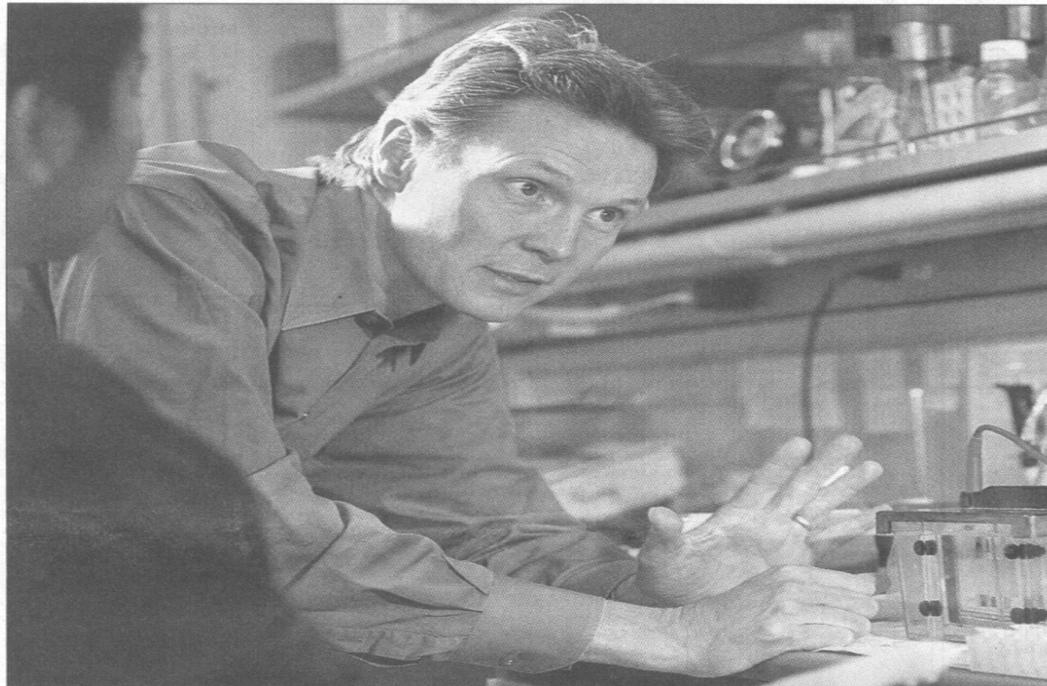




Financial Conflicts of Interest in Clinical Research

**Presentation to the NIH Department of
Clinical Bioethics, November 5, 2003
David Korn, M.D.**



Photos by Martin Klimek for USA TODAY

Tinkering around: Professor Charles Craik, 49, works with a student at the University of California, San Francisco, pharmaceutical chemistry lab. Seeking biotech jobs — which pay an average of \$50,000 a year or more — more states are trying to lure professors like Craik to fuel biotech start-ups.

States flock to biotech like gamblers to lottery tickets

But luring industry's a tricky bet

By Jim Hopkins
USA TODAY

SAN FRANCISCO — More states than ever are gambling millions of dollars on a bet that biotechnology can be their next job engine.

Florida lawmakers last month approved a \$310 million biotech research center proposed by Gov. Jeb Bush just three months ago. New York launched a media campaign in September to woo more biotech investors. In the past two years, New Mexico, Kentucky and Arkansas started venture-capital funds to attract and nurture biotech start-ups.

Dozens of other states might be next. A recent Brookings Institution report notes that biotech ranked as the No. 1 or No. 2 target for 83% of 113 state and local economic agencies nationwide.

"Bio has become everybody's best friend," says Rick Weddle, head of the International Economic Development Council.

The efforts are similar to those taken by states during the Internet boom to lure dot-coms and to those in the late 1990s to win computer chip plants. Jobs are the key.

Biotech jobs pay \$50,000 or more a year — double the U.S. median. In the next seven years, life sciences is expected to be one of the faster-



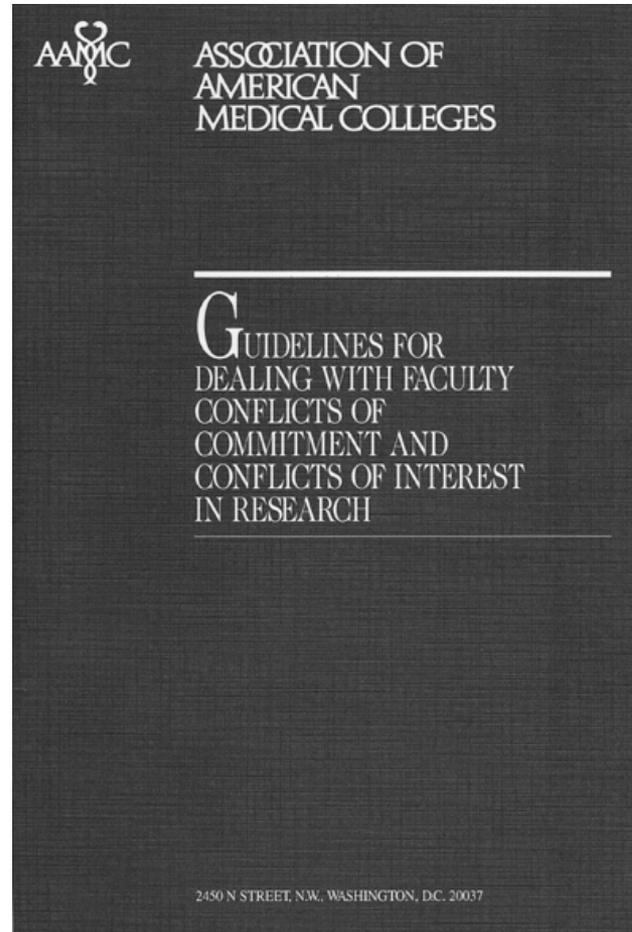
What is biotech?

- ▶ **Health care.** Diagnosing and treating illnesses such as cancer with new drugs, software and medical instruments.
- ▶ **Agriculture.** Genetic engineering of plants and animals to make them more resistant to pests. Also, engineering crops to make industrial chemicals.
- ▶ **Manufacturing.** Processing food so it's less likely to spoil.

Please see COVER STORY next page ▶



1990 Guidelines for Dealing with Faculty Conflicts of Commitment and Conflicts of Interest in Research





ASSOCIATION OF
AMERICAN
MEDICAL COLLEGES

Protecting Subjects, Preserving Trust, Promoting Progress:

Policy and Guidelines for the Oversight of Individual
Financial Interests in Human Subjects Research

Task Force on Financial Conflicts of Interest
in Clinical Research

December 2001

2001 Policy and Guidelines for the Oversight of Individual Financial Interests in Human Subjects Research



AAMC Task Force on Financial Conflicts of Interest in Clinical Research

**“Life is short, the art long,
opportunity fleeting, experiment
treacherous, judgment
difficult.”**

Hippocrates, *Aphorisms*



Task Force on Financial Conflicts of Interest In Clinical Research (2000)

- *Composition:* Broadly representative of stakeholders in human subjects research
- *Goal:* Create a model for effective and credible self-regulation
- *Philosophy:* Protect human subjects and preserve public trust while promoting medical progress



Task Force on Financial Conflicts of Interest in Clinical Research

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Rebuttable Presumption Against Significant Financial Interests in Human Subjects Research

- **Core Principle:** high standard of prior review
- ***Not an absolute prohibition:*** investigator may rebut upon a demonstration of “compelling circumstances”
- **Circumstances may be compelling if the research could not otherwise be conducted as safely or as effectively**
- **Magnitude and “relatedness” of interest, and degree of risk to human subjects are key considerations**



Internal Reporting Guidelines

- Extend PHS thresholds for annual faculty reporting to all research
- Report all equity interests in non-publicly traded companies
- Report all royalty interests
- Report service as officer or director, even if uncompensated
- Report any remuneration outside compensation for reasonable costs of research
- Extend reporting requirements to students/staff who “conduct” research (design, direct, enroll, analyze or report data)



Process Guidelines

- Standing COI Committee
- COI committee review of *all significant financial interests* in *all human subjects research* (regardless of sponsorship) prior to final IRB approval
- When permitted, significant financial interests in human subjects research must be subject to rigorous, disinterested oversight, and must be disclosed
- COI committee must recommend appropriate monitoring or other conditions
- COI committee should summarize findings and recommendations in report to IRB



Disclosure Guidelines

When COI Committee will permit financial interest in human subjects research, require:

- **Summary report to IRB**
- **Disclosure in compliance with state and federal requirements**
- **Disclosure in publications and presentations**
- **Disclosure to subjects**
 - **IRB determines form of disclosure; however**
 - **Consent form must indicate that additional information (to include nature and details of the financial interest) is available to subjects upon request**



Additional Policy Guidance

- Affirmation of institutional policies on intellectual property and publication rights
- Protection of students and trainees
- Education, compliance monitoring, sanctions
- Adequate resources for compliance
- Assessment of COI oversight as an element of accreditation for human research protection programs (e.g., AAHRPP)



**AAMC Task Force on
Financial Conflicts of Interest
in Clinical Research**

***Principles and Recommendations
For Oversight of An Institution's
Financial Interests in
Human Subjects Research***

December 2002

Protecting Subjects, Preserving
Trust, Promoting Progress II:

Principles and Recommendations for Oversight of
an Institution's Financial Interests in Human
Subjects Research

Task Force on Financial Conflicts of Interest
in Clinical Research

October 2002

2002 Principles and Recommendations for Oversight of an Institution's Financial Interests in Human Subjects Research



AAUP Declaration of Principles (1915)

“All true universities, whether public or private, are public trusts designed to advance knowledge by safeguarding the free inquiry of impartial teachers and scholars. Their independence is essential because the university provides knowledge not only to its students, but also to the public agency in need of expert guidance and the general society in need of greater knowledge; and...these latter clients have a stake in disinterested professional opinion, stated without fear or favor, which the institution is morally required to respect.”



AAMC Task Force on Financial Conflicts of Interest in Clinical Research

Institutional financial conflicts of interest in clinical research, or even the reasonable appearance thereof, become especially problematic because of the remarkable deference to university autonomy and self-governance that has been built into our system of federal oversight of sponsored academic research.



AAMC Task Force on Financial Conflicts of Interest in Clinical Research

“As an initial response to a problem of remarkable complexity, this report...does not provide a comprehensive scheme for the oversight of all institutional relationships with commercial research sponsors. Instead, the report offers a conceptual framework...and specific recommendations for the oversight of certain financial interests...that...are especially problematic and must therefore receive close scrutiny.”



Defining the Problem

ICOI may exist whenever the financial interests of the institution, or of an institutional official, might affect or reasonably appear to affect institutional processes for the conduct, review, or oversight of human subjects research.



Fundamental Principle: Primum non Nocere

Institutional policies should affirm that the welfare of human subjects and the integrity of research will not be compromised – or appear to be compromised – by competing institutional interests or obligations.



Fundamental Principle: Separation of Function

Institutions should ensure that in practice, the functions and administrative responsibilities related to human subjects research are separate from those related to investment management and technology licensing.



Research Officials

In some cases, an individual's position may convey an authority over research that is so pervasive or a responsibility for research programs and administration that is so direct that a conflict between the individual's financial interests and the institution's human subjects research should also be considered an institutional conflict of interest.



Circumstances that *May* Create ICOI and *Must* Receive Close Scrutiny

- **Royalties**
- **Equity in non-public sponsor**
- **Equity > \$100,000 in public sponsor**
- **Research officials with SFI in HSR**



Other Financial Relationships That May Warrant Close Scrutiny

- **Research officials participate materially in non-routine purchases from sponsor**
- **Substantial gift history from sponsor**
 - **Magnitude?**
 - **Held for express benefit of research subunit?**
 - **Research official helped solicit?**



ICOI Reporting and Review

- **Standing ICOI Committee**
- **Review annual financial reports for research officials and university officers**
- **Review licensing agreements conveying ownership interest in sponsor**
- **Review specified financial interests**
 - **Apply “rebuttable presumption”**
 - **Require recusal where appropriate**
 - **Report to IRB**



The IRB

- **IRB is an instrument of institutional oversight**
- **IRB COI is ICOI**
- **Recommendations modeled on procedures of NIH advisory bodies:**
 - **Disclosure**
 - **Recusal**



Disclosure of ICOI

- **Disclosure to the IRB of record, to research subjects, and in publications, whenever**
 - **A specified institutional financial interest**
 - **Is or could reasonably appear to be in conflict with proposed HSR project, and**
 - **Conflict has not been eliminated through recusal or otherwise**
- **IRB specifies the form and content of disclosure**



Additional Recommendations

- **Multi-Center trials**
- **External monitoring of primary site trials**
- **External IRB review**
- **Affiliates as separate entities**
- **Accreditation**