

# NIH Office of Biotechnology Activities and IBCs: Promoting Synergy in Oversight



# IBCs and OBA

- **IBCs and OBA are key components in a matrix of rDNA oversight, biosafety surveillance, and human subjects protections.**

# Oversight for Basic rDNA Research

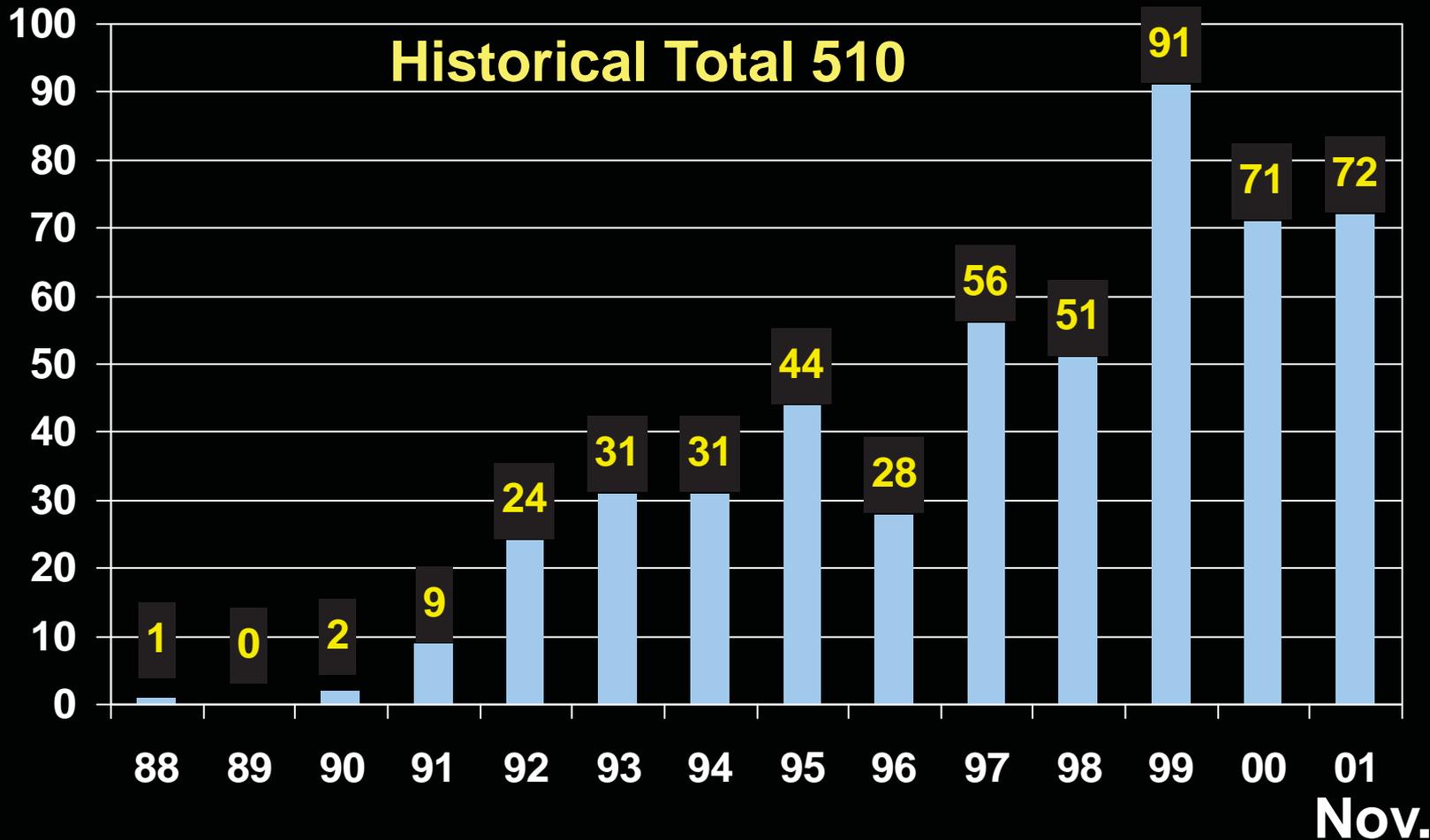
*“Coordinated Framework”*

FEDERAL		LOCAL
Regulatory Policies	Research policies	
USDA	NIH	Institution
FDA	NSF	IBC
EPA	EPA	Investigator
OSHA	OSHA	

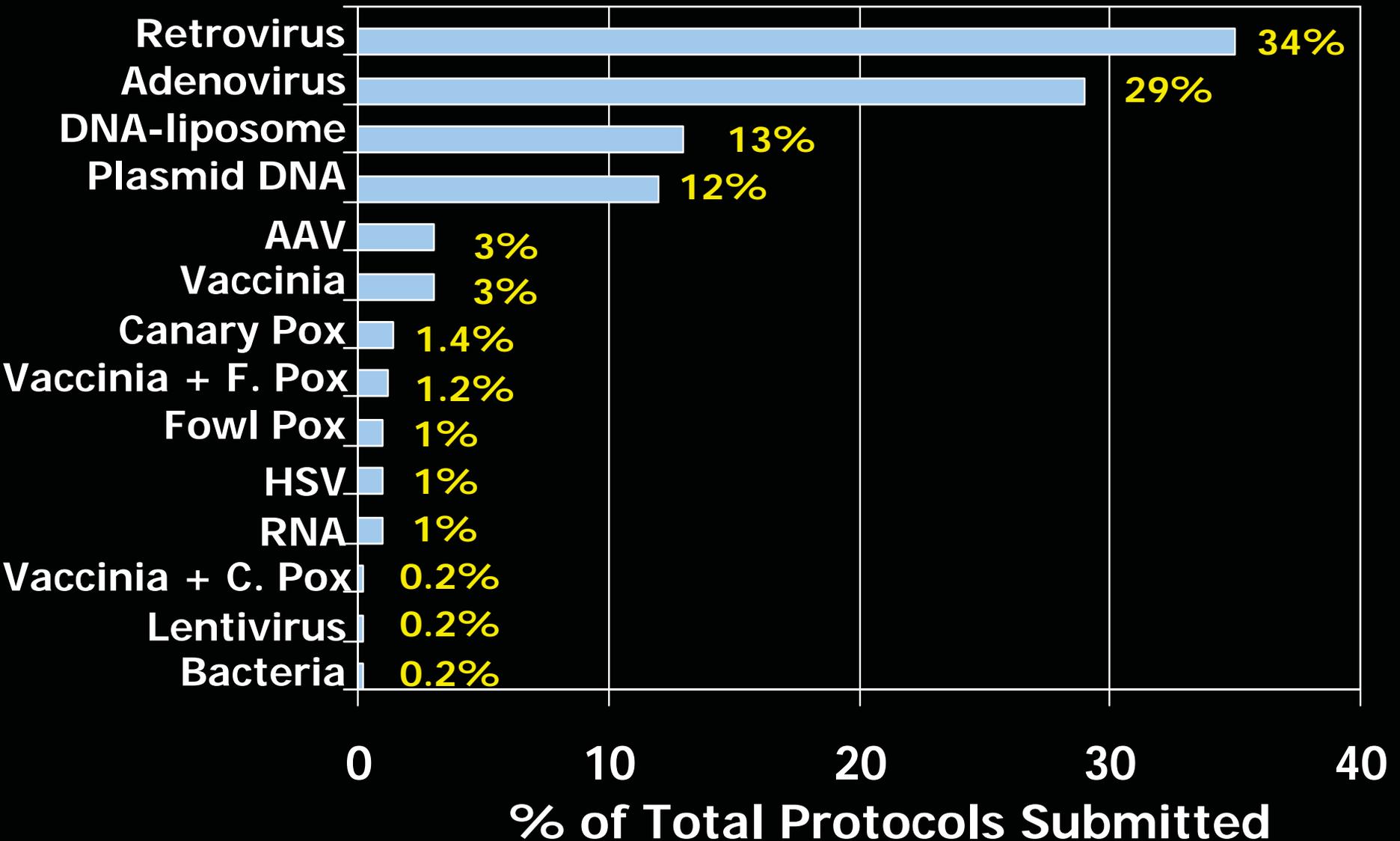
# Oversight for Human Gene Transfer Research

<b>FEDERAL</b>	<b>LOCAL</b>
<b>OHRP</b>	<b>Institution</b>
<b>FDA</b>	<b>IRB</b>
<b>NIH</b>	<b>IBC</b>
	<b>Investigator</b>

# Gene Transfer Trials by Year



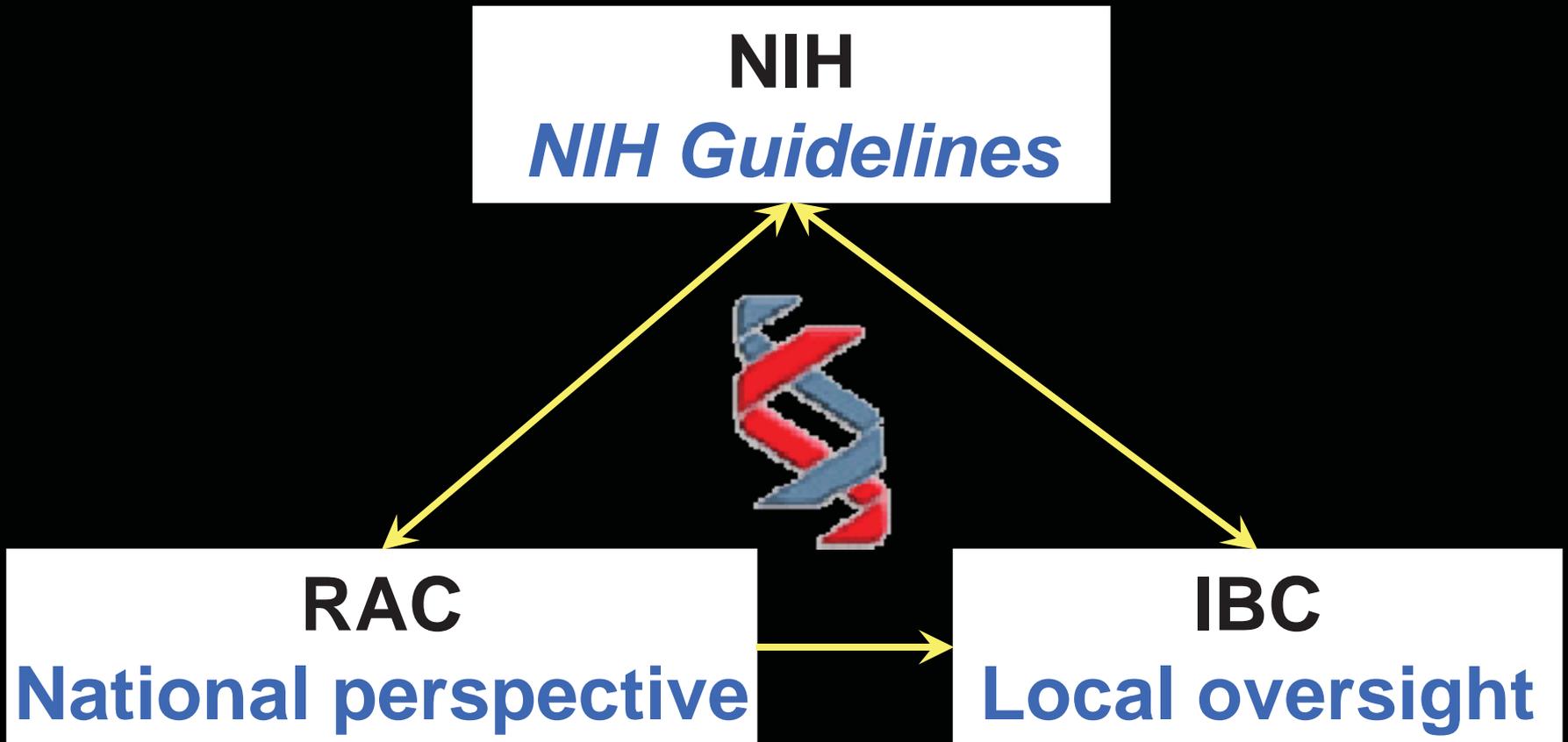
# Gene Transfer Trials By Delivery System



# IBCs and OBA

- **IBCs and OBA are key components in a matrix of rDNA oversight, biosafety surveillance, and human subjects protections.**
- **IBCs are an extension of NIH oversight**

# IBCs Are an Extension of NIH Oversight



# *How do IBCs and OBA interact?*

## **First point of contact: Registration**

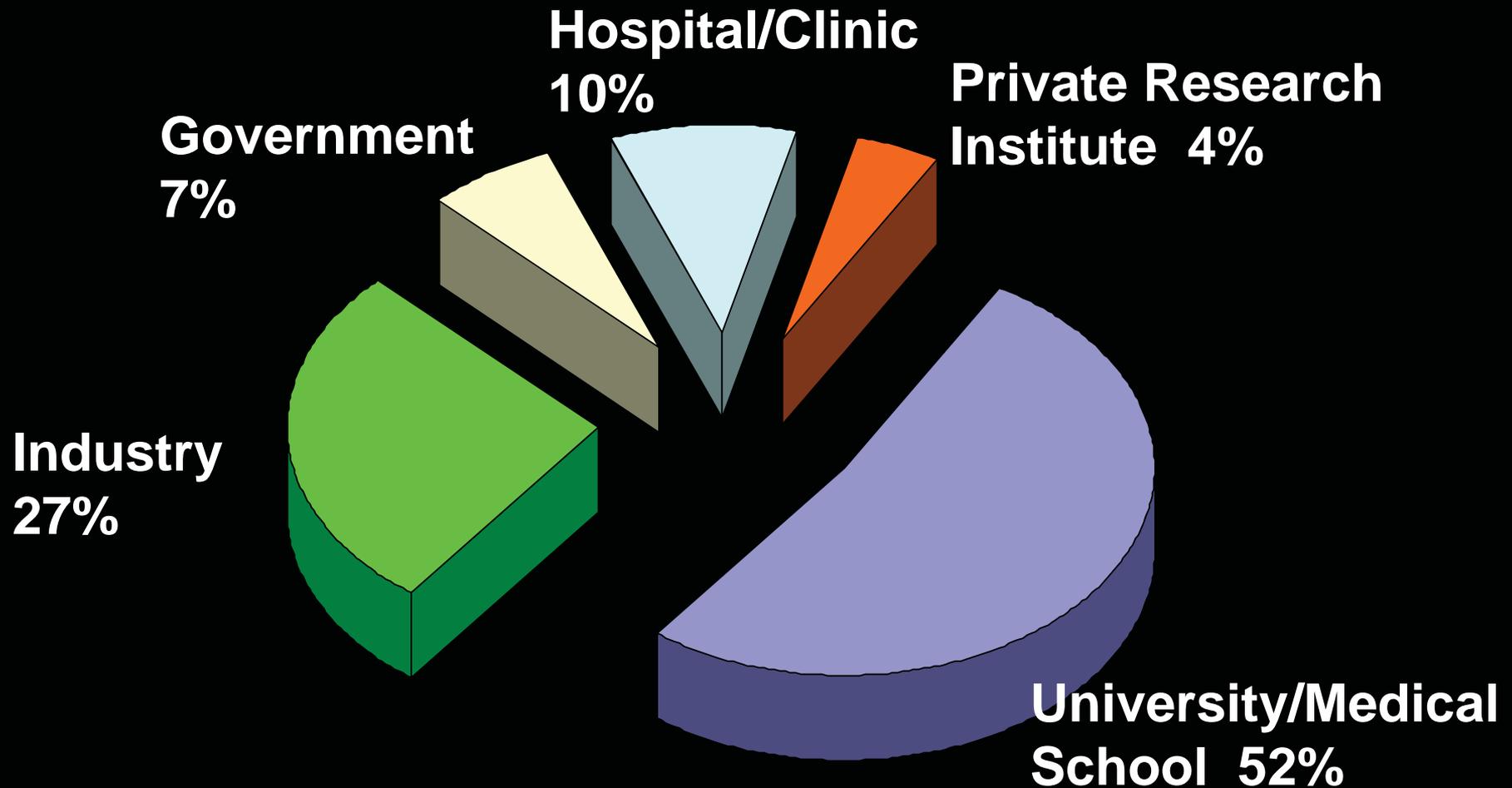
- **Provides assurance of local review of biosafety risks**
- **Allows OBA to see that general IBC expertise consistent with *NIH Guidelines***

## **Registration (cont'd):**

- **Identifies the institutional point of contact and responsibility in case of problems, questions, concerns**
- **Provides census of field**
  - **Where is rDNA research being conducted?**

# Institutional Biosafety Committees

n=450



# *How do IBCs and OBA interact?*

## **Subsequent contact: Annual reports and updates**

- **Keeps contact information current**
- **Allows OBA to know of the ongoing status of the institution's rDNA research program**

# *How do IBCs and OBA interact?*

## **Most important forms of interaction:**

- **IBC**s serve as sentinels for issues in the field
- **OBA** serves as a resource for **IBC**s
  - ◆ **OBA** has scientific and medical staff available to answer queries
    - ★ **Interpretation of NIH Guidelines**
      - **Containment**
      - **Exemptions**
      - **Risk group classification**



"Uh-oh."

# *How do IBCs and OBA interact?*

- **OBA serves as a resource for IBCs**
  - ◆ **OBA can provide information on risk assessment and containment practices on specific protocols similar to yours**
    - ★ **Results of RAC review**
      - **Meetings minutes**
      - **RAC findings and recommendations**

# Organization of the *NIH Guidelines*

- **Section I – Scope**
- **Section II – Safety Considerations**
- **Section III – Types of Experiments Covered**
  - **IIIA – IBC Approval, RAC Review, NIH Director Approval Mandatory**
  - **IIIB – NIH/OBA and IBC Approval Mandatory**
  - **IIIC – IBC and IRB Approval, RAC Review Mandatory**
  - **IIID – IBC Approval Before Initiation**
  - **IIIE – IBC Notification At Initiation**
  - **IIIF – Exempt Experiments**
- **Section IV – Roles and Responsibilities**

# New NIH OBA Initiatives

- **NIH Gene Transfer Safety Assessment Board**
- **National Database**
- **Clinical Safety Symposia**

# NIH Gene Transfer Safety Assessment Board (GTSAB)



# Functions of GTSAB

- **Analyze safety information across all trials**
  - ◆ **Recognize trends early**
  - ◆ **Report findings, conclusions, aggregated trend analysis for public discussion at RAC meetings**
- **Analyses will inform the IBC community, research participants, clinical investigators, basic scientists, IRBs, and the public**

# Operation of GTSAB

- **Meets quarterly in closed session, prior to RAC meetings**
- **Provides reports to the RAC**
- **Publishes periodic summary reports**
- **Staffed by NIH OBA**
- **Implementation – collaboratively with FDA**

# Development of a National Database for Gene Transfer Clinical Research



# Genetic Modification Clinical Research System (GeMCRIS)

## Key Features:

- **Relational database**
- **One electronic AE reporting format for two Federal agencies**
- **Query capable**
- **Web-based**
  - ◆ **Publicly accessible**
  - ◆ **Fire-wall to protect trade secret and confidential commercial information**

# Genetic Modification Clinical Research System (GeMCRIS)

## Key Functions:

- **Serve as an analytic tool for NIH, FDA, and advisory boards**
  - ◆ **Facilitate the evaluation and analysis of safety information from all gene transfer clinical trials**
- **Provide database reports that will inform diverse user groups**
  - ◆ **IRBs, IBCs, local DSMBs, investigators, research participants, and the general public**

# Diverse User Groups

- **Federal Agencies**
- **National Advisory Committees**
- **IBCs and IRBs**
- **Policy Makers**
- **Patients**
- **General Public**
- **Investigators**
- **Sponsors**
- **Media**

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# GeMCRIS

Genetic Modification  
Clinical Research  
Information System  
Version 1.0

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Welcome to the NIH OBA Gene Transfer Clinical Research Information System -- Phase II. This system provides a more powerful tool for dissemination of gene transfer clinical research—particularly for Department of Health and Human Services users involved in pre-market reviews of clinical trial data. Additionally, we are using this Phase II system as a platform for gathering feedback on what other types of information public users would like to see. Please take a moment to respond to a series of questions that appear on a feedback form at the bottom of this page. Your feedback is critical to the ongoing design of future versions of the product, and it will help us take your needs into consideration as the development of the database continues.



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**Related Information**

- ▶ [About RAC](#)
- ▶ [NIH Guidelines](#)
- ▶ [Documents \(With Quarterly Reports\)](#)

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Local intranet

# Selection for Organization Reference Table Maintenance

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Address http://sherlock.resva.trw.com/gemcris10dev/Contents/GC\_HOME.asp

# GeMCRIS

Genetic Modification  
Clinical Research  
Information System  
Version 1.0

Home
Public Information ▾
DHHS Functions ▾
Investigator AE Reporting
System Help



### Support

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Welcome to the NIH Information System, a powerful tool for disseminating research—particularly Services users involved in clinical trial data. Additionally, we are using this Phase II system as a platform for gathering feedback on what other types of information public users would like to see. Please take a moment to respond to a series of questions that appear on a feedback form at the bottom of this page. Your feedback is critical to the ongoing design of future versions of the product, and it will help us take your needs into consideration as the development of the database continues.

Data Collection ▶	Protocol Registration	IND Information
Safety Surveillance Reports ▶	Product Registration	Organization
Browser	AER Registration	Person
System Administration	Reference Tables	Unit of Measure
Management Reports	and Human	Protocol Status
Safety Surveillance Query	f clinical trial data.	Person Role
		Intervention
		Route of Administration
		Gene Vocabulary ▶
		Vector Vocabulary ▶
		VPS Cell Vocabulary ▶
		Ex-Vivo Cell Vocabulary ▶
		Lab Test
		PE Condition
		Person Degree
		Country

Done
Local intranet

# Gene Transfer Clinical safety Symposium



# Gene Transfer Clinical Safety Symposia

- **Public discussion of the most current medical and scientific data**
  - ◆ **2 to 4 times per year**
  - ◆ **Focus on classes of research (e.g., vector, clinical indication, patient population)**
- **Enhance research participant safety**
- **Optimize clinical trial design and development**

# Gene Transfer Clinical Safety Symposia

- **December 1999**      **Adenoviral Vector Safety and Toxicity – *prototype***
- **March 2000**      **Internally Deleted, Helper Dependent (“gutless”) Adenoviral Vectors**
- **December 2000**      **Cardiovascular Clinical Gene Transfer Research**
- **March 2001**      **Adeno-Associated Virus**

# Other ways OBA wishes to be a resource for IBCs:

- OBA is working with professional societies and associations to assist with professional development for IBCs
- OBA is exploring policy concerns germane to how IBCs function

# *Why a policy conference now?*

**Little re-examination of IBC requirements in  
25 years since the Guidelines first drafted**

- ◆ **Do the requirements still make sense?**
- ◆ **Have the requirements kept pace with  
changing landscape of clinical  
research?**
- ◆ **How do new clinical research and IBC  
paradigms and the *NIH Guidelines*  
mesh?**

# *What do the NIH Guidelines say about IBCs?*

## **For all types of rDNA research:**

**“The institution shall establish an Institutional Biosafety Committee whose responsibilities need not be restricted to recombinant DNA.”  
(Section IV-B-2)**

- ◆ **What does it mean to “establish” an IBC (where? locally? how? by contract?)**
- ◆ **How many members must have a formal institutional affiliation?**

# *What do the NIH Guidelines say about IBCs?*

## **For gene transfer in humans:**

**“...no research participant shall be enrolled...until...Institutional Biosafety Committee approval (from the clinical trial site) has been obtained...”**

**(Section I-A-1-a and elsewhere)**

- ◆ **What is the “site” for purposes of IBC approval (organizational entity? physical location?)?**

# What do the *NIH Guidelines* say about IBCs?

Also, for gene transfer in humans:

**“Institutional Biosafety Committee approval must be obtained from the institution at which recombinant DNA material will be administered to human research participants (rather than the site involved in manufacturing gene transfer products)”**

**(Appendix M preamble)**

- ◆ **Should approval come from other types of “sites” (e.g., clinical follow-up)?**

# General Policy Questions:

- What does the “I” in IBC mean?
- What is the nature of local oversight?
- In what ways should IBCs reflect community concerns?
- How should IBCs relate to the IRB?

# What do we want from this conference?

- Specific comments about the expectations we should have of IBCs and their characteristics
- Views about how OBA should review and handle registrations of “non-traditional” IBC arrangements
- Opinions about how the *NIH Guidelines* should address IBCs