agents, rDNA, AWC or CPHS, personnel, and location.

Questions

If you have any questions or concerns, please contact the Biological Safety Program at 713-500-8170

UTHealth Houston