Requirements for Institutional Biosafety Committees (IBCs) under the *NIH Guidelines*

IACUC Training Presentation

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Today's Agenda

- NIH slides: introduction to IBC requirements and duties

NIH National Institutes of Health
Office of Biotechnology Activities

- Relationship between IBCs and IACUCs
- How to apply to the CSU IBC
- When is IBC review required?
- Intro to the NIH Guidelines and exemptions to IBC review
- Specific details about mouse work
- 2024 revisions to the *NIH Guidelines* (CRISPR)

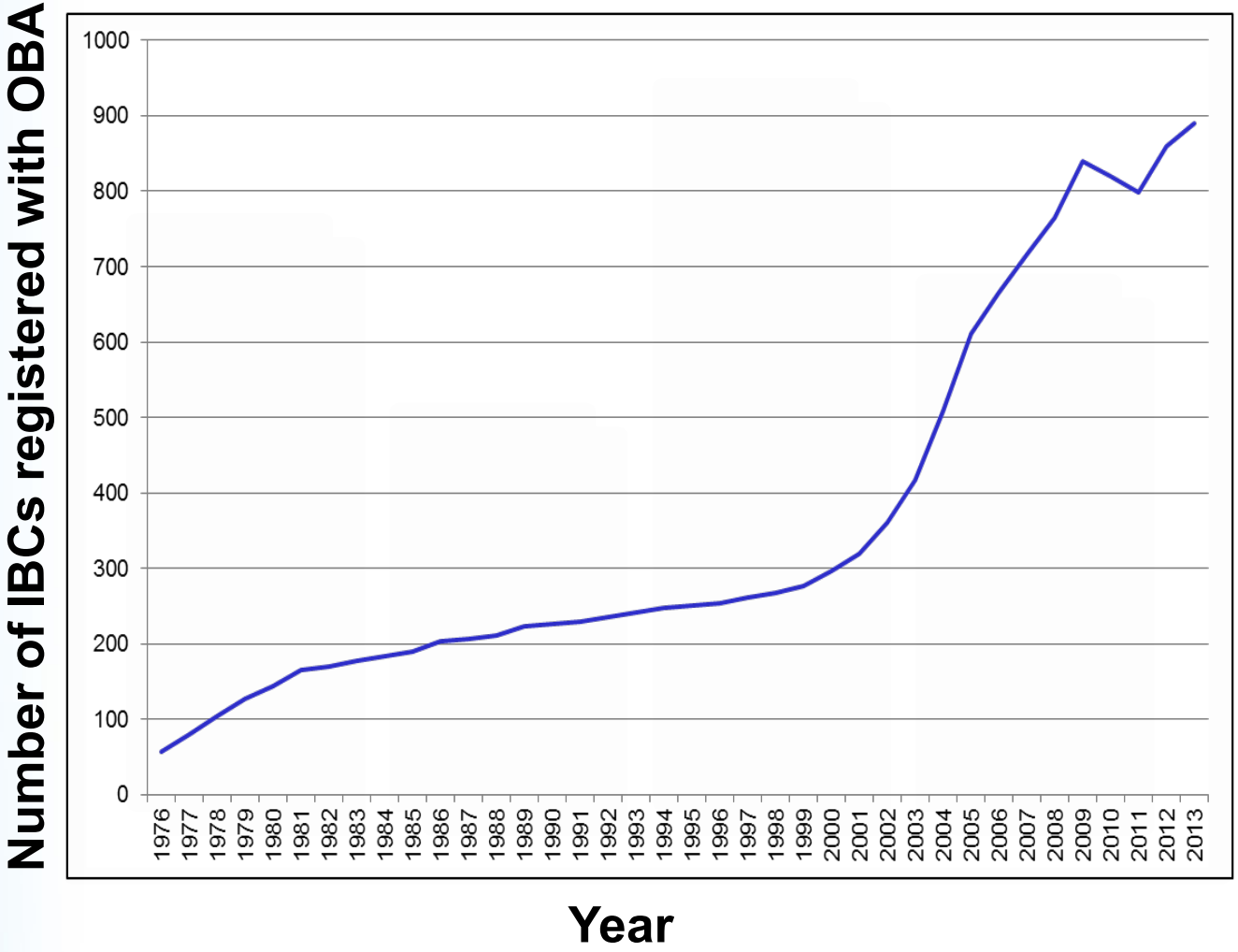
Institutional Biosafety Committees (IBCs)

- Responsible for providing *local oversight* of research involving recombinant and synthetic nucleic acid molecules
- Required under the *NIH Guidelines for Research Involving Recombinant or Synthetic DNA Molecules (aka the NIH Guidelines)*

History of IBCs

- 1975: The Asilomar Conference established guidelines for research using recombinant nucleic acids
- 1976: The first *NIH Guidelines* were drafted & the Recombinant DNA Advisory Committee (RAC) was formed
- 1978: Review responsibilities were delegated to local IBCs at research establishments
- NIH funding is contingent on compliance with the *NIH Guidelines*

IBC Registration Trends



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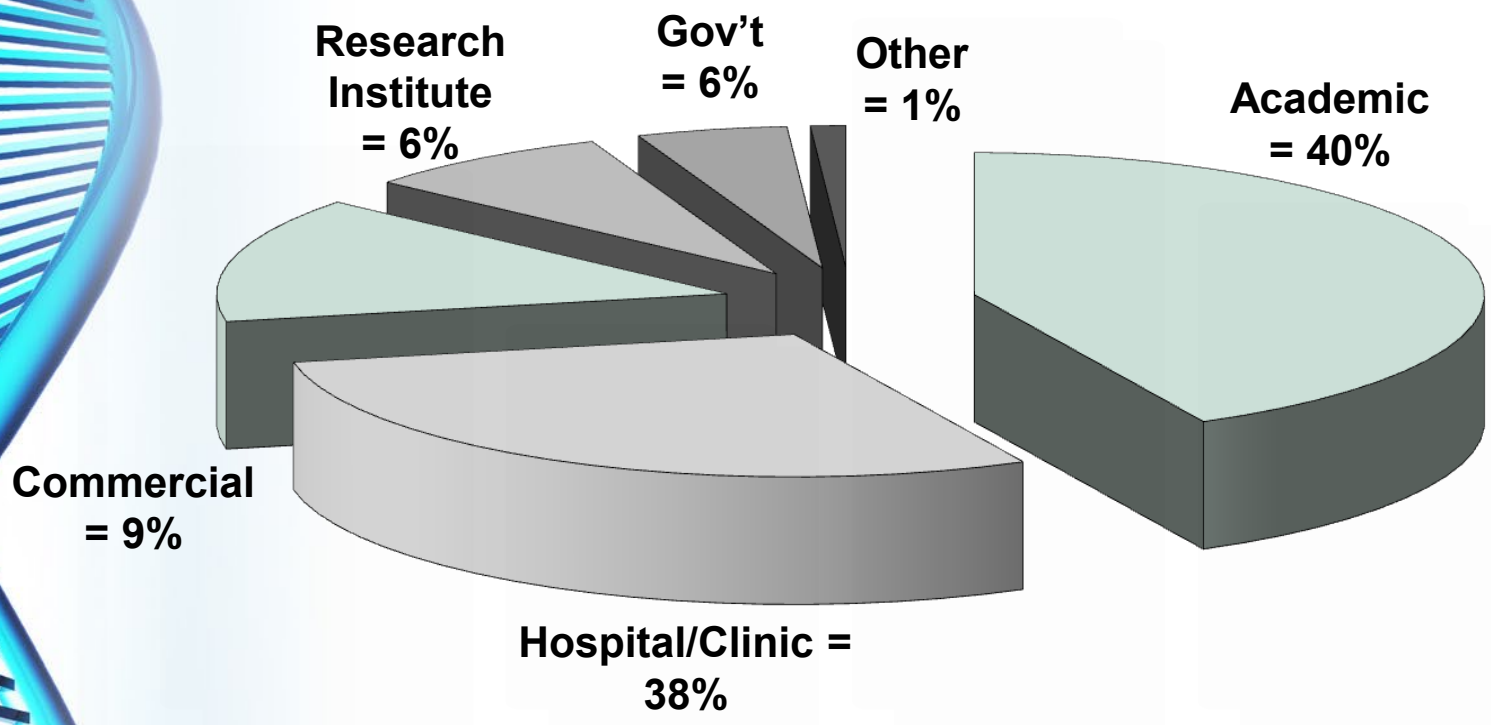
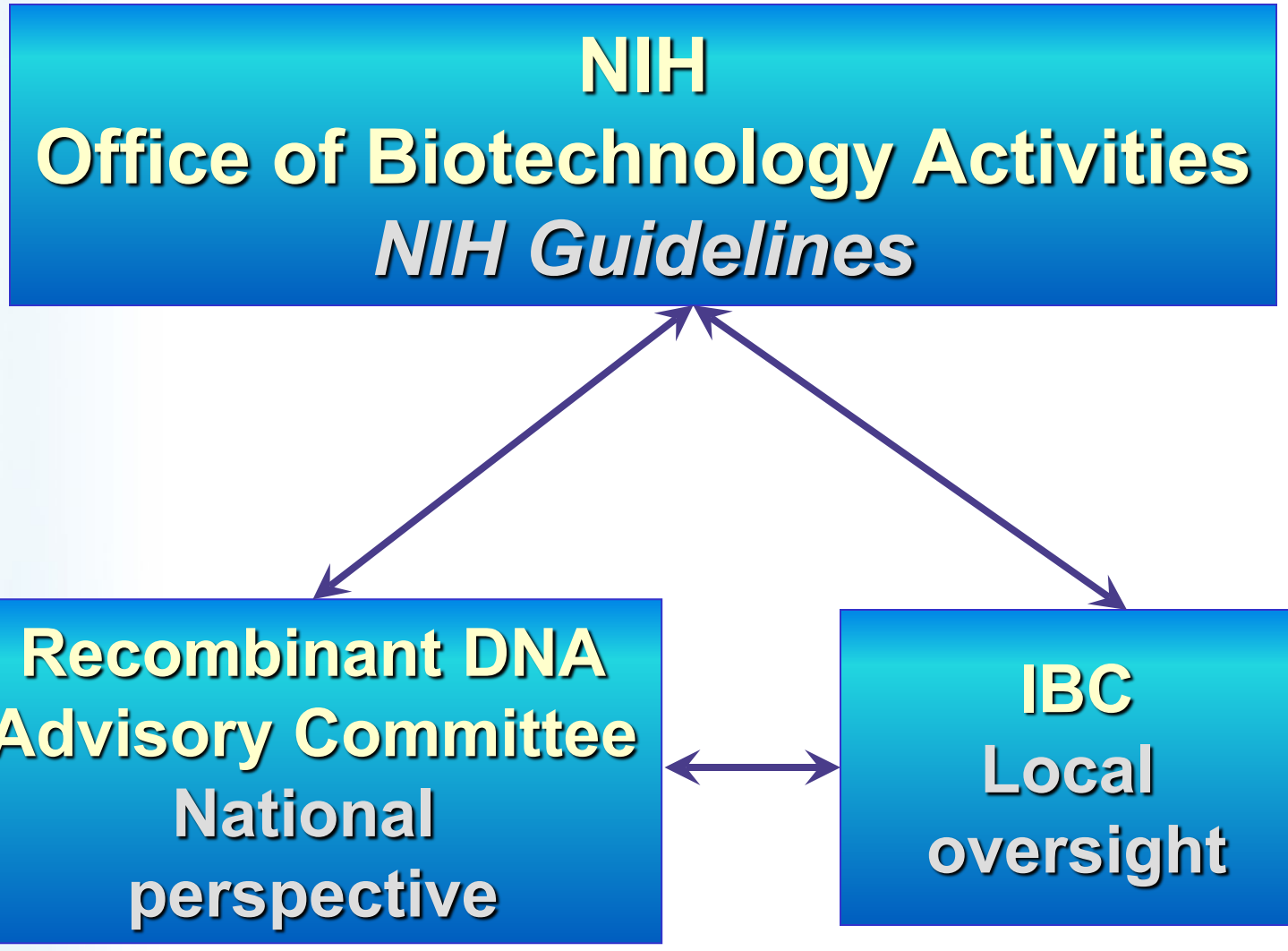
IBCs Registered with NIH



IBCs and NIH - Partners in Oversight



Institutional Biosafety Committees

- **IBCs may be assigned additional review responsibilities**
  - Select agents and toxins
  - Blood borne pathogens
  - Xenotransplantation
  - Stem cell research
  - “Dual Use” research
  - Nanotechnology
- **Broader purview is a matter of institutional discretion**

Assembling an IBC

- **Membership**
  - At least five individuals
  - Appropriate recombinant and synthetic nucleic acid expertise collectively
  - Plant and animal experts, biosafety officer as appropriate
  - At least two members not affiliated with the institution

Assembling an IBC

- **Expertise**
  - Expertise in assessment of risk to environment and public health
  - Knowledge of institutional commitments and policies, applicable law, professional standards, community attitudes, and environment
  - Biological safety and physical containment
  - Laboratory technical staff (recommended)

Assembling an IBC

- **Biological Safety Officer (BSO)**
  - A BSO must be a member of the IBC if the institution conducts recombinant or synthetic nucleic acid research at:
    - Large scale (>10 L)
    - High containment (BL-3 or BL-4)

Assembling an IBC

- **The BSO's duties include:**
  - Periodic inspection of labs
  - Reporting of any problems, violations, and research-related accidents or illnesses to the IBC and institution
  - Developing emergency plans for handling accidental spills and personnel contamination
  - Advice on lab security
  - Technical advice to PIs and the IBC on research safety procedures

Assembling an IBC

- **Non-institutional members**
  - Representatives of community interests with respect to health and protection of the environment
  - *e.g.,* officials of state or local public health or environmental authorities, local government bodies, persons with medical, occupational, or environmental expertise
  - They should be individuals who “represent community attitudes”

Staffing the IBC

- **Not prescribed in the *NIH Guidelines***
  - IBC Administrator
  - Biological Safety Officer
  - Compliance Officer
  - Environmental Health and Safety Professionals
  - Others

CSU's IBC Membership

Aaron Severson (BGES), Chair
Robert Howerton (EHS)
Barsanjit Mazumder (BGES), *ex officio* as IACUC Chair
Lou Turchyn (Animal Research Facility Mgr.)
Carrie Millward (BGES Lab Mgr.)
Andy Resnick (Physics)
Bibo Li (BGES)
Geyou Ao (Chem. Biomed. Engineering)
Nithya Gnanapragasam (BGES)
Vania De Paoli (Chemistry)
Jim Lissemore (John Carroll University, Biology)
Dave Diggins (Nestle)
Nneha Sakre (Stanford University, SLAC Nat'l Accelerator)

https://www.csuohio.edu/sprs/ibc

Registering an IBC

- **IBCs must be registered with OBA and file annual membership updates**
  - A roster of IBC members
    - Clearly indicate chair, contact person, and special expertise as appropriate (BSO, animal, plant, human gene transfer)
  - Biographical sketches of all members

Registering an IBC

- **Purpose of registration and <u>annual updates</u>**
  - Provides assurance of local review of biosafety risks
  - Allows OBA to see that IBC expertise is consistent with the *NIH Guidelines*
  - Indicates institutional point of contact
  - Provides census of the field: where research subject to the *NIH Guidelines* is being conducted

IBC Responsibilities

- **In a nutshell, what must IBCs review?**
  - Research involving recombinant or synthetic nucleic acid molecules for conformity with the *NIH Guidelines*
  - Potential risk to environment and public health
    - Containment levels per *NIH Guidelines*
    - Adequacy of facilities, SOPs, PI and lab personnel training
    - Institutional and investigator compliance; *e.g.,* incident reports

IBC Responsibilities

- **In basic and preclinical research, IBCs have authority to:**
  - Lower containment levels for certain experiments in which nucleic acid from Risk Group 2-4 is cloned in non-pathogenic organisms
  - Set containment levels for experiments involving whole plants and animals
  - Periodically review institutional compliance with *NIH Guidelines*
  - Adopt emergency plans covering spills, contamination, other accidents

IBC Responsibilities

- **For human gene transfer research, IBCs must also ensure:**
  - No participant enrolled in a trial until RAC review, IBC and IRB approval has been obtained
  - Issues raised by the RAC in public review are considered
  - Final IBC approval occurs only after RAC review
  - PI compliance with surveillance, data reporting, and adverse event reporting

IBC Responsibilities

- **Incident reporting:**
  - IBCs must report to the NIH "...any significant problems, violations of the *NIH Guidelines*, or any significant research-related accidents and illnesses"
  - Escaped transgenic animal
  - Needle stick
  - Spills of materials requiring BL2 containment resulting in overt exposure
  - Spills of materials requiring BL3-4 containment resulting in overt or potential exposure

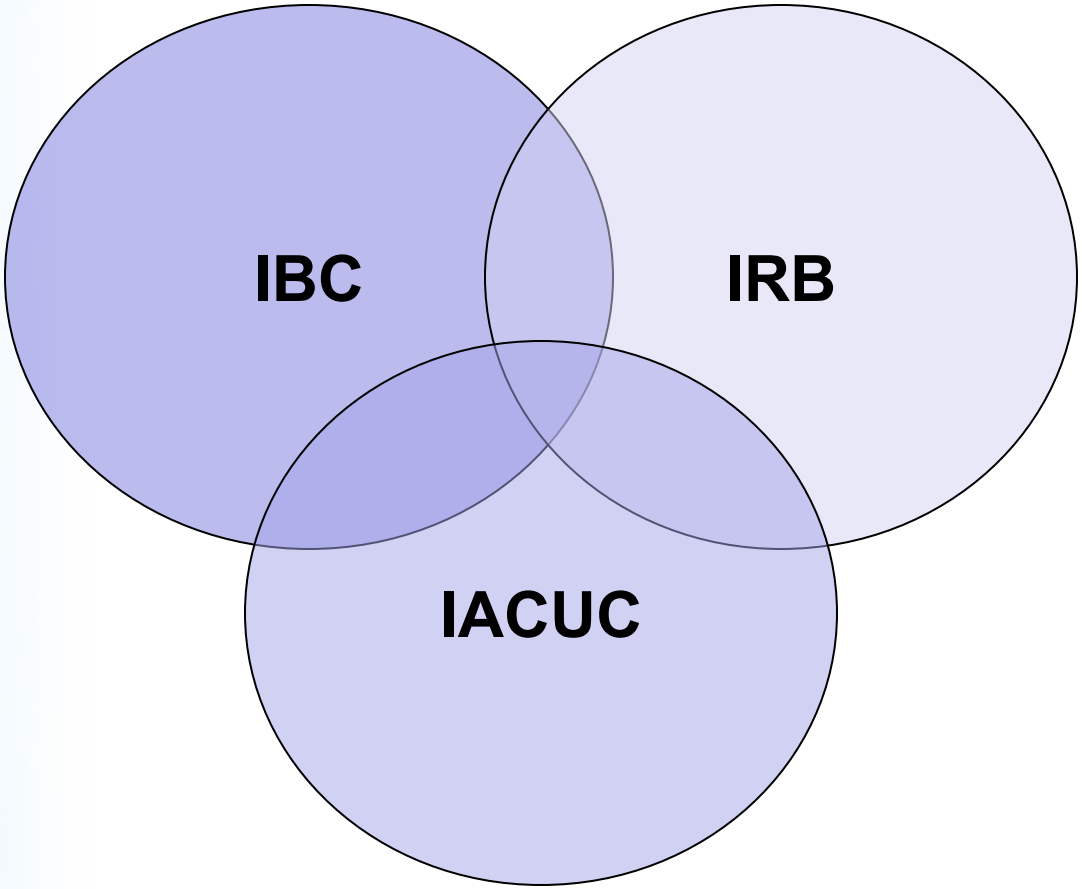
IBCs and Exempt Research

- **Who should determine what research is exempt? IBCs? The PI?**
  - A matter of institutional policy
  - IBC may wish to designate the chair, a member, or the BSO to conduct an initial review to confirm what is exempt and what requires full IBC review
  - NIH OBA can help with determinations
  - The PI is ultimately responsible for ensuring compliance with the *NIH Guidelines*. IBCs cannot review what they do not know about.

IBCs and Exempt Research

- **Who determines whether research is exempt <u>at CSU</u>?**
  - PIs should read and interpret the *NIH Guidelines* to determine exemption status
  - PIs should consult with the IBC Chair if they are uncertain
  - When in doubt, ***ASK***. If the IBC doesn't know the answer, we can look it up or ask NIH OBA for guidance.

IBCs and Other Institutional Research Oversight Committees



CSU IBC currently enjoys little overlap with IRB purview, some with IACUC

IBC Coordination with Other Institutional Oversight Committees

- Not prescribed in the *NIH Guidelines*
- Institutions should determine the best way for these committees to interact and share information
- Case IACUC will not review protocols w/ recombinant DNA until the IBC has approved
- CSU IACUC chair is *ex officio* on IBC & *vice versa*.
- CSU IBC chair conducts pre-review on all IACUC applications.

IBCs and IACUCs – Oversight of Animal Research

- **Joint purview & ideally collaborative review of certain types of research**
  - Transgenic or cloned animals
  - Use of recombinant or synthetic nucleic acid molecules in animals
  - Pre-clinical studies and data assessment for human gene transfer protocols

IBC and IACUC Review of Animal Research Subject to the *NIH Guidelines*

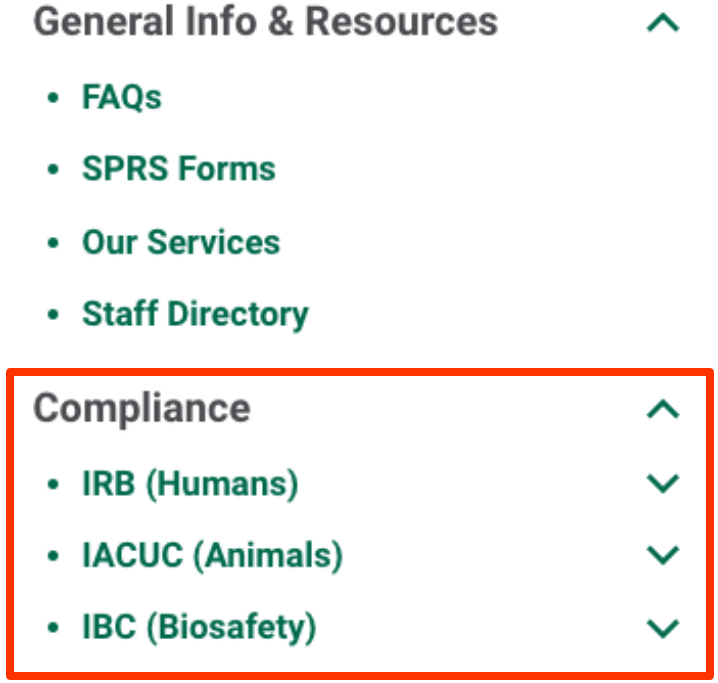
IBC Review	IACUC Review
Risks to human health - Transfer of genetically altered material, viral vectors etc. **Risks to the environment** - Escape and establishment in the wild - Interbreeding with wild stock - Consumption by other animals	**Animal welfare** - Pain and distress from adverse phenotypes (behavioral, anatomical and physiological abnormalities) - Risks to other animals in the facility from the inadvertent spread of vectors

IBCs and NIH OBA

- **NIH Office of Biotechnology Activities provides oversight, guidance, and resources for IBCs**
  - Staff and information resources available to help ensure IBCs, their institutions, and investigators are compliant with the *NIH Guidelines*
  - Scientific and medical staff available to answer queries
    - Interpretation of *NIH Guidelines*
    - Containment
    - Exemptions
    - Risk group classification
- **If local expertise is not available, the IBC can ask the NIH OBA**

How to Apply to CSU IBC

https://csuohio.edu/sprs/ibc



How to Apply to CSU IBC

Links to the NIH Guidelines, the Biosafety in Microbiological and Biomedical Laboratories (BMBL) 5th edition, and other biosafety guidance is available under the Links section.

IBC FORMS FOR DOWNLOAD

- IBC Application Form
- Examples
- Application Continuation Pages
  - S2A Continuation Page
  - S4C Continuation Page
  - S5 Continuation Page

EXEMPTIONS SPECIFIED IN THE NIH GUIDELINES

- Does your *E. coli* experiment require IBC review?
- Does your *S. cerevisiae* experiment require IBC review?
- Does your mouse experiment require IBC review?
- Does your tissue culture experiment require IBC review?

IBC REQUIREMENTS

- Biosafety Level 1 Requirements
- Biosafety Level 2 Requirements
- Biosafety cabinets (BSC) OSHA requirements
- Requirements for IBC's (Presentation)

Site will always have current forms!

Application and Examples (SAMPLE TEXT)

Application and process modeled after CWRU (Survived NIH OBA Audit)

What do BSLs mean?

This slide deck will be posted soon!!!

How to Apply to CSU IBC

¶

1C. Application Date¶

5/20/2020¶

¶

1D. Is this a new submission, resubmission, renewal, or amendment? *New submissions are applications that have not been previously submitted. Resubmissions involve applications that have been previously rejected or returned for revision. Renewals allow the project to continue beyond the prior approval period. Amendments update the project when there are changes in personnel or experimental details before a renewal is required.*¶

New Submission →¶

¶

Approvals are good for 3 years, but an amendment should be submitted if there are major changes.

For example:

- New recombinant/synthetic nucleic acids
- Adding lentiviral transduction

How to Apply to CSU IBC

Statement·of·safety·procedures·in·place:↵
This·CRISPR·design·does·package·the·gRNA·and·CAS9·enzyme·within·the·same·viral·particle.·In·addition·to·safety·protocols·designed·to·prevent·exposure·(described·below),·the·risk·to·researchers·is·mitigated·by·the·exclusive·targeting·of·mouse·genes·within·our·mouse·oligodendrocyte·progenitor·cells.·Although·the·targeted·genes·are·conserved·between·mouse·and·human,·the·guides·we·have·chosen·show·low·complementarity·to·the·human·homolog·sequence·(and·other·human·genomic·sequences)·as·indicated·by·BLAST·alignment.↵
↵
Numerous·administrative·controls,·engineering·controls,·and·use·of·proper·personal·protective·equipment·support·the·safety·of·these·proposed·experiments.↵
↵

- Safety procedures, decontamination, PPE, and waste disposal are very important parts of the application.
- Documenting appropriate training is critical!
- The IBC needs to understand <u>what</u> you are doing and <u>how</u> you're doing it
- Superficial applications will be returned

How to Apply to CSU IBC

3F. What is the proposed Risk Group/Biosafety Level (BSL)/Animal Biosafety Level (ABSL) for this project:

☐ Risk Group 1	☐ BSL 1	☒ ABSL 1
☐ Risk Group 2	☒ BSL 2	☐ ABSL 2
☒ Risk Group 3	☐ BSL 3	☐ ABSL 3
		☐ ABSL N/A

For more info on Risk Groups/BSLs/ABSLs please refer to the Biosafety in Microbiological and Biomedical Laboratories (BMBL) at the following link:
https://www.cdc.gov/labs/pdf/CDC-BiosafetyMicrobiologicalBiomedicalLaboratories-2009-P.PDF
Reference pages 10, 24, and 61

- The PI should propose a suitable Risk Group and Biosafety Level.
- The IBC will make the final determination of Risk Group and containment.

How to Apply to CSU IBC

- Completed applications should be emailed (along with any continuation pages, maps of viral vectors, etc) to:

  biosafetycommittee@csuohio.edu

- Upon receipt, the application will be assigned to an IBC member for review and an IBC meeting will be scheduled.
- IBCs CANNOT review proposals by email.
- IBC is currently meeting “as needed.”

Who must apply to IBC?

- The *NIH Guidelines* apply to:

  "*Research that is conducted at or sponsored by an institution that receives <u>any support</u> for recombinant or synthetic nucleic acid research from NIH.*"

- <u>All research</u> at CSU must comply with the *NIH Guidelines*, regardless of funding source.
- <u>All research</u> at CSU must be approved by IBC unless exempt under the *NIH Guidelines.*

When is approval required?

- **The *NIH Guidelines* specify three major classes of experiments:**

1. Experiments that must have IBC approval before initiation **(Section III-D):**

   RG≥2 vector, DNA from RG≥2 organism cloned into host-vector system, some whole animals or plants, >10L of culture, Lentivirus, etc.

2. Experiments that require IBC notice simultaneous with initiation **(Section III-E):**

   BL1 containment, some whole rodents, some AAV, etc.

3. Exempt experiments **(Section III-F & Appendix C)**

What research is exempt?

- **Exemptions are listed in *Guidelines* Section III-F and Appendix C:**
  - Nucleic acids that cannot replicate (oligos, miRNAs, siRNAs not expressed from plasmid)
  - Recombinant or synthetic nucleic acids in tissue culture
  - *E. coli* K12 host-vector systems (BL21 is NOT a K12 strain and is NOT exempt!)
  - *Saccharomyces* host-vector systems
  - Some exceptions: cloning ≥RG3 DNA, >10L cultures, >1/2 viral genome, etc.

Exemptions for Rodents

- **Exemptions are listed in *Guidelines* Section III-F and Appendix C:**
  - Purchase, transfer, or breeding of transgenic rodents (< ½ genome from single viral family)
  - If creating new transgenic mouse *at CSU*, IBC must approve before initiation
  - CSU IBC does not need to approve creation of a new transgenic mouse by a company or a collaborator at another institution (<u>just notify IBC by email</u>)

Non-exempt Rodent Work:

- Creating a new transgenic mouse *at CSU*
- Injecting a mouse with virus (recombinant or wild type)
- Introducing recombinant cell lines into mice (xenografts, allografts)
- Xenografts using non-recombinant cell lines require IBC notification – contact IBC chair for more information.

Changes in the April 2024 NIH Guidelines:

- Most changes relate to gene drive experiments
- CRISPR can allow genome editing w/o viral vectors or integration of r/sNA into a genome. Nevertheless, it is not exempt.

Changes in the April 2024 NIH Guidelines:

Section III–C–1: Experiments Involving the Deliberate Transfer of rsNA Molecules, or DNA/RNA Derived From rsNA Molecules, Into One or More Human Research Participants

Human gene transfer is the deliberate transfer into human research participants of either:

1. Recombinant nucleic acid molecules, or DNA or RNA derived from recombinant nucleic acid molecules, or
2. Synthetic nucleic acid molecules, or DNA or RNA derived from synthetic nucleic acid molecules, that meet any one of the following criteria:
    a. Contain more than 100 nucleotides; or
    b. Possess biological properties that enable ~~integration~~ introduction of stable genetic modifications into the genome (*e.g.*, cis elements involved in integration, gene editing); or
    c. Have the potential to replicate in a cell; or
    d. Can be translated or transcribed.

Section III-F: Exempt Experiments

The following recombinant or synthetic nucleic acid molecules are exempt from the NIH Guidelines and registration with the Institutional Biosafety Committee is not required; however, other federal and state standards of biosafety may still apply to such research (for example, the Centers for Disease Control and Prevention (CDC)/NIH publication Biosafety in Microbiological and Biomedical Laboratories).

Section III–F–1. Those synthetic nucleic acids that:

(1) Can neither replicate nor generate nucleic acids that can replicate in any living cell (*e.g.*, oligonucleotides or other synthetic nucleic acids that do not contain an origin of replication or contain elements known to interact with either DNA or RNA polymerase), and

(2) Are not designed to ~~integrate into DNA~~ introduce a stable genetic modification, and

(3) Do not produce a toxin that is lethal for vertebrates at an LD50 of less than 100 nanograms per kilogram body weight.

If a synthetic nucleic acid is deliberately transferred into one or more human research participants and meets the criteria of Section III–C, it is not exempt under this Section.

Questions?