

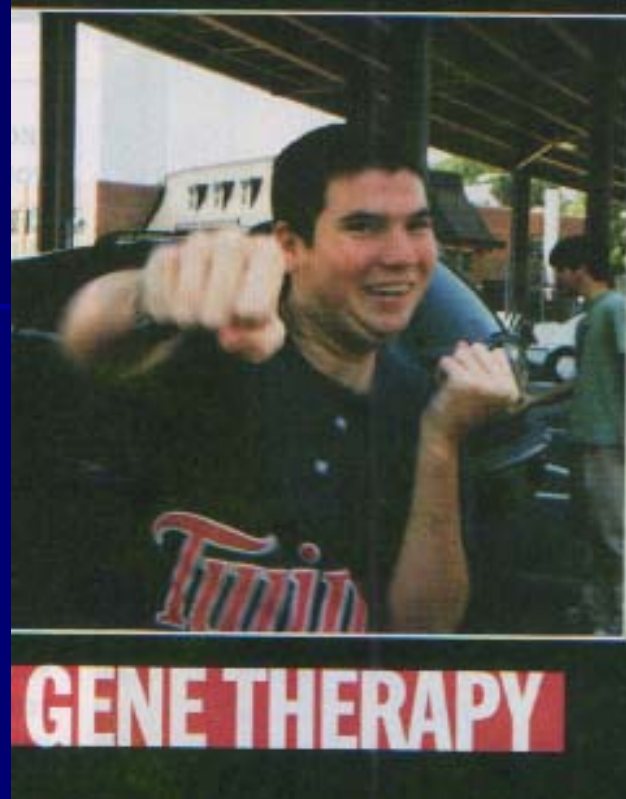
# Genetic Research and Use of Stored Genetic Samples

# Genetic Research

- Genetic Testing & Genetic disease
- Behavioral Genetic Studies
- Data and Tissue storage
- Gene Transfer Research

# Gene Transfer Research

- Technique to substitute absent or faulty genes (causing the disease)
- Carrying the gene fragment to the cells
- Use of vectors (viral or bacterial)



Jesse Gelsinger: Age 18 years  
The FDA argued that he should  
never have been given the genes.

# Gene Therapy

- What did they test?

A new way to replace defective genes in order to treat enzyme disorder.

- Whom did they try it on?

Eighteen patients with mild deficiencies

# Gene Therapy

- What went wrong?
- Injection of the genes - modified cold viruses
  - The immune system fought against the wildly proliferating viruses
  - Next day, slipped into a coma

# Gene Transfer Research

- Subject to FDA regulations as biological products
- IRB responsible for ensuring that recombinant DNA research is conducted according to guidelines

# General concepts for consent form associated with gene transfer trial

- What measures have been taken to minimize the risks of transmission?
- If transmission were to occur, what would be the consequences?
- The use of the terms “therapy/treatment/drug” should be avoided, “agent” is preferred
- The use of recombinant DNA should be clearly stated.
- The potential for recombinant DNA remaining in the body should be addressed.



# General concepts for consent form associated with gene transfer trial

- What are the risks for vector to activate an oncogene or inactivate a tumor suppressor gene leading to vector-related malignancy?
- Are there any special issues related to this gene transfer trial, such as uncertainty associated with short and long term risks and benefits or the possibility of media attention ?
- The possibility that subjects may be contracted for life long follow up should be clear

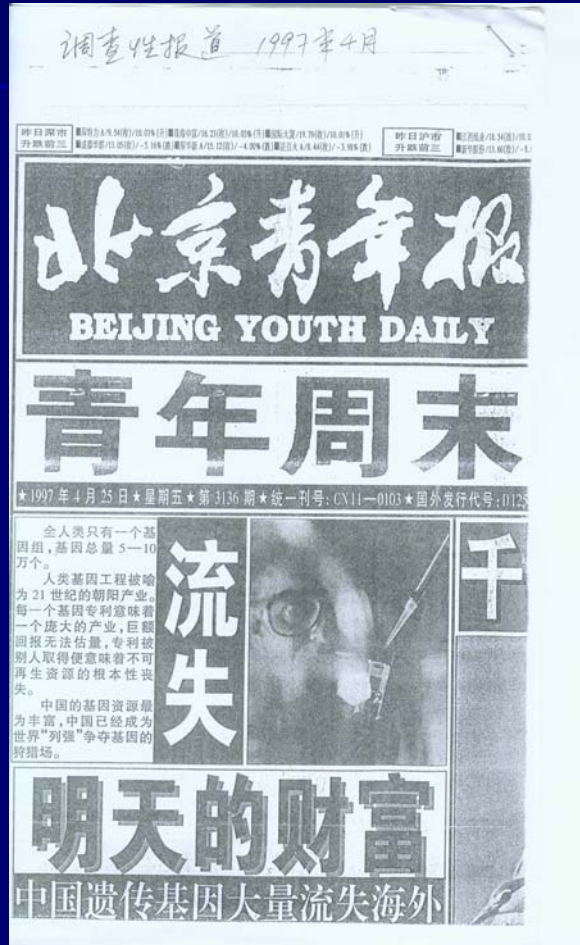
# General concepts for consent form associated with gene transfer trial

- Use of contraception should be explicitly stated for both males and females.
- Potential need for confinement should be outlined
- Potential exposure for family members should be outlined
- Risk of media exposure should be explained.
- Subjects should be informed that an autopsy will be requested

# Data and Tissue Storage

# Gene Wars, Spring 1997

- The ensuing alarm by scientists and the media in China halted many (but not all) international genetics studies until genetic resources regulations were posted in the fall of 1998



# Ethics

- The Harvard-Anhui case also illustrates complex ethical issues in genetics field surveys in China.



■ "What happened was wrong and it was badly wrong."

■ "It's the responsibility of the dean of the School of Public Health and, ultimately, it's my responsibility as president of the university to see to it that where wrong can be put right it is and, more importantly, to see to it that it never happens again." [i]

- Lawrence Summers, President of Harvard University, Peking University, May 14, 2002

[i] Gerstein, Josh. In China, Harvard head laments study. *The Boston Globe*, May 15, 2002. Page A12.

## The Boston Globe In China, Harvard head laments study

By Josh Gerstein, Globe Correspondent, 5/15/2002

BEIJING - Harvard's president, Lawrence Summers, in remarks to Chinese students yesterday, expressed deep regret that a dozen Harvard-run genetic studies in China failed to give test subjects adequate information about potential pitfalls.

"What happened was wrong and it was badly wrong," Summers said, answering a question following his speech at Peking University. "It's the responsibility of the dean of the School of Public Health and, ultimately, it's my responsibility as president of the university to see to it that where wrong can be put right it is and, more importantly, to see to it that it never happens again."

In March, the US Department of Health and Human Services faulted the Harvard School of Public Health, Brigham and Women's Hospital, and the Massachusetts Mental Health Research Corp. for their procedures involving research conducted in China. Officials at the federal Office for Human Research Protections found that participants risked not being treated for health problems that might be diagnosed in the studies, that they faced job discrimination if medical problems were discovered by the subjects' employers, and that some consent forms were too complex for rural Chinese.

In addition, significant changes to the studies were made without necessary approvals, federal investigators reported. The studies sought genetic and environmental causes for ailments that included asthma, obesity, miscarriage, and schizophrenia.

Summers said Harvard has since changed the way it handles studies of human illnesses. "We have revised in a drastic way all our procedures for research at the public health school," he told the Chinese students. "The interests of individual human beings should never be sacrificed to some concept of abstract scientific inquiry."

During the federal investigation, Harvard suspended the studies and reprimanded the lead researcher on most of the projects, Dr. Xiping Xu, an associate professor of occupational epidemiology. In previous statements, university officials said they agreed with the thrust of the federal government's investigation, but stressed that no harm had been done to the people.

The Harvard studies have been the subject of numerous articles in China's state-run news media, which have generally portrayed the research as exploitative.

Summers wrapped up a five-day trip to China yesterday. On Sunday, he inaugurated a program to bring about 50 Chinese bureaucrats to Cambridge each year to study at the Kennedy School of Government. On Monday, the Harvard leader and former treasury secretary met briefly with China's president, Jiang Zemin.



# OHRP Guidance: Components of Repositories

- Repository activities involve three components, each of which must satisfy certain requirements:
  - Collection of tissue samples
  - Repository and data management
  - Receipt by investigators

**Collector(s)**

**Repository**

**Recipient(s)**



**IRB Review**

**IRB Review**

**Recipient  
Agreement**

**Informed  
Consent**

**Sample Informed  
Consent**

**Submittal  
Agreement**

**Certificate of  
Confidentiality**



# Ethical Issues

- Is it appropriate to use stored biological materials in ways that originally were not contemplated, by source or collector
- Does such use harm anyone's interest?
- Does it matter whether material is
  - from an identified, or identifiable, source
  - linked, or linkable, to medical or personal data regarding the source

# National Bioethics Advisory Commission (NBAC)

- The extent to which a sample is linked with the identity of its source
  - significantly affects the risks and potential benefits
- <http://bioethics.georgetown.edu/nbac/hbm.pdf>

# Categories of human biological materials (samples)

## ■ Unidentified samples:

- anonymous
- supplied by repositories to investigators from collection of **unidentified** human biological specimens

## ■ Unlinked samples:

- anonymized
- lack identifiers or codes that link sample to a particular human being

# Categories, cont'd

## ■ Coded samples:

- linked or identifiable
- supplied by repositories to investigators from **identified** specimens with a code rather than personally identifying information

## ■ Identified samples:

- supplied by repositories from identified specimens with a personal identifier
- researcher able to link biological information derived from research directly to the individual

# Ethical Issues

- Is it appropriate to use stored biological materials in ways that originally were not contemplated, by source or collector
- Does such use harm anyone's interest?
- Does it matter whether material is
  - from an identified, or identifiable, source
  - linked, or linkable, to medical or personal data regarding the source

# Data and Tissue Storage

Lists of questions concerning tissue and data storage for future research:

- **Explicit mention in the consent form of the duration and data storage**
- **How such tissue and data will be used in the future?**
- **Whether such uses will be limited to the studying disease for which the tissue was obtained to begin with.**
- **The issues of whether and how future genetic testing results will be conveyed to study subjects.**

# Data and Tissue Storage

Lists of question concerning tissue and data storage for future research:

- Will tissues samples and data be distributed to investigators outside of the study during the future research ?
- Where will tissue and data be stored?
- Will tissue and data be discarded at the conclusion of the study?
- Will tissue and data be retained for future research, including Genetic testing?

# Data and Tissue Storage

Questions concerning tissue and data storage for future research: :

- Will there be secondary distribution of tissue and/or data and how will subjects' confidentiality be protected?
- How will the results of the future genetic testing be handled with respect to person?
- When withdrawing from participation in a study can subjects request that sample be destroyed or anonymized or require that the data does not be used.





# OFFICE FOR PROTECTION FROM RESEARCH RISKS

Issues to Consider in the  
Research Use of Stored Data  
or Tissues

# IRB Review

- Regulatory requirements in each component
- Informed consent
- Submittal agreement
- Sample Informed consent
- Certificate of Confidentiality
- Recipient Agreement
- Local policies

# Some points to consider

- Genetic research is rapidly changing. Investigators need to keep their IRB informed of the recent developments
- The result of the genetic testing not only affect the subjects but their families as well
- The consent process and genetic counseling

# Suggestion

- In the consent form, give subjects a chance to consent to any of the choices
  - I agree to have my blood sample used for future research,
  - I agree to have my blood sample used only for a specific purpose for 5 years.
  - I don't agree to have my blood sample used for future research.

# Common Rule

*Provides **flexibility** for IRBs to review non-biomedical research*

- Exempt Research
- Expedited Review
- Waiver of Consent and/or Documentation of Consent

# Consent Waiver

- Written informed consent is not always **appropriate**
- IRBs have **flexibility** and **authority** to modify or waive consent requirements

# Waiver of Documentation

- presents **no more than minimal risk**;

and

- involves procedures that do not require written consent when performed **outside of a research setting**.

45 CFR 46.117(c)(2)

# Waiver of Documentation

- principle risks are those associated with a **breach of confidentiality** concerning the subject's participation in the research; and
  - consent document is the **only** record linking the subject with the research
- 45 CFR 46.117(c)(1)



# Waiver of Consent

- No more than minimal risk to subjects;
- Waiver will not adversely affect the rights and welfare of subjects;
- could not practicably be carried out without the waiver; and
- Provide pertinent information after participation

45 CFR 46.116(d)

# Points to Remember

- IRB must find and **document** that the research meets the criteria when consent is waived
- Deception research requires a waiver of consent with appropriate **documentation**

# Points to Remember

- "Passive consent" or "implied consent" is not consent and requires a waiver with appropriate **documentation**
- IRBs exercise their waiver authority and **document** appropriately

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