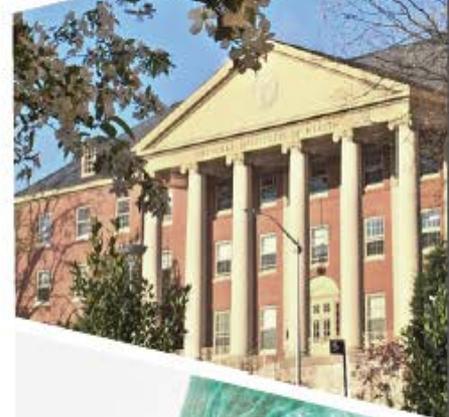
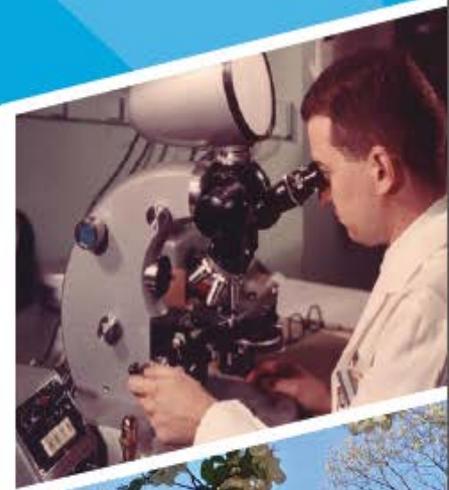


NIH Guidelines: Honoring the Past, Charting the Future

Session II:

The Current NIH Framework for the Oversight of Research with Recombinant or Synthetic Nucleic Acid Molecules



Goals of Session II

Explore the current framework established by the *NIH Guidelines*, including the roles of Institutional Biosafety Committees (IBCs) and the Recombinant DNA Advisory Committee (RAC)

Jessica Tucker, Ph.D.

Stephen J. Libby, Ph.D.

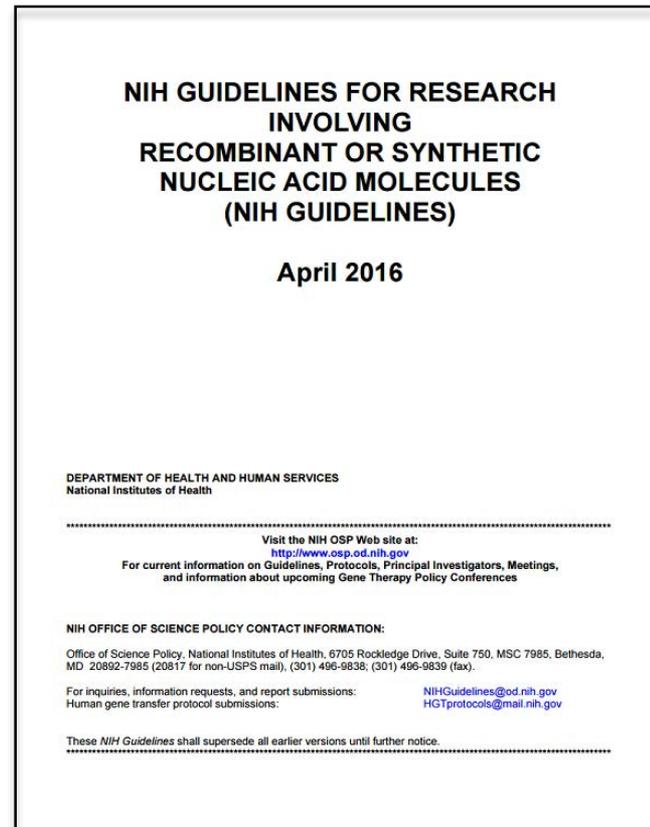
Hans-Peter Kiem, M.D., Ph.D.

NIH Framework for Oversight of Recombinant and Synthetic Nucleic Acid Research

- **NIH biosafety guidelines**
 - *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)*
- **Local review of risks and implementation of *NIH Guidelines***
 - IBCs
- **National advisory body**
 - RAC

NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules

- **A scientifically responsive document that has continually evolved to keep pace with scientific advances**
 - **Amended many times since 1976**
 - **Latest version April 2016**



NIH Guidelines and Emerging Technologies

“The *NIH Guidelines* cannot anticipate every possible situation... As new techniques develop, the *NIH Guidelines* should be periodically reviewed to determine whether and how such research should be explicitly addressed. It is the responsibility of the institution and those associated with it to adhere to the intent of the *NIH Guidelines* as well as to their specifics.”

Content of the *NIH Guidelines*

- **Section I – Scope of the document (purpose, definitions, applicability)**
- **Section II – Safety considerations (risk groups, risk assessments, containment)**
- **Section III – Types of experiments covered**
- **Section IV – Roles and responsibilities**
- **Appendices**

The NIH Guidelines Apply to...

- **Research with recombinant or synthetic (or both) nucleic acid molecules that is performed at or sponsored by an institution that receives any NIH funding for such research**
- **Term and condition of NIH funding for research with recombinant or synthetic nucleic acid molecules**

NIH Guidelines – Risk Groups

RG 1	RG 2	RG 3	RG 4
<p>Agents that are not associated with disease in healthy adult humans</p>	<p>Agents that are associated with human disease which is rarely serious and for which preventive or therapeutic interventions are <i>often</i> available</p>	<p>Agents that are associated with serious or lethal human disease for which preventive or therapeutic interventions <i>may be</i> available (high individual risk but low community risk)</p>	<p>Agents that are likely to cause serious or lethal human disease for which preventive or therapeutic interventions are <i>not usually</i> available (high individual risk and high community risk)</p>

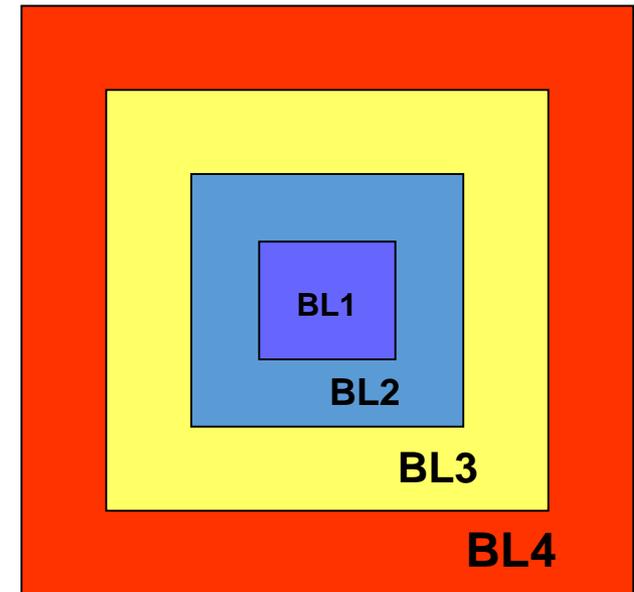
NIH Guidelines – Containment

■ Physical (Biosafety Levels)

- Practices
- Equipment
- Facilities

■ Biological

- Survival
- Transmission



NIH Guidelines

Roles and Responsibilities

- **NIH**
- **Institution**
- **IBC**
- **Biological Safety Officer (BSO)**
- **Principal Investigator (PI)**

NIH Responsibilities under the *NIH Guidelines*

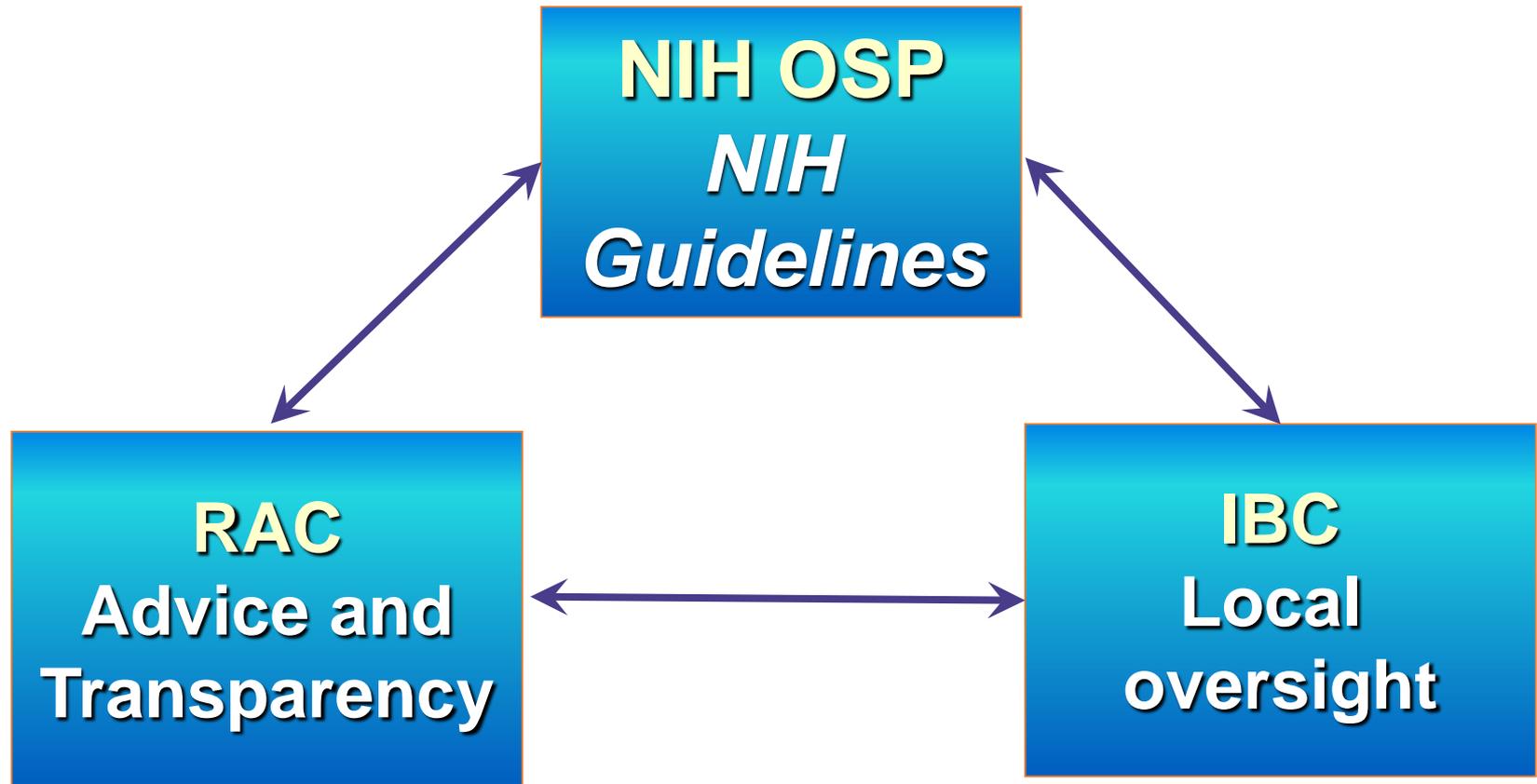
■ NIH Director

- Establishing the *NIH Guidelines* and overseeing their implementation
- Establishing and maintaining the RAC
- Approving or rejecting Major Actions (after receiving advice from the RAC)
- Promulgating and amending a list of classes of recombinant or synthetic nucleic acid molecules to be exempt from the *NIH Guidelines*
- Certifying new host-vector systems
- Adopting changes to the *NIH Guidelines*

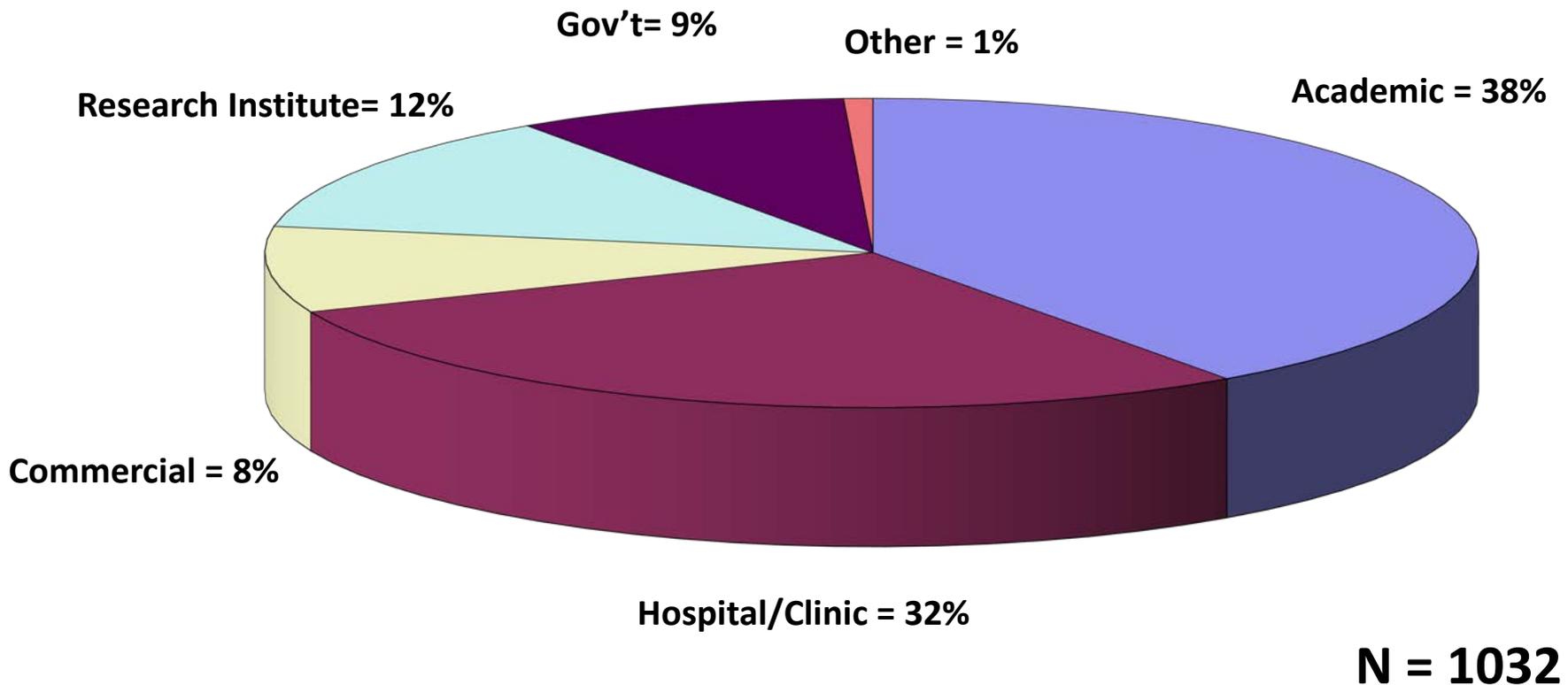
NIH Responsibilities **under the *NIH Guidelines***

- **NIH OSP (on behalf of the NIH Director)**
 - **Review of certain basic recombinant or synthetic nucleic acid molecule experiments**
 - **Minor Actions**
 - **Review and approval of certain toxin experiments**
 - **Review of containment lowering requests**
 - **Approval of “restricted” experiments**
 - **Conduct and support training for IBCs, Investigators, BSOs, and all those involved in the conduct or oversight of research subject to the *NIH Guidelines***

IBCs, RAC, and NIH – Complementary Roles



IBCs Registered with the NIH OSP July 2017



IBC Responsibilities

- Review research involving recombinant or synthetic nucleic acid molecules for conformity with the *NIH Guidelines*
- Assess potential risk to environment and public health
 - Containment levels per *NIH Guidelines*
- Ensure adequacy of facilities, SOPs, PI and lab personnel training
- Periodically review research
 - Ensure Institutional and investigator compliance
- Adopt emergency plans covering spills, contamination, other accidents

IBC Responsibilities

- **For contained laboratory research**
 - **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**

Functions of the RAC

- **Provide a transparent forum for the discussion of novel scientific, ethical, and safety issues associated with recombinant and synthetic nucleic acid research**
- **Advise the NIH Director on:**
 - ❑ **Clinical trial design for specific human gene transfer experiments to identify unique scientific and ethical issues, and to promote a culture of safety for research participants**
 - ❑ **Appropriate biosafety protections for researchers, health care workers, and close contacts of research subjects, for recombinant and synthetic nucleic acid research**
- **Inform the deliberations of Federal and local oversight bodies**

The RAC and Biosafety

- **Reviews and Advises the NIH Director on Major Actions**
 - **The deliberate transfer of a drug resistance trait to microorganisms that are not known to acquire the trait naturally if such acquisition could compromise the ability to control disease agents in humans, veterinary medicine, or agriculture**
 - **Major Actions discussed at recent RAC meetings**
 - **Transfer of tetracycline resistance to Chlamydia**
 - **Transfer of chloramphenicol or tetracycline resistance to different strains of Rickettsia**

The RAC and Biosafety

- **Provide advice on biosafety issues**
 - **“Institutional Biosafety Committees may consult with NIH OSP regarding experiments that are not Major Actions but nonetheless raise important public health issues. NIH OSP will consult, as needed, with one or more experts, which may include the RAC.”**
 - **Biosafety issues discussed at recent RAC meetings**
 - **Biosafety of cloning RG4 *Mononegavirales* in *E. coli***
 - **Containment for certain research with defective strains of Lassa, Ebola, and hemorrhagic fever viruses**
 - **Housing of non-human primates in BL4 containment**

The RAC and Biosafety

- **Provide advice on amending the *NIH Guidelines***
 - **Examples include:**
 - **Amending the scope to provide biosafety guidance for synthetic biology research**
 - **Providing additional biosafety guidance for research with Risk Group 3 influenza viruses with increased pandemic potential**
 - **Supplementing biosafety guidance for research involving mammalian-transmissible HPAI H5N1**
 - **Providing guidance to allow the housing of non-human primates in open cages in a dedicated animal room provided certain conditions are met**

The RAC and Biosafety

- **Provide a forum for public discussion of biosafety issues or emerging technologies at workshops**
 - **Biosafety workshops**
 - **Primary Containment of Non-human Primates in Biosafety Level 4 Laboratories: Challenges and Best Practices**
 - **Biosafety Considerations for Research with Highly Pathogenic Avian Influenza Virus H5N1 that is Transmissible between Mammals by Respiratory Droplets**
 - **Public Health and Biosafety Practices for Research with 1918 H1N1 Influenza Viruses**
 - **Recombinant DNA Research with Non-contemporary Influenza Viruses and Highly Pathogenic Avian Influenza Viruses**
 - **Safety Considerations in Recombinant DNA Research with Pathogenic Viruses**
 - **NIH Public Consultation on Proposed Changes to the *NIH Guidelines* for Synthetic Nucleic Acids**
 - **National Science Advisory Board on Biosecurity/RAC Roundtable on Synthetic Biology**
 - **Emerging Technologies Workshops**
 - **Genome Editing: Establishing Preclinical Toxicology Standards**
 - **Gene Therapy: Charting a Future Course**
 - **RNA Oligonucleotides: Emerging Clinical Applications**
 - **Prenatal Gene Therapy: Scientific, Medical, & Ethical Issues**