

**Introduction to the  
National Institutes of Health  
Office of Biotechnology Activities**



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# NIH Mission

- **Discover new scientific knowledge that will improve human health**
- **NIH funds, conducts, and oversees biomedical research**
  - **Over 50,000 extramural scientists**
  - **Over 2,000 research institutions**
  - **Over 5,000 intramural scientists**
  - **27 Institutes and Centers**



# NIH Stewardship Responsibilities

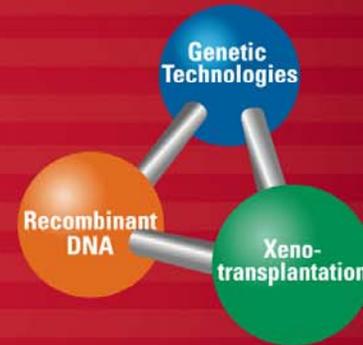
- **Invest wisely taxpayer dollars entrusted to it for the support and conduct of biomedical research**
- **Apply and communicate the knowledge gained from research**
  - ❑ **Improve the design and conduct of ongoing and future studies**
  - ❑ **Efficiently advance development of new treatments and cures**
  - ❑ **Optimize patient safety**



National Institutes of Health

## Office of Biotechnology Activities

Promoting safe and ethical science through education, communication, and sound public policy.



OBA accomplishes its mission through analysis, deliberation, and communication of scientific, medical, ethical, legal, and social issues.

**Recombinant DNA** • **Genetic Technologies** • **Xenotransplantation**

# NIH Office of Biotechnology Activities

- **Within the Office of Science Policy, Office of the Director, NIH**
- **Five programs:**
  - ❑ **Recombinant DNA (RAC)**
  - ❑ **Genetics (SACGHS)**
  - ❑ **Xenotransplantation (SACX)**
  - ❑ **Biosecurity (NSABB)**
  - ❑ **Outreach and Education**



# Recombinant DNA Program

- **Oversee recombinant DNA research, including human gene transfer**
- **Manage the Recombinant DNA Advisory Committee (RAC)**
- **Administer the *NIH Guidelines for Research Involving Recombinant DNA Molecules***
- **Partner with Institutional Biosafety Committees in the oversight of recombinant DNA research**



# Recombinant DNA Program

- **Disseminate information on technical and policy matters concerning recombinant DNA research**
  - RAC recommendations on clinical protocols
  - Interpretations of the *NIH Guidelines*
  - Scientific symposia and policy conferences
- **Develop and contribute to public policy on recombinant DNA research**
  - Interagency oversight of biotechnology

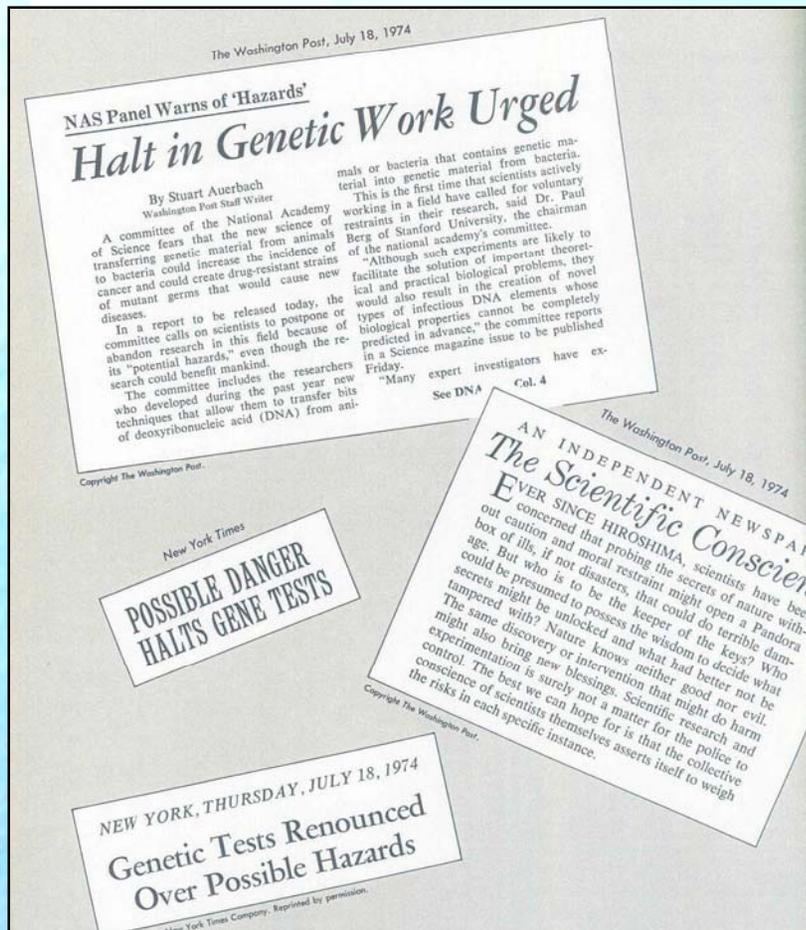


# A Brief History of Recombinant DNA Oversight

- **Emergence of recombinant DNA technology (Mid 1970's)**
- **Concerns among both scientific community and general public**
  - **Public health and safety**
  - **Environmental impact**
  - **Potential ethical and social implications**



# A Brief History of Recombinant DNA Oversight



- **NAS Committee Report (July 1974); called for**
  - a moratorium on certain experiments
  - development of NIH guidelines for conduct and review of recombinant DNA experiments

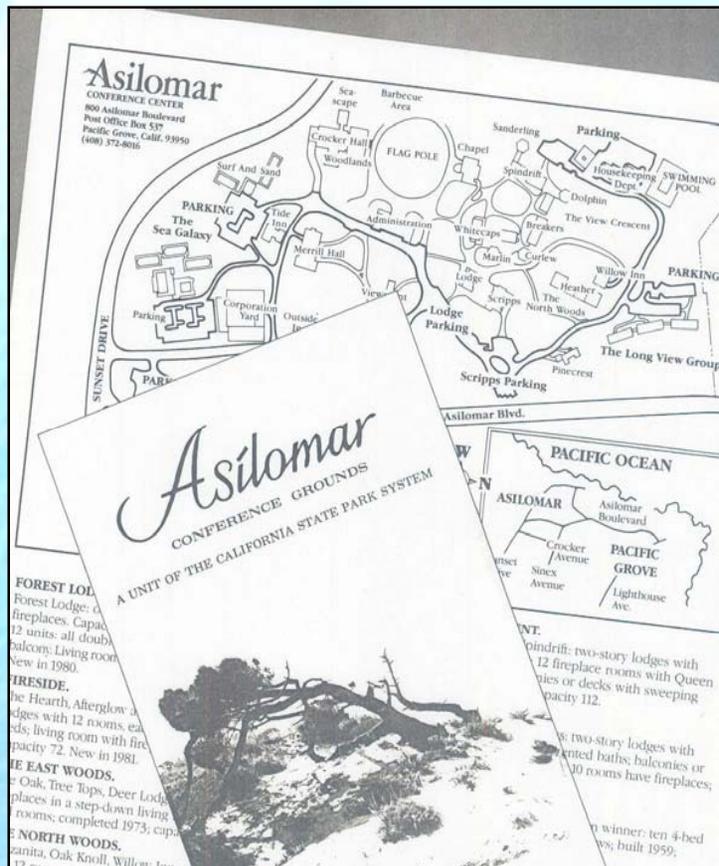


# A Brief History of Recombinant DNA Oversight



## ■ Asilomar Scientific Summit (1975)

- Premise: Scientists taking responsibility for the risks of their own research activities
- Outcomes
  - Reaffirmation of the need for guidelines
  - Establishment of a new federal oversight committee



# A Brief History of Recombinant DNA Oversight

- **NIH Recombinant DNA Molecule Program Advisory Committee**
  - **First federal advisory committee**
  - **Launched process of developing NIH guidelines for recombinant DNA oversight**
  - **Made recommendations about local oversight**
    - **NIH grants using rDNA be awarded only after review of risks by an institutional “biohazards” review committee**
      - **Review of physical containment and facilities**
      - **Consideration of local circumstances**



# The First *NIH Guidelines*

- Published in July 1976
- Established responsibilities of investigators and institutions

**federal register**

WEDNESDAY, JULY 7, 1976



PART II:

DEPARTMENT OF  
HEALTH,  
EDUCATION, AND  
WELFARE

National Institutes of Health

▪  
RECOMBINANT DNA  
RESEARCH

Guidelines



# Local Community Involvement

## Policing genetic research

THE WASHINGTON POST Friday, July 9, 1976

### City Blocks DNA Research

By Edward Schumacher  
Special to The Washington Post  
CAMBRIDGE, Mass., July 8—  
The Cambridge City Council early this morning voted a three-month moratorium on potentially dangerous genetic research at Harvard University and Massachusetts Institute of Technology that federal research officials fear will set a precedent of community control over such work.

The nine-member council voted 5 to 3 with one abstention to establish a review committee of scientists and citizens to recommend by the end of the moratorium a city policy on the "recombinant DNA" research. The city has the legal power to ban the experiments by declaring them a public health hazard.

Mayor Alfred E. Vellucci, who is also head of the city council, said today, "Cambridge has six square miles and we're boss here. They're going to do what we tell them."

The moratorium will have little effect on the university for the time being. Harvard does not plan to have the requisite laboratory until next spring. MIT has a lab, but it has not been certified yet under new federal guidelines on such research.

The experiments involve combin-

anism. The possibility exists that it will be an unknown one and that its properties will be unpredictable, scientists on all sides of the issue agree.

The fear is that new diseases with unknown cures will be created and spread.

Proponents of the research say that it offers the basic scientific understanding of cell reproduction that could lead to cures for cancer and other diseases, as well as to the production of organic things such as insulin and self-fertilizing plants.

William J. Garland, head of genetic research at the National Institutes of Health, attended the five-hour hearing, which was packed with several hundred local residents, students, scientists and two Nobel laureates. He later said the council's action may be "obstructive" by starting a wave of non-uniform regulations across the country.

He said the recombinant research is expected to escalate rapidly. A voluntary national moratorium on the research had been in effect since 1974 until two weeks ago when NIH issued long-awaited guidelines on the safety issue.

Mayor Vellucci, a hard-core

intellectuals opposing the genetic research. These include outspoken Nobel laureate George Wald and his wife, Ruth Hubbard, as well as many of the university students Vellucci has ridiculed in the past.

"It's nice to know the city can expose an issue like this and have all the Nobel scientists come to us" Vellucci said.

Attention has centered on Harvard, where recently the administration approved plans for a recombinant DNA lab in the biology building after months of debate among students and professors. One biology professor opposing the work has since demanded her office be moved farther away from the lab.

Harvard geneticist William Petrie said at the hearings that the lab should be moved to a desert area. "If it blows up, only a few persons will be hurt," he said.

But Matthew S. Meselson, chairman of the department of biochemistry and molecular biology and a supporter of the research, said that if he thought the lab were dangerous, "I would not subject myself to it . . . The work is too important to be stopped."

- Local communities (e.g., Cambridge) begin establishing their own oversight frameworks
- Local review and citizen involvement key characteristics of oversight



# First Major Revisions (1978)

- **Relaxed certain restrictions deemed no longer scientifically necessary, while:**

***“...increasing significantly public access to information about recombinant DNA research activities and increasing public participation in the administration of the guidelines in local communities.”***

***(HEW Secretary Califano)***



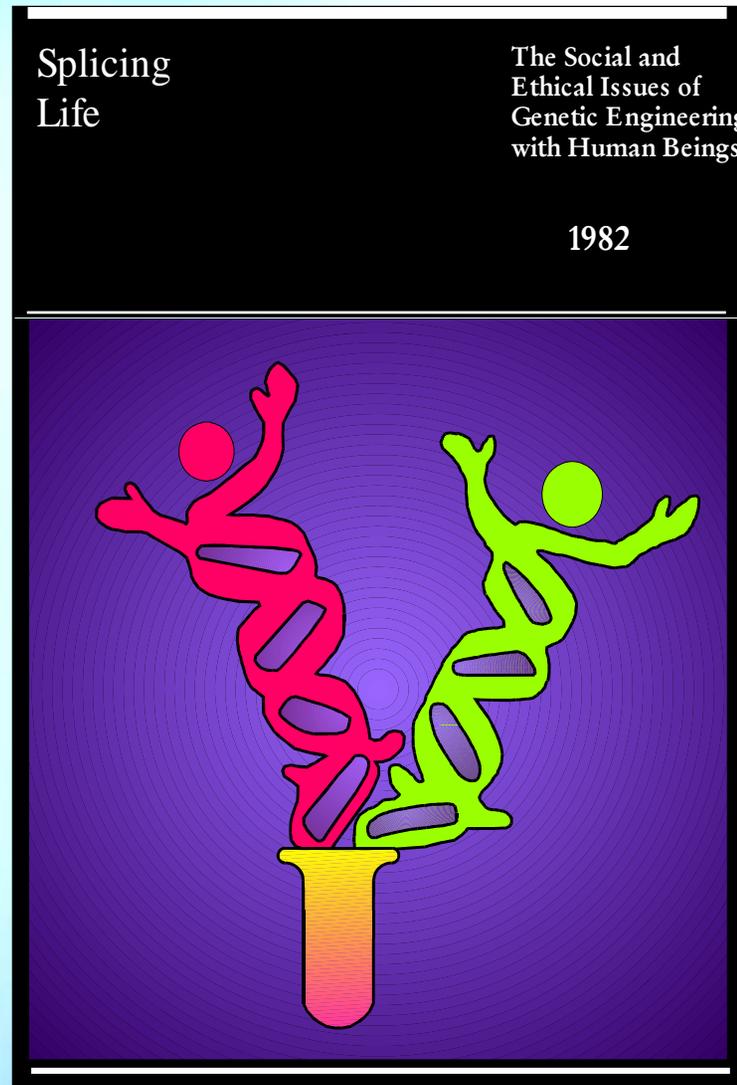
# Enhancing Public Access (1978)

- **At least two, and no less than twenty percent, of IBC members had to represent the general public and have no connection to the institution**
- **“Important records” of IBC’s had to be publicly available**
  - **In addition to minutes: MUAs, reports of violations, and other materials submitted to the federal government**
- **“Major actions” only on advice of RAC and after public and Federal agency comment**
- **Public participation continues to be a hallmark of rDNA oversight**



# 1982

- **President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research**
  - ***“Splicing Life: Social and Ethical Issues of Genetic Engineering with Human Beings”***



# Revised NIH Guidelines

## April 1984

- **IBCs become responsible for review of human gene transfer research**
- **New responsibility pursuant to recommendations of RAC Working Group for Development of Response to President's Commission Report on Ethical and Social Issues**
- **Subsequently, RAC Working Group on Human Gene Therapy embarks on "Points to Consider"**



# Revised NIH Guidelines

## May 1986

- **Adoption of “Points to Consider” guidance document for gene therapy protocols**
- **IBC approval prior to submission to NIH**
- **Points for IBC consideration and review**
  - **Characteristics of the biological system**
  - **Pre-clinical risk assessment studies**
  - **Public health**



# 1989/90

- **1989: NIH Director approves 1<sup>st</sup> human gene transfer protocol**
- **1990: “Points to Consider” added to *NIH Guidelines* as Appendix M**
  - **Requirements for submitting human gene transfer protocols to NIH for review and approval**
  - **Emphasis on gene transfer not therapy**



# Revised NIH Guidelines July 1994

- **Adoption of Appendices  
P (plants) and Q (animals)**
  - **Containment guidance for IBC's**
  - **Augments IBC membership**



# Revised NIH Guidelines

## October 2000

- **Amended requirements for submission of gene transfer protocols**
  - Protocols require RAC review prior to IBC approval
- **Rationale**
  - Research participants are assured that prior to their enrollment in a gene transfer clinical trial that is either novel or raises significant ethical or safety concerns, their local IRB and IBC, and PI are apprised of the results of public RAC review and discussion.



# Revised NIH Guidelines

## October 2000

- **IBC functions specified for review and approval of gene transfer protocols**
  - **Ensure PI addresses all aspects of Appendix M**
  - **Ensure new enrollment requirements are met**
  - **Ensure appropriate consideration by PI and IBC of results of public RAC review**
  - **Ensure final IBC approval is granted after RAC review process**
  - **Ensure compliance with surveillance and reporting requirements**



# Why is Biosafety Review of Recombinant DNA Needed Today?

- **Hasn't history proven the technology to be safe?**
- **Why have a technology-based approach to oversight instead of one that is based on the risks of individual products?**
- **Are there really any residual scientific or public concerns?**



# Hasn't History Proven the Technology to be Safe?

- **Many of the catastrophic dangers originally feared never materialized**
- **The oversight system changed to respond to this new understanding**
  - **The RAC no longer reviews and approves most basic science protocols**
- **Local review is still important to ensure biological safety (medical, occupational, environmental) and responsible scientific practice**



# Why a Technology-Based Approach to Oversight (Instead of Product Based)?

- **The NIH review system encompasses technology and product, as they are intertwined**
- **The products of recombinant techniques can have unpredictable characteristics that are unlike the source or host organisms**
- **This unpredictability warrants a local case-by-case assessment**



# Are there Really Any Residual Concerns?

- **The public here and abroad is still concerned about many aspects of this technology**
- **Our oversight system has provided scientifically-based surveillance of this research that has reassured the public and permitted the science to move forward safely**
- **Human gene transfer continues to raise many safety, ethical, and scientific issues in need of public discussion and analysis**



# Morning Session: The Fundamentals

- Introduction to the National Institutes of Health Office of Biotechnology Activities
- Overview of the Current *NIH Guidelines for Research Involving Recombinant DNA Molecules*
- Requirements for IBCs in the *NIH Guidelines*
- Open Forum
- Break
- Role of the Recombinant DNA Advisory Committee and the Protocol Review Process
- Case Studies

