THE FOURTH ANNUAL MEDICAL RESEARCH SUMMIT APRIL 21-23, 2004

"The Use of Hazardous Materials in Human Subject Research"

Kenneth L. Dretchen, Ph.D.
Georgetown University
Moderator

Susan M. Martin, MS, CSHM
Georgetown University

Sheila Cohen Zimmet, BSN, JD
Georgetown University

Susan L. Rose, Ph.D.
Univ. of Southern California

How to Facilitate Research Efforts While Maintaining Regulatory Compliance

Susan Martin, MS, CSHM
Director, EH&S
Georgetown University

Georgetown University
Office of Regulatory Affairs
Five Oversight Committees for Hazardous Materials

- **IBC** (*Institutional Biosafety Committee*)
- **CSRC** (*Chemical Safety Review Committee*)
- **RSC** (*Radiation Safety Committee*)
- **IACUC** (*Institutional Animal Care & Use Committee*)
- **IRB** (*Institutional Review Board: Human Subject Research*)

Biological Safety Program

&

Institutional Biosafety Committee (IBC)

Subject: All Research Involving Use of:

- Infectious/Biohazardous Agents
- Recombinant DNA Molecules
- Transgenic Animals (Creation of)

Regulated By:

- Center For Disease Control (CDC)
- National Institutes of Health (NIH)
- U.S. Department of Health and Human Services (HHS)
- US Patriot Act

Requirements:

- Protocol Approval
- 5 Year Protocol Renewal
- Annual Registration
- Training
- Personal Protective Equipment (PPE)
- Inspections
- Medical Surveillance
- Emergency Response
- Disposal & Waste

Biological Safety (Cont.)

"Bloodborne Pathogens; Exposure Program

Subject:

Standard applies to any employee who has a reasonably anticipated exposure to human blood, and/or body fluids.

Regulated By:

OSHA Standard 1910-1030

Requirements:

- Develop Exposure Control Plan & Policy
- Training: Initial & Annual
- HBV Vaccination (Offered)
- Personal Protective Equipment (PPE)
- Inspections
- Medical Surveillance
- Emergency Response
- Disposal & Waste

Chemical Safety

Chemical Safety Review (CSR)

Subject:

Any research involving use of Particularly Hazardous Chemicals

Regulated By:

- Occupational Safety and Health Administration (OSHA)
- National Fire Protection Association (NFPA)
- Environmental Protection Agency (EPA)

Requirements:

- Laboratory Specific Chemical Hygiene Plan
- Standard Operating Procedures
- Training
- Personal Protective Equipments (PPE)
- Inspections
- Medical Surveillance
- Emergency Response
- Disposal & Waste

Radiation Safety

Radiation Safety Committee (RSC)

Subject:

All Research Involving the Use of
- Radioactive Materials
- Radiation Producing Devices
- Cesium-137 Research Irradiator

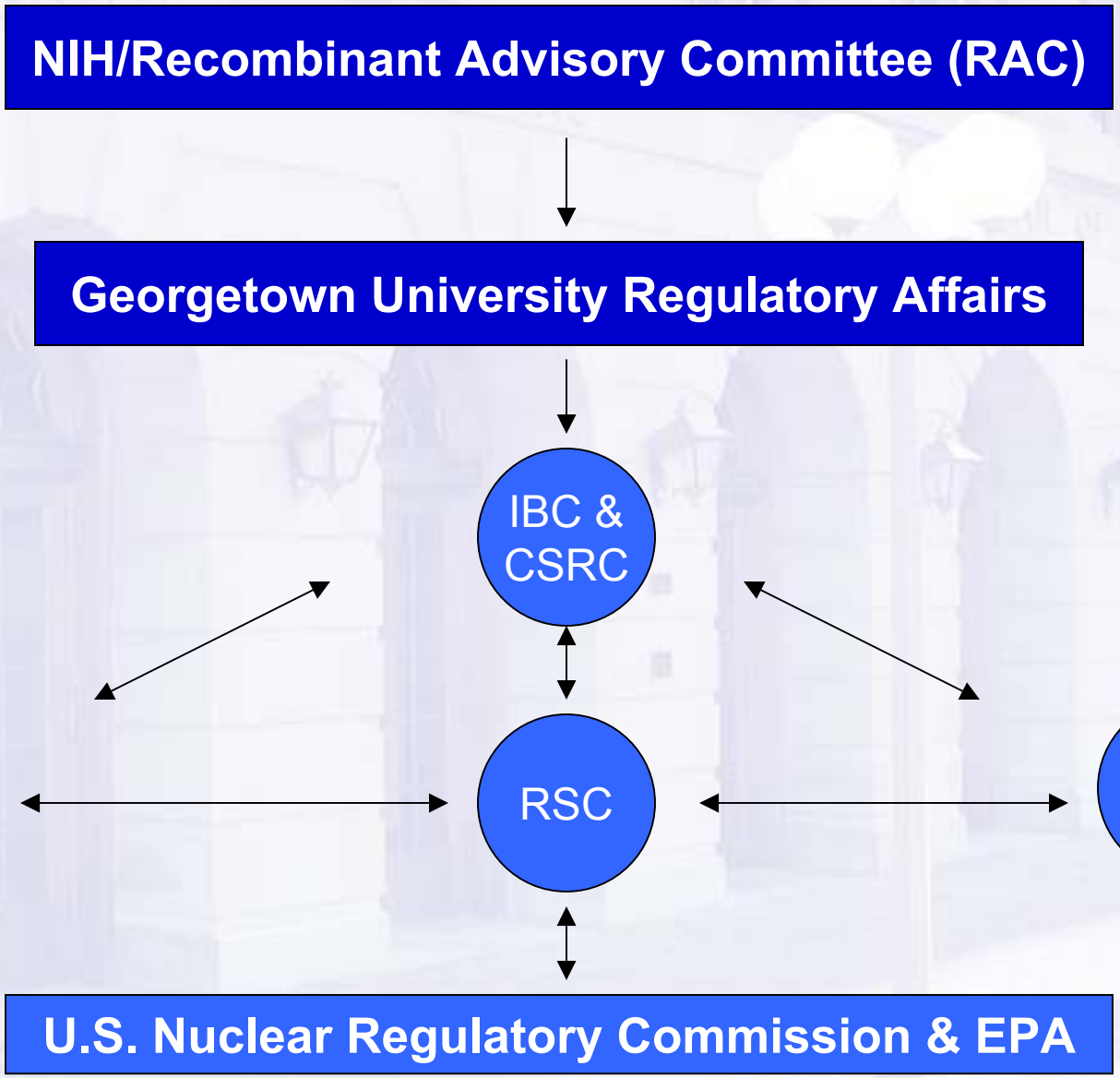
Regulated By:

- US Nuclear Regulatory Commission (10 CFR)
- District of Columbia – Department of Health

Requirements:

- Authorized User and Protocol Approvals
- RSO Policy and Procedure Approvals
- 3 Year Renewals
- Training
- Personal Protective Equipment (PPE)
- Inspections
- Medical Surveillance
- Emergency Response
- Disposal & Waste

Hazardous Materials Interrelationships



Functional Relationships

- Applications Filed Simultaneously
- Cross representation by committee members
- Communication among administrative personnel
- Grants and Contracts Submission Form
- Cross References In Application Forms

Institutional Biosafety Committee Protocol for Research Involving Biological Hazards & Chemical Safety Review

Protocols for all research at Georgetown University involving **Biological Hazards** must be submitted to the **Institutional Biosafety Committee (IBC)** for review. **For purposes of the IBC, Biological Hazards include: A) Recombinant DNA, B) Infectious Agents, C) Hazardous/Carcinogenic Chemicals, and D) Transgenic Animals.** Research protocols involving the use of any of these entities must contain a detailed description of potential danger(s) posed by the agent(s), **And** a summary of safeguards, training, and procedures which will be employed to protect both laboratory personnel and the GU community.

Will this protocol involve the use of Radioactive Materials? (1)

Will this protocol involve the use of Animals?(2)

Will this protocol involve Human Subjects? (Clinical Trials)(3)

(1)**For research involving the use of Radioactive Materials or Radiation Producing Equipment . . ., a copy of this protocol must also be submitted to the Radiation Safety Office.**

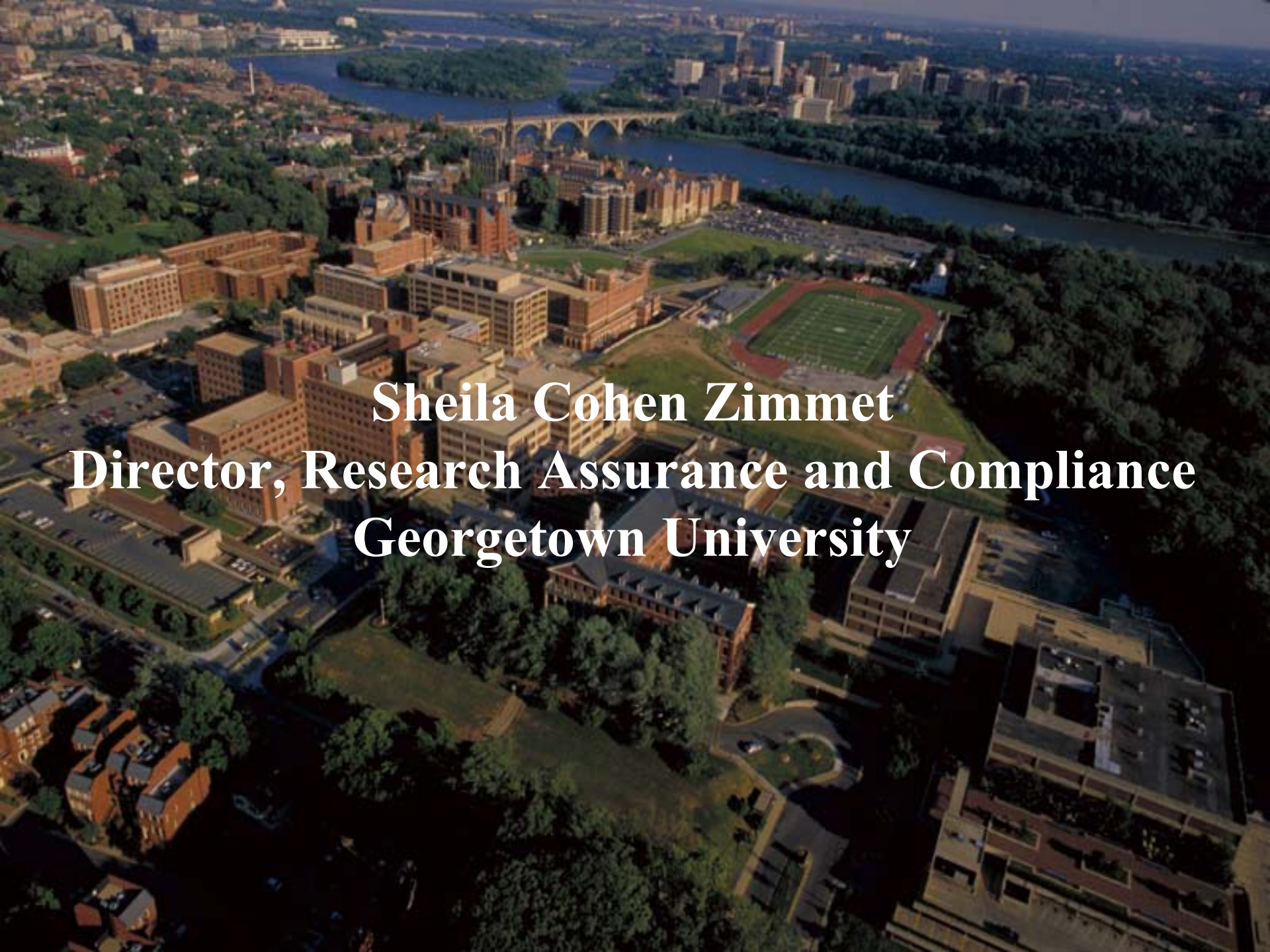
(2)**For research involving Animals, a copy of this protocol must also be submitted to the GUACUC.**

(3)**For research involving Human Subjects, IRB [prior] approval must be demonstrated.**

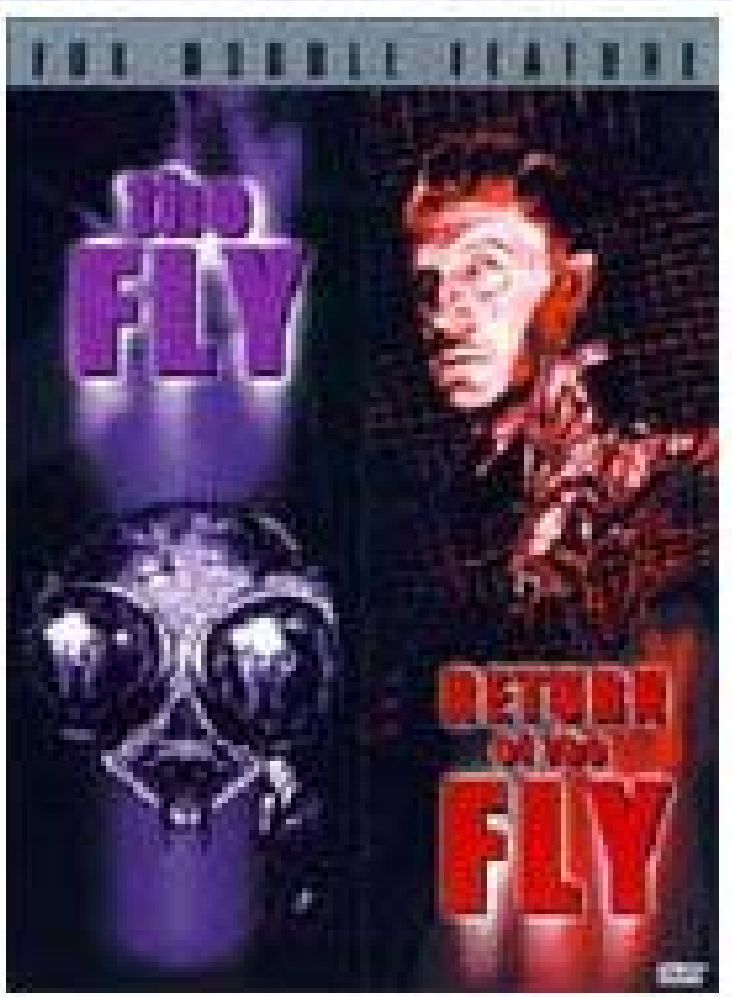
Overall Approaches to Facilitate These Interactions

- Electronic links
  - Who, What and Where?
- Program Orientation and Review (Initial and Annual)
  - Annual Training Sessions for All Faculty and Research Staff
  - New P.I. (one on one)
  - New Research Staff
  - New Employee Support Staff
- Monitoring to Insure Compliance
  - Pre-Inspection
  - Quarterly Review
  - Annual Review
  - Close-Out Inspection
- Disciplinary Action (If necessary)
  - Suspension
  - Termination

"I hope there's nothing genetically modified in this"



Sheila Cohen Zimmet
Director, Research Assurance and Compliance
Georgetown University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What did they do wrong?

No IRB review
No OBA/RAC review

Administration of a Recombinant DNA molecule to a human requires prior OBA/RAC review.

NIH Office of Biotechnology Activities
(Recombinant DNA Advisory Committee)
http://www4.od.nih.gov/oba/

Any questions: e-mail: oba@od.nih.gov
Phone: 301-496-9838
FAX: 301-496-9839

Georgetown University Institutional Review Board Application Protocol for Biomedical IRB Review

Section Two: Additional Georgetown University Regulatory Information

1. Does this project involve the use of biohazardous materials, recombinant DNA and/or gene therapy?

☐ Yes. If so, Institutional Biosafety Committee (IBC) approval must be obtained.

☐ No

Has the Institutional Biosafety Committee approved the protocol?

Approved **Date Approved:**

Application Pending **Date Submitted:**

2. Does this project include the use of radioisotopes and/or radiation-producing devices regardless of whether the use is incidental to the project?

☐ Yes. If so, all protocols must be submitted to the RSC along with a completed RSC-4 or RSC-5 form. The forms require information on the use of radioisotopes and radiation-producing devices and must include dose calculations.

☐ No

Has the Radiation Safety Committee approved the protocol?

Approved **Date Approved:**

Application Pending **Date Submitted:**

Study#1: Study of early immune response in advanced cancer patients with CEA expressing carcinomas to vaccination with CEA-based vaccines using infectious agents, Vaccinia virus and Fowlpox, as viral vectors.

Scientific review, including animal studies

OBA/RAC approval

Adequacy of safety precautions for subjects, family members and other close contacts, pharmacy, and medical and nursing staff – including opt out for staff, especially those with small children at home or pregnant staff;

What did they do wrong?

No IACUC Review

Vertebrate Animal

Animal Welfare Act

Was there adequate animal testing before initiating human clinical trial?

Was animal data accurate and complete?

Georgetown University Animal Care and Use Committee (GUACUC) Proposal to Use Laboratory Animals in Research and Teaching

Special Concerns

Yes ☐ **No** ☐ Does the project involve recombinant DNA (including) transgenic animals), toxic, carcinogenic or infectious agents **in animals**? If yes, submit one copy of the Protocol for Research involving Biologic and Chemical hazards Form to the Institutional Biosafety Committee (IBC).

If yes, provide: a. A copy of the signed approval letter from the IBC must be provided.

b. a completed IBC application with description of **potential dangers,** and **safety precautions and levels** relevant to the animal colony and personnel to the GUACUC.

c. a safety strategy meeting is required before animals can be ordered.

What did they do wrong?

No reporting Of:

Adverse Event

Unexpected Occurrence

Study #2 Cancer vaccine trial using sequential vaccination with ALVAC-CEA and Vaccinia-CEA.

ALVAC-CEA supplied by NCI. Shipped ALVAC-IL2 – package labeled ALVAC-CEA and administered to 6 subjects. (No injury subject Resulted)

Telephone notification from NCI; followed by written notice
Notice to IRB; approved written notice to subjects and supplemental consent; written reports from PI
Written notice to subjects and supplemental consent forms.
Office of Biologic Activities notified; verified FDA, NIH, OPRR notified.
Sentinel event investigation, report and recommendations - new pharmacy procedures
OHRP investigation and criticism for lack of direct notice of unanticipated occurrence.

Subject of Congressional inquiry into adequacy of government oversight of adverse event data from gene therapy trials.

Pre-Belmont Report and Pre-Common Rule

Tuskegee syphilis study

Intentional exposure of soldiers to radiation in the 1940s and 1950s

Secret administration of LSD to soldiers by the CIA and Army in the 1950s and 1960s

Jewish Chronic Disease Hospital Study (injection with cancer cells)

[Japanese “plague bombs”]

[Nazi experimentation]

Stuttering as a learned condition

We hold that … a parent, appropriate relative, or other applicable surrogate, cannot consent to the participation of a child or other person under legal disability in nontherapeutic research or studies in which there is any risk of injury or damage to the health of the subject. Grimes v. Kennedy Krieger Institute, et al., 366 Md. 29, 782 A.2d 807 (Ct App Md 2001)

Paul Gelsinger, addressing a meeting of the Recombinant DNA Advisory Committee on December 10, 1999:

> "All these people who participated in this trial did a wonderful thing. They came in with the same intent my son had. It doesn't get any purer."

(quoted by Sheryl Gay Stolberg in "Tribute and Apologies in Gene Therapy Death," December 10, 1999) http://www.frrenchanderson.org/history/tribute/pdf

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Olmstead v. United States, 277 U.S. 438, 479, 48 S.Ct. 564, 572-573 (1928), cited in Grimes v. Kennedy Krieger Institute, et al.

"Experience should teach us to be most on our guard to protect liberty when the Government's purposes are beneficent. Men born to freedom are naturally alert to repel invasion of their liberty by evil-minded rulers. The greatest dangers to liberty lurk in insidious encroachment by men of zeal, well-meaning but without understanding." (Brandeis dissenting)

Georgetown University
Office of Regulatory Affairs
http://ora.georgetown.edu

(IRB, IBC, IACUC, Radiation Safety, HIPAA, complaints/concerns)

Office of Biotechnology Activities
(Recombinant DNA Advisory Committee)
http://www4.od.nih.gov/oba/

"Compliance with the NIH Guidelines for Research Involving Recombinant DNA Molecules"
http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-02-052.html

NIH Guidelines stipulate biosafety and containment measures
http://www4.od.nih.gov/oba/rac/guidelines/guidelines.html

Office for Human Research Protection (OHRP)
http://ohrp.osophs.dhhs.gov/

OHRP Compliance Activities: Determination Letters
http://ohrp.osophs.dhhs.gov/detrm_letrs/lindex.htm

Office of Research Integrity
http://ori.dhhs.gov

OIG