

Biological Use Authorization

What is it and when is it need?

Philip Barruel, Biosafety Officer
Environmental Health and Safety
UC Davis

Outline

- What is biosafety?
- Levels of oversight
- Types of biohazardous materials used at UC Davis
- Institutional Biosafety Committee
 - Biological Use Authorizations
- Biosafety trigger words
- Biosafety coordination

Medical Advances

Year	Medical Advancement
1790s	Smallpox vaccine developed
1880s	Rabies vaccine developed
1900s	Life cycle of malaria described
1920s	Pathogenesis of typhus discovered
1930s	Tetanus vaccine developed
1950s	Polio vaccine developed
1960s	Rubella vaccine developed
1980s	Prions better characterized

Source:
"The Proud Achievements
of Animal Research"
Foundation for Biomedical
Research, 2001

Research is not Risk-Free

- Work with microorganisms (bacteria, viruses, fungi, etc.)
 - Work with recombinant organisms
 - Laboratory-acquired infections
 - Elizabeth R Griffin (B virus)
 - Malcolm Casadaban (attenuated strain of the plague)
-
- There is a program that helps ensure the safety of these valuable research activities – safety committee (e.g. IBC)



External and Internal Oversight

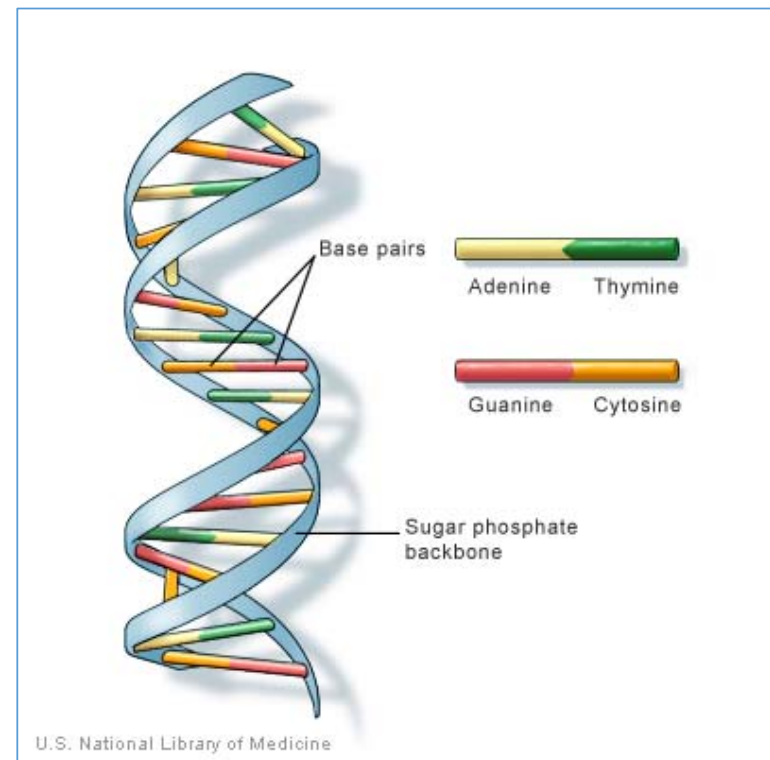
- Federal
 - NIH Guidelines for Research Involving Recombinant and Synthetic Nucleic Acid Molecules (NIH OSP)
 - Select Agent Laws and Regulations (CDC and USDA)
- State
 - Medical Waste Management Act (CDPH)
 - Cal/OSHA Standards
 - 5193 (Bloodborne Pathogens)
 - 5199 (Aerosol Transmissible Diseases)
 - 5199.1 (Zoonotic Aerosol Transmissible Diseases)
- UC Davis
 - P&P 290-55 (Biological Safety)

Biosafety Terms

- **Biosafety**
 - Pertains to “the safe handling and containment of infectious microorganisms and hazardous biological materials to prevent transmission of biohazardous agents to workers, other persons, and the environment” (BMBL, 5th edition)
- **Risk Groups**
 - The relative hazard that an infectious or pathogenic agent presents to human and animal health (1=least, 4=greatest)
- **Biological Safety Level (BSL)**
 - The suite of containment barriers and protective practices that are appropriate to the hazards presented by a particular microbiological experiment (BSL-1=lowest, BSL-4=highest)

Recombinant DNA or RNA Molecules

- Molecules constructed by joining natural or synthetic DNA or RNA segments to DNA or RNA molecules that can replicate in a living cell, or nucleic acid molecules that result from their replication (NIH Guidelines definition)



Biohazards at UC Davis

- Recombinant DNA
 - Viral vectors
 - Transgenic animals
 - Transgenic plants
- Biohazardous animals and their tissues
 - Non-human primates (especially macaques)
 - Ungulates (especially sheep and goats)
 - Field studies (*Peromyscus*, bats, turtles)

Biohazards at UC Davis (cont.)

- Human source materials
 - Bloodborne Pathogens: Infectious agents generally associated with human blood, tissues and body fluids, especially including HIV, HepBV, and HepCV
 - Examples:
 - Human cells and cell lines
 - Human blood and blood products
 - Human tissues
- Infectious agents
 - Human pathogens
 - Plant pathogens
 - Animal pathogens
 - Zoonotic agent transmission

Types of research that require BUAs

- Recombinant or synthetic nucleic acid experiments
- Infectious agent studies (to humans, animals, or plants)
- Human source materials or non-human primate source materials (including established cell lines)
- Storage of biohazardous materials

Institutional Biosafety Committee

- National Institutes of Health (NIH) requirement
 - Institutions that receive NIH funding for research involving recombinant or synthetic nucleic acid molecules
 - <https://osp.od.nih.gov/biotechnology/nih-guidelines/>
- UC Davis-specific policy (PPM 290-55)
 - Also includes infectious materials
 - <https://ucdavispolicy.ellucid.com/documents/view/303/323/>

**NIH GUIDELINES FOR RESEARCH
INVOLVING
RECOMBINANT OR SYNTHETIC
NUCLEIC ACID MOLECULES
(NIH GUIDELINES)**

April 2016

DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

Visit the NIH OSP Web site at:
<http://www.osp.od.nih.gov>

For current information on Guidelines, Protocols, Principal Investigators, Meetings,
and information about upcoming Gene Therapy Policy Conferences

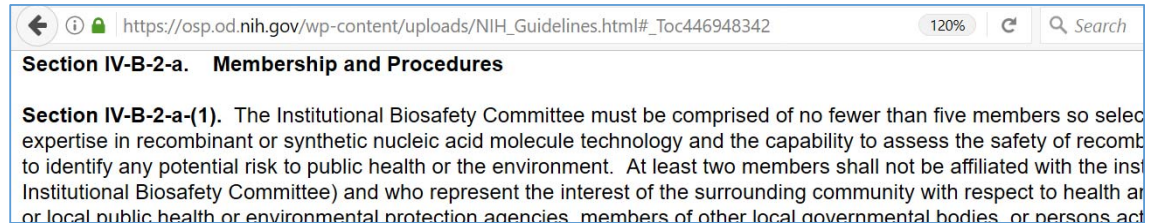
NIH OFFICE OF SCIENCE POLICY CONTACT INFORMATION:

Office of Science Policy, National Institutes of Health, 6705 Rockledge Drive, Suite 750, MSC 7985, Bethesda, MD 20892-7985 (20817 for non-USPS mail), (301) 496-9838; (301) 496-9839 (fax).

For inquiries, information requests, and report submissions:
Human gene transfer protocol submissions:

NIHGuidelines@od.nih.gov
HGTprotocols@mail.nih.gov

IBC Membership



- NIH Guidelines requirements:
 - Have no fewer than five members
 - Experience and expertise in recombinant or synthetic nucleic acid molecule technology
 - At least one member knowledgeable in animal containment principles, if these experiments involve rDNA
 - Plant, plant pathogen, or plant pest containment principles expert, if these experiments involve recombinant or synthetic nucleic acid molecules (rDNA)
 - Biological Safety Officer if research involves rDNA that require BSL-3 or BSL-4 containment or if rDNA culture is >10 liters (Large Scale)
 - Two unaffiliated members to represent local community interest

IBC Membership (cont.)

- In addition to fulfilling the NIH Guidelines membership requirements, the UC Davis IBC has members whose expertise include proper containment of non-rDNA pathogens

UC Davis Policy and Procedure Manual

Chapter 290, Health and Safety Services

Section 55, Biological Safety

Date: 3/7/13

Supersedes: 4/27/07

Responsible Department: Environmental Health and Safety (EH&S)

Source Documents: National Institutes of Health (NIH) Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules; Select Agent Regulations 42 CFR § 73, 9 CFR § 121, 7 CFR § 331.

I. Purpose

This section establishes the authority of the Institutional Biosafety Committee (IBC), outlines the policies governing the acquisition and use of biological hazards, select agents, and details IBC approval requirements for human gene transfer research.

II. Definitions

- A. Biological hazard—infectious agents (human, animal, or plant), potentially infectious materials (e.g., human tissues, cell lines, blood), recombinant and synthetic nucleic acids, toxins.

IBC Responsibilities

- Review IBC protocols (BUAs)
- Ensure compliance with the NIH Guidelines, pertinent regulations and campus policies
- Report loss of containment of rDNA materials to NIH Office of Science Policy (OSP) immediately
- Propose campus policies regarding biosafety

Biological Use Authorization (BUA)

- At UC Davis, IBC protocols = “Biological Use Authorization” (BUA)
 - UC Davis uses an online BUA form (Biosafety Information Online – BIO)
 - <https://ehs.ucop.edu/bio>

UC Safety | BIO - Test

BUA: R2570
Submitted Date:
Renewal Date:
PI: Philip Barruel

- 1. Project Summary
- 2. BUA Locations
- 3. Biological Categories
- 4. Biological Materials
- 5. Biological Links
- 6. NIH Guidelines
- 7. Risk Assessment
- 8. Attachments
- 9. PI Contacts
- 10. Authorized Personnel
- 11. Biological Safety Data Sheets
- 12. BUA Preview

Project Summary

Project Title: * ?
Test BUA

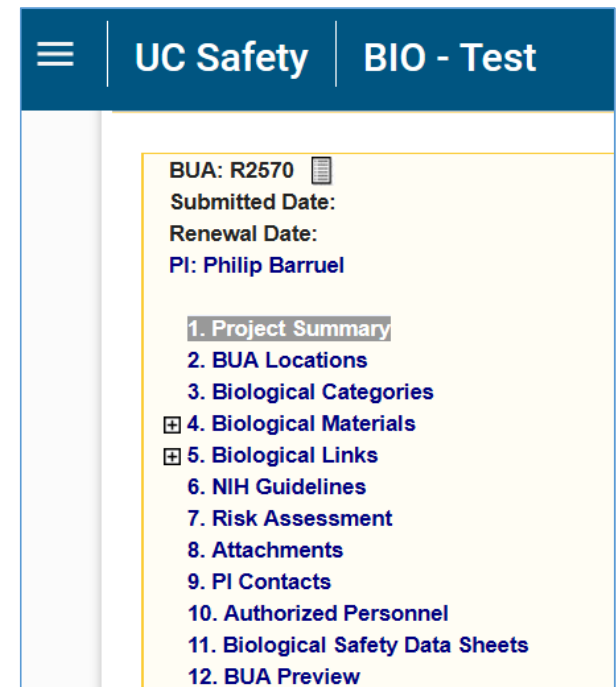
Project Summary: * ?
It is important to use language that will be detailed enough for scientific non-scientific backgrounds. Please provide sufficient information for

- What is the primary hypothesis and objectives of your research?
- What is the overall goal and specific objectives of the work with the
- What are the experimental procedures involving biohazardous materials or procedures that will be taken to prevent exposure to
- What are the conditions for collection, growth, maintenance, and

Test project summary

Biological Use Authorization (BUA) (cont.)

- PIs are to provide the following information in their BUAs
 - Project summary
 - Locations used
 - What biological materials are used
 - Relevant NIH Guidelines sections, if applicable
 - Description of experiments involving biohazardous materials
 - Risk assessment
 - Research personnel involved and their training



The screenshot shows a web interface for managing Biological Use Authorizations (BUAs). At the top, there is a dark blue header with a hamburger menu icon on the left, and the text "UC Safety" and "BIO - Test" on the right. Below the header, the main content area has a light yellow background. It displays the following information:

- BUA: R2570 [document icon]
- Submitted Date:
- Renewal Date:
- PI: Philip Barruel

Below this information is a list of sections, each with a small square icon to its left:

1. Project Summary
2. BUA Locations
3. Biological Categories
4. Biological Materials
5. Biological Links
6. NIH Guidelines
7. Risk Assessment
8. Attachments
9. PI Contacts
10. Authorized Personnel
11. Biological Safety Data Sheets
12. BUA Preview

BUA Review

- Determine the Risk Groups of all experimental components, as applicable
- Determine the “typical” containment (biosafety) level
- Consider the experimental conditions and other modifying factors
- Verify the appropriate Sections of the NIH Guidelines
- Arrive at a final risk assessment
- Determine appropriate containment for rDNA or infectious agents

Risk Assessment

- Understanding of risks is critical to working safely
 - Analysis of the components and the procedures
 - Training of personnel who perform them
 - Equipment used
 - Consider most common issues (how does the risk affect the “typical” person?)
 - Also consider less common concerns such as immunocompromised people

BUA Review Outcomes

- Approved
- Conditionally Approved
- Tabled
- Denied

BUA Timeline

- BUA submission deadline: first day of the month
- BUAs submitted by the deadline are almost always reviewed by the IBC during that month's meeting
 - The IBC meets on the fourth Mondays of the month
- BUAs are approved for three years
 - Exception: Human Gene Transfer BUAs
 - Approved for one year, but needs to be kept active until the end of the project
 - Requires an annual report

BUA Profile

- Many BUAs are for rDNA and bloodborne pathogens
- Some BUAs are for work at BSL-1 (plant rDNA and infectious agents, some animal pathogens, some other rDNA work)
- Many BUAs are amended for additional materials, locations, procedures, or personnel

BUA Profile (cont.)

- Schools and colleges that have BUAs:
 - School of Medicine
 - School of Veterinary Medicine
 - College of Biological Sciences
 - College of Letters and Science
 - College of Agricultural and Environmental Sciences
 - College of Engineering

Some Biosafety Trigger Words

- Recombinant
- Viral vector
- Transgenic
- Knockout
- Targeted gene
- Infect, infected
- Mouse Biology Program or MBP (and other core facilities that generate transgenic mice)
- Plasmid
- iPSC (induced pluripotent stem cells)
- Stem cells (human or NHP)
- Infectious agents
- Pathogens
- Xenograft
- Human cells, tissue, blood, or other body fluids (some exceptions)
- Non-human primate cells, tissue, blood, or other body fluids (some exceptions)

Biosafety Coordination

- IACUC
- IRB
- SCRO
- Sponsored Programs
- Other units in EH&S
- Export Control
- Departmental Safety Coordinators and College Safety Officers
- Purchasing
- Distribution Services (Shipping Dangerous Goods)
- EH&S outreach program for new PIs

Biosafety Office

- Philip Barruel (Biosafety Officer)
- Chelsea Schiano (High-Containment Facility Officer)
- Vivian Xian (Associate Biosafety Officer)
- Adrienne Zweifel (Associate Biosafety Officer)
- Jim Baugh (Associate Biosafety Officer)
- Students
 - Thuong Nguyen, Sarah Goldberg, Izzy Huang, Carly Aozasa
- biosafety@ucdavis.edu

Thank you

- Comments or questions?