Biosafety and the NIH Guidelines

This section will explore:

• Why the NIH Guidelines are important
• The definition of recombinant or synthetic nucleic acid research

✓ Content of the NIH Guidelines

Section III - Experimental Classifications

• What is an IBC and its function?
• How to submit a research proposal to the IBC for review
Content of the *NIH Guidelines*

- Section I – Scope
- Section II – Safety Considerations
- **Section III – Experimental Classifications**
- Section IV – Roles and Responsibilities
- Appendices
NIH Guidelines – Section III

Levels of Review

- IBC, RAC, NIH Director (III-A)
- IBC, PBBP (III-B) (in consult with experts)
- IBC, IRB, RAC (III-C)
- IBC (III-D)

University of Pittsburgh
IBC Registration only

RISK
Section III-A

Requires: NIH Recombinant Advisory Committee (RAC) review, NIH Agency Director approval, and IBC review and approval before initiation

Transfer of a **Drug Resistance Trait** may be considered to be a “**Major Action**” in the *NIH Guidelines*...

The deliberate transfer of a drug resistance trait to microorganisms that are:

a) not known to acquire the trait naturally, if such acquisition

b) could compromise the use of the drug to control disease agents in humans, veterinary medicine, or agriculture
Section III-B

Requires: NIH/OBA Office review and IBC review and approval before initiation

- **III-B-1**: Experiments involving the cloning of Toxin molecules with LD50 of less than 100 nanograms per kilogram body weight

- **III-B-2**: Experiments similar to any identified as previously approved (under Section III-A) as a “Major Action” under the *NIH Guidelines*
Section III-C

Requires: IBC and review for recommendation to NIH, NIH Registration, then approval before initiation

Human gene transfer (HGT)
Deliberate transfer into human research participants of either:

(i) Recombinant nucleic acid molecules, or DNA or RNA derived from recombinant nucleic acid molecules, **OR**

(ii) Synthetic nucleic acid molecules, or DNA or RNA derived from synthetic nucleic acid molecules, that meet any one of the human gene transfer criteria
Section III-C-1

Human Gene Transfer: Does the clinical research meet any one of the following criteria?

- Contain more than 100 nucleotides; **OR**
- Possesses biological properties that enable integration into the genome; **OR**
- Has the potential to replicate in a cell; **OR**
- Can be translated or transcribed
“Vaccine Exemption” Footnote of Appendix M

Human studies in which a) induction or enhancement of an immune response to a vector-encoded microbial immunogen is the major goal, and that b) it has been demonstrated in model systems, and c) the persistence of the vector-encoded immunogen is not expected.

However, it is NOT exempt IBC review!
How to initiate IBC review for clinical study:

- Complete the *NIH Guidelines* training module at Hsconnect/ISER
- Go to the IBC web portal and complete the on-line application: [www.MyIBC.pitt.edu](http://www.MyIBC.pitt.edu)
- IBC application must be reviewed and approved before IRB review
- Contact the IBC Office for assistance with determining criteria for IBC review (evaluation)
Section III-D

Section III-D describes experimental classes that require IBC review and approval before initiation

- IBC approvals must occur at a convened meeting of the membership (transparency in research)
- IBC meetings are scheduled monthly

- Section III-D describes the seven (7) sub-classifications of experiments
  - III-D-1 through III-D-7
Section III-D-1

Includes experiments using any of the following:

- Risk Group 2 *(Adenovirus, Herpes)*
- Risk Group 3 *(HIV, MERS)*
- Risk Group 4, *(Ebola, Marburg)*
  or
- Any Restricted Agent *(Anthrax)*
  (such as a Select Agent or a regulated toxin)

...as the Host-Vector System
Section III-D-2

Includes experiments in which **Nucleic Acids** from a:
- Risk Group 2,
- Risk Group 3,
- Risk Group 4, **OR**
- Any Restricted Agent (such as a Select Agent or a regulated toxin)

are cloned into a:
- *Non*pathogenic Prokaryotic
  **OR** a
- Lower Eukaryotic

**Host-Vector System**
Section III-D-3

Includes experiments that involve the Use of:

▪ Infectious DNA or RNA Viruses

OR

▪ Defective DNA or RNA Viruses in the presence of Helper Virus in Tissue Culture Systems (in vitro)
Section III-D-4

Includes experiments where:

- An animal’s genome has been altered by stable introduction of recombinant or synthetic nucleic acids into the *germline* (transgenic animals)

- Viable recombinant or synthetic nucleic acid molecule-modified microorganisms are tested on whole animals (*in vivo*)
Section III-D-5

Require IBC review and approval before initiation

Includes experiments in which:

- Plants are genetically engineered by recombinant or synthetic nucleic acid molecule methods
- Plants are used with recombinant or synthetic nucleic acid molecule containing insects
- Dependent on risks (BSL-2 through BSL-4)
Section III-D-6

Experiments that Require IBC review and approval before initiation

- More Than 10L of Culture at one time

This section applies to all cultures or viable organisms that contain recombinant or synthetic nucleic acid molecules in large quantity volumes

* Also See Appendix K
Experiments involving Influenza Viruses:

- Generated by recombinant or synthetic methods shall be conducted under containment corresponding to the source virus of the majority of gene segments in the construct.

- Influenza viruses or constructs containing genes or segments from selected influenza strains shall be conducted under BSL-3 enhanced containment (RBL)
  - 1918-1919 H1N1 (1918 H1N1) human
  - H2N2 (1957-1968) human
  - HPAI H5N1 (high-path avian strains within the Goose/Guangdong/96-like H5 lineage)
End of Chapter 2