

biology that variation is a key to evolutionary development?

It is true that sociology, with its broad range of interests and methods, has indulged in more than its share of social scientific foolishness. It is also true that the same broad range has given sociology more than its share of social scientific successes. When people have money to invest in social research, they tend to spend it on methods invented by sociologists; modern demographic methods and modern market research are two obvious examples. Most of the decent social data on the United States and its population has been gathered by sociologists or by people using methods that sociology pioneered.

After a decade of applying to social data the dynamic algorithms that were originally developed for the analysis of DNA, I am somewhat surprised to discover that I am afraid of biology. Should I expect a delayed reaction? Will I recant? Are there colleagues out there in biophilic social scientific disciplines who have already done this work and published it where my research assistants and I can't find it?

Andrew Abbott

*Department of Sociology,
University of Chicago,
Chicago, IL 60637, USA
E-mail: abbot@cicero.spc.uchicago.edu*

If sociologists do not know much biology, so biologists do not know much sociology. Otherwise the former head of the Alcohol, Drug Abuse, and Mental Health Administration would not have compared the U.S. inner cities to the jungle and researchers would be looking at guns, not genes, for the origins of the homicide rate.

John H. Gagnon

*Department of Sociology,
State University of New York,
Stony Brook, NY 11790, USA*

■ Morality Play

In her 26 July editorial ("A cautionary tale," p. 411), Dorothy S. Zinberg reviews the suppression of data for a levothyroxin bioequivalence study funded by Boots Laboratories at the University of California, San Francisco (UCSF), which showed no difference between the Boots drug Synthroid and three generic products. As the UCSF scientist who reviewed the work for the university and attempted to mediate the differences between the company and the investigators, I share Zinberg's concern about the morality of the actions of both the company and the university.

As I was quoted in the *Wall Street Journal* exposé of the issues (1), I continue to believe that "the Boots people were deceptive and self-serving" in their review and analysis of the study. At this time, however, I am extremely frustrated to find that the results of the UCSF study are not available to the medical community, with the authors' analysis of the implications of their study, as originally accepted for publication in the *Journal of the American Medical Association*. The paper was withdrawn at the insistence of the university, who presumably feared a lawsuit from the pharmaceutical company.

Zinberg does not mention that Boots Pharmaceuticals has published the results of the study and their interpretation of the data in a new periodical (2). The senior author of the paper, Boots' Gilbert Mayor, serves as an associate editor of the new journal.

Leslie Z. Benet

*Department of Biopharmaceutical Sciences,
School of Pharmacy, University of California,
San Francisco, CA 94143-0446, USA
E-mail: benet@itsa.ucsf.edu*

References

1. R. T. King Jr., *Wall Street Journal*, 25 April 1996, p. 1.
2. G. H. Mayor, T. Orlando, N. M. Kurtz, *Am. J. Therapeut.* 2, 417 (1995).



So far, systems in the ÄKTA design family include:

- ÄKTAexplorer, for method development and scale up of every biomolecule
- the new ÄKTApurifier, for purification of peptides, oligonucleotides and other biomolecules

I agree somewhat with Zinberg that there is a question as to "how long will corporations that are committed to funding genuinely basic research projects be willing to do so if their motives are tarnished by the fallout from incidents such as the [Boots case]?" But only somewhat. It appears to me that the case involves good, but routine, testing and statistical analysis. This is not research. At one time it was usual to differentiate between research and development; the former had distant and often ill-defined goals, while the latter was well focused, with surprises allowed; and the consequences of the sought results were foreseen. In many cases today, university research is developmental work designed principally to earn revenue. Yet for faculty retention, promotion, and salary increases, the academic zoo requires publication, which is usually manifested in journals under the guise of research.

Thus, basic and applied research (development) are facts of life, and corporations, which are usually not philanthropic organizations, pay for development projects in one form or another. A broad spectrum of companies, from automotive to pharmaceutical, pay for so-called research at universities because then they do not need to incur the overhead to conduct the work themselves.

They create a "virtual laboratory" thereby. Universities must understand that such companies are looking for short-term results and cannot interest their stockholders in underwriting basic research. Thus, I doubt that corporations will ever consider anything but "less-than-disinterested research sponsorship," and they undoubtedly will not worry about "the long-term consequences of their actions."

The solution of the dilemma "to take the testing money or not" appears simple. Accept legitimate and interesting applied research contracts from companies while understanding that a relationship something like that between lawyer and client will exist. Read the fine print in the contracts. Charge accordingly, and not a pittance—about \$30,000 per year to cover a \$600-million annual turnover for the product cited. Create balance in the investigative work at the university. Use the profits from applied research to fund basic studies. Push the latter activity and tolerate the former to pay for real needs. Use the experiences gained in applied research to formulate a more general research program. Publish those results that you may, whatever the source of funding. Reward workers for the quality of their work even if it remains unpublished. Try to survive in a climate in

which governmental largess in research funding has become a thing of the past without losing your mission in life. Know that the ethical underpinning of scientists-in-training does not depend on the source of research support, but that it is preached by professors of unassailable character in subtle and manifold ways.

That's my view, but then I'm from Lake Wish-I-can, where all the men are strong, the women outstanding, and our researchers avidly looking for funding.

Walter R. Debler

Professor Emeritus,

College of Engineering,

University of Michigan,

Ann Arbor, MI 48109-2125, USA

E-mail: debler@engin.umich.edu

What weakens UCSF integrity is a failure to honor the terms of a valid contract. What also weakens its integrity is to back down because of the threat of a lawsuit rather than acknowledge that one of its researchers did not comply with a contract. *Science*, by publishing Zinberg's editorial, has given voice to a moral deficiency and in so doing has aided and abetted the effort to make public by indirect means that which was protected by the terms of the contract.

ÄKTAdesign: an open purification platform for all of your biomolecules

What type of purification is going on in your lab? Do some of your colleagues develop methods and optimize schemes to purify peptides, proteins, or oligonucleotides at every purification scale? Are others purifying natural, synthetic and recombinant peptides? Are yet others purifying native or recombinant proteins? Or perhaps you do all of this yourself.

Doing individual types of purification has meant following individual working procedures—until now, that is. Until ÄKTAdesign (ÄKTA is the Swedish word for real; it's pronounced eckta).

**With ÄKTAdesign, your purification systems
won't act like strangers to one another**

ÄKTAdesign is the name of a new platform for a family of purification systems and pre-packed columns exclusively from us, Pharmacia Biotech. The platform integrates fully-biocompatible hardware solutions with a control system that gives you control over purification systems from lab to production scales. It lets everyone use the same better, smarter way of doing purification. All of which means you can operate every ÄKTAdesign system once you've used any one of them.

Each ÄKTAdesign system lets you use pre-set protocols that automatically resolve all major purification tasks—including automatic method scouting. Each system gives you pre-set running parameters for most purification techniques. Each system is supported with an extensive range of technique-specific, pre-packed columns. Each system automatically prepares buffers from stock solutions—without manual titration. And each system operates via UNICORN®—with this single control system, you can instantly transfer your methods to purification systems at all scales.

What does your lab want to purify today? A version of ÄKTAdesign will suit all your needs. Call us: 1 (800) 526 3593 from the USA; +81 (0)3 3492 6949 from Japan; or +46 (0)18 16 50 11 from Europe and the rest of the world. Ask for a free brochure. Or meet us on the Internet at <http://www.biotech.pharmacia.se>.



Circle No. 24 on Readers' Service Card

James R. Thomen
Modern Management Associates, Inc.
Post Office Box 3754,
Wilmington, DE 19807, USA

Zinberg states that the potential hero, UCSF's governing board, backed down when faced with the prospect of a massive lawsuit and the university became the main "victim." Yet, as Zinberg reports the facts, UCSF was seriously misled by the researcher who (i) did not have the contract subjected to prior review by UCSF, as Zinberg implies that university policy required; and (ii) worse, agreed to a clause that the results could not be published without prior written consent of the company. Under these circumstances, there appears to be absolutely no legal defense to the actions of the company, and UCSF had no leverage in the situation.

Ernest B. Hook
School of Public Health,
University of California,
Berkeley, CA 94720-7360, USA
E-mail: ebhook@garnet.berkeley.edu

The issues Zinberg raises touch on some of the most important questions currently surrounding medical research funding: What is the appropriate relationship between aca-

demia and industry? How can medical research best be advanced and the interests of the patient best protected?

However, by relying as heavily as she does on one article in the *Wall Street Journal*, Zinberg passes up an important opportunity to help advance the discussion of these matters. We regret, for example, that Zinberg did not contact the Knoll Pharmaceutical Company (formerly Boots) in the preparation of her piece.

One should also be aware of the inherent difficulties, and in certain instances even dangers, involved in substituting a generic product for a brand-name levothyroxine sodium drug such as Synthroid. Unlike many other prescription drugs, levothyroxine sodium has an unusually narrow therapeutic range. A difference of 12.5 micrograms can generate a clinically significant response. For this reason, levothyroxine substitution without retesting and retitration might actually prove harmful to patients and, ultimately, more costly to the health care system.

We are committed to strong industry-academic research partnerships, and we stand ready to participate in an ongoing discussion of what the future relationship between the private sector and university researchers should be. But such a discus-

sion should avoid representing any one constituency as a villain or a victim.

Carter Eckert
President, Knoll Pharmaceutical Company,
3000 Continental Drive North,
Mount Olive, NJ 07828-1234, USA

Response: Each of the letters cited here—and many of the others written to me directly—raise interesting, for the most part valid, points that reenforce the one I tried to make in a short editorial, namely, the unusual set of circumstances that the *Wall Street Journal* reported (1) provided a magnifying glass with which to view potential traps in industry funding of university research. It is only because the researcher signed an agreement not to publish, and then tried to do so, that the issue came to light.

The larger question is whether university researchers hard-pressed for funds are explicitly or tacitly agreeing not to publish results at the behest of the grantors. In a 1994 study of U.S. university-industry research centers (2), researchers at Carnegie Mellon University reported that 35% of their sample had signed agreements whereby the sponsor(s) could require that "information can be deleted from publication," and 53% agreed that

Six Hot Careers: Biotechnology, Pharmaceuticals and Beyond

A SCIENCE Advertising Supplement

A look at the hottest fields in research...

The special advertising supplement, Six Hot Careers, in this issue of SCIENCE looks at:

- Bioinformatics
- Consulting for Life Scientists
- Combinatorial Chemistry
- Genomics
- Patent Law
- Regulatory Affairs

SCIENCE

Turn to page 1887

"publication can be delayed." More than 30% had accepted both strictures. Is this practice gaining as standard operating procedure about which there is too little discussion?

To explore in greater depth the complicated details of the UCSF/Boots case and its implications for the openness of university research would have required an extensive research project. The *Wall Street Journal* article (1) (which to date has not been cited for gross errors) provided the warning, as does the Carnegie Mellon report, that a larger public should heed.

Benet's frustration is only too understandable. Boots Pharmaceuticals has a new name, Knoll Pharmaceutical Company. The company has indeed published the results of the UCSF study, not in the refereed *Journal of the American Medical Association (JAMA)*, but in a new journal (3) where one of its own scientists serves as an associate editor. (Eckert does not mention whether the journal has JAMA's stringent peer-review standards.) The data appear to have been interpreted according to the company's own interests ("might actually prove harmful to patients").

Debler makes an important point about the difference between research and testing and the intentions of industry to have testing carried out at significantly less cost in universities. But as the work at UCSF demonstrated, the results are not always to the advantage of the sponsor, and even "testing" findings could go awry. Should the public be locked out from the pertinent differences of opinion? I disagree with Debler's proposals for a new relationship between universities and industry because I believe it will set universities on the road (one already too well traveled) to becoming nothing more than job shops. Despite Debler's restrained doubts regarding no-strings-attached grants from industry to university, many scientists—perhaps less so in schools of engineering, but certainly in the basic sciences—can report years of funding from corporations that believe it is in their long-term interest to support a thriving research enterprise even when the short-term results do not benefit their own endeavors.

Using only the information published in the *Wall Street Journal's* extensively documented article (1), I did not know other relevant facts. In a more recent letter (12 September 1996) I received from Benet in answer to several of my posthoc questions—Who actually received the money at the university? Why did this office not question the contract? Or did the money go directly to the researcher? Or to an amorphous fund that does not follow university regulations?—he provid-

ed many of the answers. I learned that researcher Betty Dong had not received any money personally from Boots; it went through the usual university channels. What was not usual was the advice she received from the Campus Counsel after signing the contract waiving her rights to publication. She was allowed to proceed, Benet says, because there had never been a case where university investigators were not allowed to publish their results even when they had signed such an agreement—a bit of *Alice in Wonderland* in the university.

As for the published article (3), Benet observes

As you well know, data (and statistics) can be presented in a number of ways. The data in itself within the manuscript are the results of the study. . . . [but] the article and the interpretation are very slanted towards the Boots position. . . . I cannot say, however, that they misrepresented the data.

Dong's name was omitted from the publication, and the study was presented as a failed study. Where Dong and her associates interpreted their data to support bioequivalence, Boots asserted that the data proved otherwise. In this case, sponsored research carried a high price tag for maintaining the openness of scientific research in the university.

The details specific to the UCSF case are not so important as the larger issues it raises. Hence, "A cautionary tale," as the editors of *Science* so aptly titled my editorial.

Dorothy S. Zinberg

Center for Science and International Affairs,
John F. Kennedy School of Government,
Harvard University,
Cambridge, MA 02138, USA

References

1. R. T. King Jr., *Wall Street Journal*, 25 April 1996, p. 1.
2. W. Cohen, R. Florida, W. R. Goe, *University-Industry Research Centers in the United States* (Carnegie Mellon Univ. Press, Pittsburgh, PA, 1994).
3. G. H. Mayor, T. Orlando, N. M. Kurtz, *Am. J. Therapeut.* 2, 417 (1995).

Letters to the Editor

Letters may be submitted by e-mail (at science_letters@aaaas.org), fax (202-789-4669), or regular mail (*Science*, 1200 New York Avenue, NW, Washington, DC 20005, USA). Letters are not routinely acknowledged. Full addresses, signatures, and daytime phone numbers should be included. Letters should be brief (300 words or less) and may be edited for reasons of clarity or space. They may appear in print and/or on the World Wide Web. Letter writers are not consulted before publication.

Precipitate Nucleic Acids.

IN COLOR!

Pellet Paint™ Co-Precipitant

A highly visible, inert carrier for routine DNA or RNA precipitation.*

EFFICIENT PRECIPITATION OF DNA AND RNA

- Quantitative recovery of nucleic acids
- Five minute procedure
- No low temperature incubations
- Suitable for precipitation of dilute samples (<2ng/ml)

NO MORE LOST SAMPLES!

- Vivid pink pellets are easily located
- Consistent precipitation ends uncertainty
- Precipitation and resuspension steps are easily confirmed

COMPATIBLE WITH MANY APPLICATIONS

- Pellet Paint contains no DNA, RNA or nucleases
- No inhibition of downstream reactions
- Qualified for:
 - manual and Cy5** sequencing
 - restriction digestion
 - PCR† amplification
 - kinase reactions
 - cDNA synthesis
 - *in vitro* transcription
 - random priming
 - *in vitro* translation
 - transformation
 - gel electrophoresis
 - ligation

*Patent pending

**Cy5 is a trademark of Biological Detection Systems, Inc.

†The PCR process is covered by patents owned by Hoffmann-La Roche.



Circle No. 35
on Readers' Service Card

Novagen

Novagen, Inc.
597 Science Dr.
Madison, WI 53711

800-526-7319

Fax: 608-238-1388

e-mail: novatech@novagen.com

URL: <http://www.novagen.com>