

SCIENTIFIC SECRECY AND “SPIN”: THE SAD, SLEAZY SAGA OF THE TRIALS OF REMUNE

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Science is, upon the whole, at present in a very healthy condition. It would not remain so if the motives of scientific men were lowered. The worst feature of the present state of things is that the great majority of the members of many scientific societies, and a large part of others, are men whose chief interest in science is as a means of gaining money . . . —Charles Sanders Peirce (1901)¹

[T]he present concentration of industrial interest in academic science is generating no small measure of concern about whether the academy is selling its soul. —Barbara J. Culliton (1982)²

Entrepreneurialism is rampant in medicine today. —Arnold Relman (1984)³

Entrepreneurial values, economic interests, and the promise of profits are shaping the scientific ethos. . . . These changes are reflected in excessive competition among scientists, reluctant to share data, and sometimes in fraud. —Dorothy Nelkin (1998)⁴

Today’s universities are increasingly encouraging their scientists and doctors to be entrepreneurial and to commercialise their intellectual property. However, the collaboration between industry and academia . . . can easily end in tears. —The Lancet (2000)⁵

[The industrialization of science] implies the establishment within academic science of a number of practices that are essentially foreign to its culture. —John Ziman (2000)⁶

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1. CHARLES SANDERS PEIRCE, *Pearson’s Grammar of Science, Annotations on the First Three Chapters* (1901), in 8 COLLECTED PAPERS ¶143 (Charles Hartshorne, Paul Weiss, and Arthur Burks, eds. 1931–1958).

2. Barbara J. Culliton, *The Academic-Industrial Complex*, 216 SCIENCE 960, 960 (1982).

3. Arnold Relman, *Dealing With Conflicts of Interest*, 310 NEW ENG. J. MED. 1182, 1182 (1984).

4. Dorothy Nelkin, *The Performance of Science*, 352 LANCET 893, 893 (1998).

5. Editorial, 355 LANCET 857, 857 (2000).

6. JOHN ZIMAN, REAL SCIENCE 79 (2000).

I

INTRODUCTION

The story is certainly a disturbing one: A drug company funds a large-scale clinical trial of its new AIDS therapy; when the results are unfavorable, the company tries to prevent their being published; when the researchers go ahead with publication anyway, the company seeks millions of dollars in damages; eventually, newspaper headlines tell us it gets “zilch,”⁷ but the arbitration proceedings are private, so beyond that we know—well, zilch. The same year, a multi-party suit is filed alleging that the company had manipulated its stock price by misleading the public about the effectiveness of the drug;⁸ four years later, with this suit still pending, the company website affirms that “results of previous clinical trials demonstrate” that it “has the potential to slow the progression of HIV infection.”⁹

Of course, viewed more closely, things are more complicated than they seem at first; and anyway, I don’t want just to work up a good head of righteous indignation, but to offer something with real theoretical backbone. So the plan is to sketch an account of what science is and does that suggests how and why the ways in which scientific work is funded can distort or even block its progress; to put this theory to work in the course of an analysis of the troubled history of the trials, clinical and legal, of Immune Response’s AIDS drug, Remune; and to conclude with some thoughts about industrial sponsorship of scientific research in the universities.

II

WHY EVIDENCE-SHARING MATTERS IN SCIENTIFIC INQUIRY

Science, as I understand it, is a federation of kinds of inquiry into natural and social phenomena, differentiated from other kinds of inquiry such as historical or literary scholarship primarily by the sorts of question that fall within its scope.¹⁰

An inquirer’s business is to discover true answers to the questions that concern him; so his obligation is to seek out what evidence he can and assess it as fairly as possible. An advocate’s business is to make the strongest possible case that his side’s answer is the true one; so he will be most effective if he

7. *Zilch for Maker in AIDS Drug Suit*, S.F. CHRON., Sept. 11, 2001, at A10.

8. *See In re Immune Response Secs. Litig.*, 375 F. Supp. 2d 983, 994 (S.D. Cal. 2005). The case originated in ten separate class action suits, *id.* at 994 n.1; the lead plaintiff, Florence Hirschfeld, filed her case on July 10, 2001. *Hirschfeld v. Immune Response Corp.*, No. 01-CV-1237 (S.D. Cal. 2001).

9. Press Release, Immune Response Corporation, The Immune Response Corporation Announces That REMUNE Has Been Selected For A New HIV Clinical Trial Sponsored by The U.S. National Institutes of Health (March 29, 2005), *available at* <http://www.imnr.com/news/2005/2005Mar29.htm>.

10. This section presents briefly some ideas worked out more thoroughly in SUSAN HAACK, *DEFENDING SCIENCE—WITHIN REASON: BETWEEN SCIENTISM AND CYNICISM* (2003) [hereinafter HAACK, *DEFENDING SCIENCE*], especially chapters 1, 3, 4, and 11.

selects and emphasizes whatever evidence favors the proposition concerned, and ignores or plays down the rest. Strictly speaking, “disinterested inquirer” is a kind of pleonasm, and “biased inquirer” a kind of oxymoron.

Unlike advocacy, which starts from a proposition to be advanced, inquiry starts with a question. If the question can be answered by some familiar procedure, we simply follow that procedure: look up the number in the phone book, call the airline and ask, or whatever. If not, however, we have to make a conjecture about what might explain the event or phenomenon that puzzles us; figure out the consequences of its being true; check out how well those consequences stand up to any evidence we already have and any further evidence we can lay our hands on; and then use our judgment whether to accept the conjecture, modify it, drop it and start again, or suspend judgment until more evidence comes along. Our inquiries are better conducted the more insightful and informed our conjectures, the more thorough our search for evidence, and the more judicious our assessment of the worth of the evidence.

The evidence with respect to factual, empirical claims is a complex mesh in which observations (the evidence of the senses) and reasons (background beliefs) work together, rather as the clues and intersecting entries in a crossword puzzle do.¹¹ How reasonable a crossword entry is depends on how well it is supported by the clue and any completed intersecting entries; on how secure those entries themselves are, independent of the entry in question; and on how much of the crossword has been completed. Similarly, how warranted a claim is depends on how well it is supported by the evidence; on how independently secure the reasons it includes are; and on how much of the relevant evidence it includes. Put another way, evidence is stronger the more firmly it anchors the claim in experience, the more tightly it weaves the claim into an explanatory picture, and the more relevant information it takes into account.

Our capacity to inquire is a remarkable human talent; but we are fallible creatures, in more ways than one. Sometimes our imaginations fail us, and we are unable to think of a plausible hypothesis; sometimes we are unable to see, or reason, well enough. No one, moreover, is of absolutely rock-solid, across-the-board intellectual integrity; even the most honest inquirers have their prejudices and blind spots. So the distinction between inquiry and advocacy can get a little—sometimes more than a little—blurred. Sometimes the problem is not our limited and imperfect cognitive powers, but our ambivalence about inquiring, or about what we might discover if we do investigate: we don’t want to know the truth badly enough to go to all the trouble of finding out; or we

11. I first introduced this analogy in Susan Haack, *Rebuilding the Ship While Sailing on the Water*, in PERSPECTIVES ON QUINE 111, 116 (Robert Barrett & Roger Gibson eds., 1990); developed it further in SUSAN HAACK, EVIDENCE AND INQUIRY: TOWARDS RECONSTRUCTION IN EPISTEMOLOGY 81–89 (1993); and, in HAACK, DEFENDING SCIENCE, *supra* note 10, at 57–121, applied it specifically to scientific evidence and method.

really want *not* to discover truths we suspect will be unpalatable, and go to a lot of trouble *not* to find out.¹²

So successful have the natural sciences been that the words “science,” “scientific,” and their cognates, are often used as all-purpose terms of epistemological praise, meaning, vaguely, “strong, reliable, good.” This honorific usage has encouraged the idea that scientific evidence must be evidence of a peculiar, and peculiarly reliable, kind; that the sciences must owe their remarkable successes to the uniquely reliable mode of inference or procedure of inquiry that scientists use, the so-called Scientific Method; and that scientists must be unemotional and even stolid types, “objective” in a stereotypical sense.¹³ But this is all a serious misunderstanding.

Scientists are fallible human beings; and though no doubt some *are* stolid and unemotional, some are passionate—about their scientific problem, about a promising theory, about how often they are cited, and so on. Moreover, the evidence with respect to scientific claims is like the evidence with respect to empirical claims generally—only more so: it is almost always a shared resource, pooled by scientists both within and across generations; the experiential evidence on which it calls is vastly more dependent on instruments of observation; and the reasons are woven into an even denser and more complex mesh. Similarly, scientific inquiry is like empirical inquiry generally—only, again, more so: enabled, expanded, and refined by the vast array of helps to inquiry¹⁴ that scientists have gradually developed over centuries of work. As Einstein once observed, “[t]he whole of science is nothing more than a refinement of everyday thinking”;¹⁵ it represents, in Gustav Bergmann’s marvelously resonant phrase, the “long arm of common sense.”¹⁶

Among the vast array of scientific helps to inquiry are models and metaphors that have extended, refined, and amplified scientists’ powers of imagination; instruments of observation—from the microscope and the telescope to the questionnaire—that have extended, refined, and amplified unaided human senses; complex and subtle experimental designs that have extended, refined, and amplified evidential reach; and mathematical and statistical techniques and devices, from numerals to the calculus to sophisticated computer programs, that have extended, refined, and amplified unaided human

12. For amplification, see Susan Haack, *The Ideal of Intellectual Integrity, in Life and Literature*, 36 NEW LITERARY HIST. 359 (2005).

13. This honorific usage seems also to have left its mark on Justice Blackmun’s opinion in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993). See HAACK, DEFENDING SCIENCE, *supra* note 10, at 251–52; Susan Haack, *Trial and Error: The Supreme Court’s Philosophy of Science*, 95 AM. J. PUB. HEALTH S66 (2005).

14. “Helps” is Francis Bacon’s word: “Effects are produced by the means of instruments and helps, which the understanding requires no less than the hand. . . .” FRANCIS BACON, NOVUM ORGANUM (1620), Book I, aphorism 2, *reprinted in* ADVANCEMENT OF LEARNING AND NOVUM ORGANUM 309, 315 (Colonial Press 1900).

15. ALBERT EINSTEIN, *Physics and Reality, in* IDEAS AND OPINIONS 290, 290 (Carl Seelig ed., Sonja Bargmann trans., 1954).

16. GUSTAV BERGMANN, PHILOSOPHY OF SCIENCE 20 (1957).

powers of reasoning. And then there is the complicated internal social organization that has gradually evolved within and among scientific communities, which has enabled a subtle and complex division of labor, advanced the sharing of evidence, supplied the incentives of reputation and renown that motivate scientists to take the risks of frustration and failure inevitable in any serious intellectual work, and even managed, by and large and on the whole, to keep most scientists, most of the time, reasonably honest.

When one thinks of, say, the gradual evolution of today's techniques of medical imaging, each building on previous knowledge, some of it obtained in part thanks to earlier imaging technologies,¹⁷ the phrase that comes to mind (just as with a crossword) is "nothing succeeds like success." All the same, scientific helps are fallible and imperfect: a metaphor may lead in what turns out to be a fruitless direction; an observation may turn out to be an artifact of the instrumentation; an experimental design may fail to take potential interfering factors into account. For example, a carefully designed laboratory experiment relying on what are in fact false assumptions about which variables are relevant, or a carefully designed clinical trial relying on what are in fact false assumptions about background death-rates, may give quite misleading results.

Moreover, though the success of the natural sciences in devising more and more efficient technical helps has been truly extraordinary, there are no grounds for complacency. For the external environment in which scientific work is conducted can affect which questions are thought worth investigating (and which passed over because they are perceived as unfashionable, or as too sensitive to risk looking into); what kinds of results are widely reported in the media (and what politely ignored, or loudly criticized); and even, sometimes, what results are reached (and what hypotheses scientists never even consider, or don't bother to test). And the environment may be more, or less, hospitable to thorough, honest investigation.

What one might describe as "the scientific ethos" (the phrase is appropriately vague, since the phenomenon to which it refers is itself diffuse, uncodified) calls for unhampered, honest investigation and free exchange of ideas. It is embodied in the attitudes and aspirations instilled in the course of the long apprenticeship undertaken by young scientists; it is sustained by the incentives of honor, reputation, accomplishment, and workmanship that can motivate a life in science. But these attitudes and aspirations impose a considerable burden on natural human tendencies to wishful thinking and self-promotion—as William James expressed with his usual shrewd vividness when he wrote of the "patience and postponement, [the] choking down of preference" that is "wrought into [the] very stones and mortar" of "the magnificent edifice of the physical sciences."¹⁸

17. See BETTYANN HOLTZMANN KEVLES, *NAKED TO THE BONE: MEDICAL IMAGING IN THE TWENTIETH CENTURY* (1997).

18. WILLIAM JAMES, *The Will to Believe* (1896), in *THE WILL TO BELIEVE AND OTHER ESSAYS IN POPULAR PHILOSOPHY* 1, 17 (1897; repr. 1956).

As Charles Sanders Peirce observed, “A man must be downright crazy to deny that science has made many true discoveries.”¹⁹ Indeed. But the progress of science has been ragged and uneven; there is no guarantee that it will continue. No algorithmic “Scientific Method” guarantees progress; nor is there any certainty that the internal mechanisms which have thus far sustained intellectual integrity more or less adequately will continue to do so. Scientists are only human; and under the pressures, internal and external, that can disturb the delicate incentive structure of the scientific enterprise, they may be less thorough in seeking out evidence, or less scrupulously honest in assessing its worth, than they would otherwise be.

By now, though scientific discoveries are still occasionally made with tiny resources, the days in which major breakthroughs require no equipment fancier than a candle and a piece of string are, mostly, behind us. And as science gets more and more expensive, only institutions with vast resources can afford to support it: governments, either directly or through their support of universities, and large industrial concerns. Of late, moreover, the potential for scientists to make money from their discoveries has grown dramatically. Doubtless there has always been dishonesty in science, and even occasionally outright fraud; but thus far scientists’ knowledge that if their work is of any real importance cheating will probably be found out eventually has kept the temptations to dishonesty more or less in check. However, as the pressure builds for scientists to get more grant money and to publish more papers, as opportunities multiply for them to get rich from their discoveries, as the expert-witness business booms, and as industrial concerns more interested in making money than in inquiry for its own sake come to exert more and more influence over scientific work, the old safeguards against dishonesty, conscious or self-deceptive, may not be enough.

Usually, for example, the pooling of evidence is a huge cognitive advantage essential to the scientific enterprise: when numerous researchers in different locations can work together on a project in astronomy or epidemiology, for example, or when new results can be speedily published and made accessible to others in the field, a much greater range and variety of evidence is available to all than any could obtain alone. Even when it seems effortless, however, the cognitive efficiency of such evidence-sharing depends implicitly on the grounds each scientist has for justified confidence in others’ competence and honesty. And this cognitive efficiency can be hampered when, for example, too much career pressure tempts researchers to go prematurely to the press, to publish half-baked, weak, plagiarized, or fraudulent work, or simply to boost their vitae by splitting results into minimal publishable units (known in the trade as MPUs). At the same time, the overburdened process of reviewing papers for publication may get less effective at screening out the weak and the flawed, or

19. PEIRCE, *Lectures on Pragmatism, Lecture VI: Three Types of Reasoning*, in 5 COLLECTED PAPERS, *supra* note 1, ¶ 172.

even the plagiarized and the faked; and when research teams are too large and too scattered, no member may be in a position to be sure that all are competent and honest.²⁰

According to the announcement of the conference at which this paper was presented, science is “concordant with the ideals of a democratic society.”²¹ This is not entirely true, for in one respect science is more like an aristocracy, in the old, Platonic sense, than a democracy: it is, at heart, a meritocratic enterprise. The scientific community will not give much weight to Joe Public’s opinion on the age of the earth, the plausibility of string theory, the dangers of power lines or cell-phones, and so on; and rightly so, for the average lay person simply does not know enough to make an informed judgment. Nevertheless, the idea that science is democratic is true in part. For one thing, authority in science is not the privilege of any office or position: the accolades go to those with expertise, skill, persistence, and to those who have the knowledge and the wit to recognize the truth when they stumble on it accidentally, rather than to those who hold a certain position or rank (think of brash young post-doctoral fellow Jim Watson beating out Nobel Laureate Linus Pauling to solve the structure of DNA). For another, and most to the present purpose, scientific progress is enabled, as democracy is, by freedom of inquiry and the free exchange of ideas.

However, the governments and businesses on which scientists must often now rely for financial support have other interests besides arriving at the truth: both are likely to want unpalatable truths left undiscovered, or to want them covered up if scientists discover them anyway; businesses are likely to want potentially profitable truths kept from their competitors. And *any* pressure on intellectual integrity and the free exchange of ideas—whether it takes the form of incarceration in a concentration camp or mental institution for such crimethink as “Jewish physics” or “bourgeois genetics,”²² or of financial support from business conditional on sponsors’ controlling the dissemination of results—is apt to hamper scientific progress. The dangers of political interference in science are certainly neither negligible nor unimportant;²³ but the focus in what follows will be on the dangers of the influence exerted by private sponsors.

20. Problems about multiple authorship are a major theme of the short pieces in the 1998 colloquium *Publication and Promotion*, 352 LANCET 891. See, e.g., Nelkin, *supra* note 4.

21. Conference Announcement, *Sequestered Science: the Consequences of Undisclosed Knowledge*, October 14–15, 2004, (on file with Law & Contemporary Problems).

22. On Nazi science, see ALAN D. BEYERCHEN, *SCIENTISTS UNDER HITLER: POLITICS AND THE PHYSICS COMMUNITY IN THE THIRD REICH* (1977), and Alan D. Beyerchen, *What We Now Know About Nazism and Science*, 59 SOC. RES. 615 (1992). On Soviet biology, see VALERY N. SOYFER, *LYSENKO AND THE TRAGEDY OF SOVIET SCIENCE* (Leo Gruliow & Rebecca Gruliow trans., 1994).

23. See generally MORTON HUNT, *THE NEW KNOW-NOTHINGS: THE POLITICAL FOES OF THE SCIENTIFIC STUDY OF HUMAN NATURE* (1999) (arguing that the social sciences are presently stultified by pressure to be “politically correct”).

III

THE TRIALS OF REMUNE

Since the 1970s the proportion of U.S. “research and development” sponsored by the federal government has been declining, and the proportion sponsored by industry rising—from three percent of all university research in 1970 to seven percent in 2001—and now amounts to billions of dollars.²⁴ The pervasive dependence of medical research in universities on financial support from drug companies has become a particular source of concern; so “the sad, sleazy saga of the trials of Remune” is a particularly appropriate case study.

The narrative will begin with the U.S. Food and Drug Administration’s (FDA) approval of the first large-scale clinical trial of Remune, and will proceed from the early cessation of this clinical trial and Immune Response’s efforts to suppress the results, through their publication in the *Journal of the American Medical Association* (JAMA) and the ensuing legal dispute between the researchers and their sponsors, to the present state of play with respect to the drug, and the company.

Remune is an AIDS therapy “based on whole HIV particles, stripped of a protein called gp120, and killed by irradiation and chemical treatment.”²⁵ It was conceived by Jonas Salk, the pioneer of polio vaccination, and developed by Immune Response Corporation (IRC), the California biotech company he founded in 1987.²⁶ Perhaps because of the Salk connection, the drug is sometimes described as a vaccine against AIDS;²⁷ but it is intended, not to prevent infection, but to boost the immune systems of patients already infected with HIV.²⁸

In February 1996, FDA approved the first large-scale study of Remune, funded by IRC, to begin in March of that year.²⁹ At the time, a diagnosis of AIDS was in effect a death sentence, and AIDS activists were understandably anxious that FDA not delay trials of any promising-sounding therapy; nevertheless, according to an FDA spokesman, the advisory committee was “fraught with doubts” about the project, and split on whether to approve it.³⁰ The chair, Dr. Stanley Lemon of the University of North Carolina, commented that he was “not at all excited about the data” he had seen, but would be

24. Joshua A. Newberg & Richard L. Dunn, *Keeping Secrets in the Campus Lab: Law, Values and Rules of Engagement for Industry-University R&D Partnerships*, 39 AM. BUS. L.J. 187, 193 (2002). See also SHELDON KRIMSKY, *SCIENCE IN THE PRIVATE INTEREST: HAS THE LURE OF PROFITS CORRUPTED BIOMEDICAL RESEARCH?* 27–32 (2003) (providing similar statistics).

25. Paul Smaglik, *Reservoirs Dog AIDS Therapy*, 405 NATURE 270, 272 (2000).

26. The Immune Response Corporation, *Corporate Snapshot*, <http://www.imnr.com/corp/corporate.htm>.

27. See, e.g., Smaglik, *supra* note 25, at 272.

28. Thomas H. Maugh II, *Firm Disputes Handling of Drug Study*, L.A. TIMES, Nov. 1, 2000, at A3.

29. *In re Immune Response Secs. Litig.*, 375 F. Supp. 2d 983, 997–98 (S.D. Cal. 2005).

30. Amended Complaint at 8, *Hirschfeld v. Immune Response Corp.*, No. 01-CV-1237 (S.D. Cal. Jul. 10, 2001) [hereinafter *Hirschfeld* Complaint]. 405 NATURE 270, 272 (2000).

“thrilled to be proven wrong.”³¹ IRC stock soared in anticipation of FDA approval of the trial.³²

The lead researchers were medical scientist Dr. James Kahn of the University of California, San Francisco (UCSF) and statistician Dr. Stephen Lagakos of Harvard University; data were collected by a team of researchers at seventy-seven hospitals nationwide.³³ The trial eventually involved 2,527 volunteers, all of whose immune systems were already compromised by HIV, assigned at random to one of two groups.³⁴ In a double-blind test, patients in one group were given injections of Remune every three months, and those in the other group were given injections of the adjuvant alone.³⁵ At the time, FDA required that potential AIDS drugs show a decrease in progression of the disease or in death rates; and the Remune trial was designed to be sensitive to a fifty percent increase in survival rate attributable to the drug.³⁶

Shortly after the trial began, however, the FDA requirements were changed to allow the use of “surrogate markers”; which meant that even if it was not shown to lower disease or death rates, an AIDS drug could be approved if it was shown to decrease other factors associated with disease or death.³⁷ Moreover, around the same time, a new class of AIDS drugs, the protease inhibitors, was introduced; and as a result of their use the death rate from AIDS slowed from around six percent a year to less than one percent.³⁸ The trial design was quickly modified to track AIDS-related illnesses as well as deaths, and to allow patients to combine Remune with any anti-retroviral therapy they chose, including experimental treatments and protease inhibitors, or none at all.³⁹

In May 1999, on the recommendation of a five-member Data Safety Monitoring Board (DSMB) selected to help review statistics on patients’ responses, Drs. Kahn and Lagakos halted the trial.⁴⁰ According to Dr. Kahn, the reason was that preliminary data showed that the drug was ineffective: in the first two years of the study, fifty-three people in the Remune group had become sicker or had died, as had fifty-three in the control group.⁴¹ However, according to Dennis Carlo, the then-president and Chief Executive Officer of IRC, the reason was that the now lower expected death rate from AIDS meant

31. *Hirschfeld Complaint*, at 7–8.

32. *Stock Comment—New York*, MARKET LETTER, Feb. 26, 1996.

33. James O. Kahn et al., *Evaluation of HIV-1 Immunogen, an Immunologic Modifier, Administered to Patients Infected with HIV Having 300 to 549 × 10⁶/L CD4 Cell Counts: A Randomized Controlled Trial*, 284 J. AM. MED. ASS’N 2193, 2193 (2000).

34. *Id.* at 2193–94.

35. *Id.* at 2194.

36. Maugh, *supra* note 28; Kahn et al., *supra* note 33, at 2195.

37. Maugh, *supra* note 28.

38. *Id.*

39. John S. James, *Bitter Publication Dispute on Remune Study: More Than Meets the Eye?*, AIDS TREATMENT NEWS, Nov. 3, 2000, at 4.

40. Maugh, *supra* note 28.

41. *Id.*; *Hirschfeld Complaint*, *supra* note 30, at 7.

that the sample was no longer large enough to test the effectiveness of the drug.⁴² According to Dr. Robert Schooley of the NIH, the reason was that “[t]he study was doomed from the start because the whole method of treating the disease changed during the trial,” making it futile to continue.⁴³

Shortly after the Kahn-Lagakos study was halted, IRC fired nearly a third of its staff, and forced many others to take pay cuts.⁴⁴ However, in cooperation with Agouron, a unit of Pfizer to which IRC had licensed marketing rights for Remune the year before, IRC now initiated two additional Phase III surrogate-marker trials of the drug.⁴⁵ A year later, Dr. Kahn notified IRC that he intended to share his negative results with the NIH Clinical Trials Group, which had begun enrolling HIV-infected patients in a study of Remune.⁴⁶ IRC executives assured Dr. Kahn that this was unnecessary, since the company had already supplied the information; according to Dr. Lagakos, however, NIH did not have the full data until he gave it to them himself.⁴⁷ Eventually, NIH discontinued one of its Remune trials and substantially modified another.⁴⁸

Dr. Kahn and his colleagues believed that they should publish their analysis of the results of their trial. But in January 2000, Dr. Ronald Moss, medical vice-president of IRC, wrote to Dr. Kahn that the company itself, along with a third-party clinical-research outfit, should analyze the study data.⁴⁹ Dr. Kahn was “flabbergasted” by this proposal, which he described as “completely unacceptable”; Dr. Lagakos, too, said it was “inappropriate and unacceptable.”⁵⁰ In July 2000, IRC’s lawyer told Dr. Kahn that “[d]ata and analysis may be used and published only with IRC’s consent. . . . IRC does not

42. Maugh, *supra* note 28.

43. *Id.*

44. *Id.*

45. Derhsing Lai & Taff Jones, *Remune Immune Response*, 3 CURRENT OPINION IN INVESTIGATIONAL DRUGS 391, 391 (2002). The Kahn-Lagakos study was also a Phase III trial. According to an FDA program director:

Phase I studies are early clinical trials in which the principal objective is an assessment of safety. This usually involves minimal numbers of patients, usually does not include a control group and may include very limited dosage assessments. In Phase II the study is typically larger, includes dose ranging studies, and may in addition to safety endpoints, have assessments of drug activity or efficacy as well as include a control group. By Phase III it is expected that the safety profile of the product is better understood and that a potentially effective dose has been identified. These studies are predominantly aimed at efficacy evaluations, although safety is critically evaluated as well and some continued dose ranging may be done. Such studies are often the basis of product license applications if they show a favorable risk/benefit profile.

E-mail from Amy Rosenberg, Program Director, Food and Drug Administration, to Susan Haack (Nov. 3, 2005) (on file with Law and Contemporary Problems).

46. Penni Crabtree, *Scientists Say Firm Tried to Gag Them; Tell of Releasing AIDS Vaccine Data*, SAN DIEGO UNION-TRIBUNE, Nov. 7, 2000, at B1.

47. *Id.*

48. *Id.*

49. Thomas M. Burton, *Unfavorable Drug Study Sparks Battle Over Publication of Results*, WALL ST. J., Nov. 1, 2000, at B1.

50. *Id.*

consent to your proposed publication”;⁵¹ and Mr. Carlo informed him that “IRC is prepared to enforce its contractual rights,” adding that if Kahn were to make any statements suggesting that the company was not acting within its rights in this matter, IRC was prepared to take legal action against him.⁵² When Drs. Kahn and Lagakos refused to accept this, the company refused to provide them with the results of participants’ final check-ups, conducted after the trial was halted, and insisted that the results of IRC’s own, more favorable, analysis of a sub-sample of ten percent of the subjects whose blood had been tested more frequently should be included in any publication.⁵³

In the November 2000 issue of JAMA, Dr. Kahn and his colleagues published a paper⁵⁴ based on the 90–95% of the study data to which they had access. (Had the DSMB not supplied Dr. Kahn with this data, he and his colleagues would presumably have been completely stymied.) This article acknowledged that Remune “elicited significant immunogenicity” but found no significant difference in this effect between the group as a whole and the subgroup on which IRC was placing so much weight—the 200-odd patients whose blood was tested every twelve weeks instead of every twenty-four.⁵⁵ “The results of this trial,” the paper concluded, “failed to demonstrate that the addition of HIV-1 Immunogen to ART [anti-retroviral therapy] conferred any effect on progression-free survival relative to that achievable by ART alone.”⁵⁶

It is normal practice for such papers to be circulated before publication to all those contributing to the study; but in this case, Dr. Kahn claimed, IRC had refused to provide him with contact information on all the participants, so rather than circulate the paper only to those for whom he had this information, he had not circulated it at all.⁵⁷ (Dr. Moss claimed that Dr. Lagakos had all the names and addresses.)⁵⁸ Dr. John Turner, the Philadelphia physician who had monitored the group of patients tested more frequently, was reportedly “floored when [he] found out they were coming out with a paper about which [he] knew nothing.”⁵⁹ In an editorial accompanying Dr. Kahn’s paper, the editor of JAMA, Dr. Catherine DeAngelis, said the journal had decided to publish this study because “the integrity of the research process must be protected and preserved”;⁶⁰ and the deputy editor, Dr. Drummond Rennie, was

51. *Id.*

52. Crabtree, *supra* note 46.

53. Katherine S. Mangan, *Company Seeks \$10 Million from Scientist and University*, CHRON. HIGHER ED. Nov. 17, 2000, at A48, A50.

54. Kahn et al., *supra* note 33.

55. *Id.* at 2199.

56. *Id.* at 2200.

57. Maugh, *supra* note 28. See also Kahn et al., *supra* note 33, at 2202; James O. Kahn & Stephen Lagakos, *In Reply*, 285 J. AM. MED. ASS’N 2193, 2194 (2001).

58. Maugh, *supra* note 28.

59. Sabin Russell, *Firm That Paid for UCSF Study Seeks Damages*, S.F. CHRON., Nov. 1, 2000, at A3 (quoting John Turner).

60. Catherine D. DeAngelis, *Conflict of Interest and the Public Trust*, 284 J. AM. MED. ASS’N 2237, 2238 (2000).

quoted as saying that the journal had decided to go ahead with publication to “prevent the bias that comes from reporting only those results favorable to sponsors’ products.”⁶¹

Some of the letters published in response to the article raised scientific objections (the trial did not include true temporal variables⁶² or explore possible distinguishing characteristics of the sub-group whose response was more promising,⁶³ there was unpublished data showing that Remune was immunogenic, but suggesting that the response was transient, with no effect on clinical outcomes,⁶⁴ it might be the adjuvant, and not Remune, that prompted the response in the immune system.)⁶⁵ Other letters focused on the relationship between the researchers and their sponsors: one, from Peter Lurie and Sidney Wolfe of the Citizens’s Health Research Group in Washington, D.C., noted that IRC had been accused of improper attempts to influence the presentation of data on Remune before and had even received a Warning Letter from the FDA in 1995, when two subjects were found to have been excluded from a published article that claimed to include all subjects;⁶⁶ another, from Donald M. Poretz of the Georgetown School of Medicine—who had been one of the investigators in the trial and, like Dr. Turner, was upset because he had not been asked to review the manuscript before publication—observed that “[t]he intense pressure on individuals at academic institutions to publish and on the sponsoring companies to get their drugs on the market sometimes produce[s] tensions between the 2 parties, and if results are not favorable, disagreements can develop[,] leading to disputes, innuendos, and even legal action.”⁶⁷

That, to put it mildly, is putting it mildly.

By six o’clock on the evening before Dr. Kahn’s article came out, IRC stock had fallen more than nineteen percent in after-hours trading.⁶⁸ The company had spent about \$191 million on Remune⁶⁹ and had no other drug in such an advanced stage of development.⁷⁰ The Vice-President of IRC described JAMA’s involvement as “tabloid journalism” and Dr. Kahn’s article as a

61. Scott Gottlieb, *Firm Tried to Block Report on Failure of AIDS Vaccine*, 321 BRIT. MED. J. 1173, 1173 (2000).

62. Nguyen V. Dat, Letter to the Editor, *Outcomes of a Trial of HIV-1 Immunogen in Patients with HIV Infection*, 285 J. AM. MED. ASS’N 2191, 2191 (2001).

63. *Id.*

64. Frances M. Gotch & Nesrina Imami, Letter to the Editor, *Outcomes of a Trial of HIV-1 Immunogen in Patients with HIV Infection*, 285 J. AM. MED. ASS’N 2191, 2191–92 (2001).

65. Billi Goldberg & Raphael B. Stricker, Letter to the Editor, *Outcomes of a Trial of HIV-1 Immunogen in Patients with HIV Infection*, 285 J. AM. MED. ASS’N 2192 (2001).

66. Peter Lurie & Sidney M. Wolfe, Letter to the Editor, *Outcomes of a Trial of HIV-1 Immunogen in Patients with HIV Infection*, 285 J. AM. MED. ASS’N 2193 (2001).

67. Donald M. Poretz, Letter to the Editor, *Outcomes of a Trial of HIV-1 Immunogen in Patients with HIV Infection*, 285 J. AM. MED. ASS’N 2192, 2192–93 (2001).

68. Penni Crabtree, *Analysts Try to Sort Out Flap Over Remune*, SAN DIEGO UNION-TRIB., Nov. 1, 2000, at C1.

69. Cheryl Clark & Penni Crabtree, *Carlsbad Firm Under Fire on Vaccine Study*, SAN DIEGO UNION-TRIB., Nov. 1, 2000, at A1.

70. Crabtree, *supra* note 68.

“smear campaign”;⁷¹ expressing confidence that “the truth in the long run will come out,”⁷² he insisted that the company tried to prevent publication “only because we think there was important information that was excluded” about the subset of participants whose blood was tested more frequently.⁷³ Dr. Kahn replied that IRC executives were acting like “bull[ies] in a sandbox,” and that their supposedly “important information” was the result of “data dredging.”⁷⁴ IRC’s analysis stressed that in this subset there was lowered viral load and increased T-cells at weeks 36, 48, 60, 84, 96, and 120;⁷⁵ Dr. Kahn replied that “[o]ne cannot pick and choose data points to suit one’s needs,”⁷⁶ and that the company was “manipulating data to try to have a positive outcome.”⁷⁷

Participants in the study, who now learned for the first time why it had been halted in 1999, expressed concern that they had not been informed earlier of the unfavorable results.⁷⁸ IRC spokesperson Laura Hansen declined to comment, instead referring inquirers to the company’s website, where numerous news releases showing the benefits of Remune were posted; but Dr. Kahn observed that “you should tell [participants] all the information that you know,” especially since by enrolling in Remune studies they were disqualified from enrolling in many other clinical trials.⁷⁹ Indeed.

Agouron stood by Remune, and biotech stock analyst Alan Auerbach, who was advising clients to buy IRC stock, stood by Agouron: “Agouron/Pfizer is convinced [Remune] works via their analysis, and Pfizer has gotten a lot of drugs approved by the FDA,” he commented, asking, “How many drugs has James Kahn brought to the FDA?”⁸⁰ “If there isn’t [any effect on patients], why is Pfizer putting so much money into this? Are you telling me that Jim Kahn is smarter than Pfizer? I have a problem believing that.”⁸¹ But Charles Engelberg, who was advising his clients to sell IRC, disagreed: “I’ve been following this since 1993 and the company has been guilty of massaging data all along”⁸²

71. Clark & Crabtree, *supra* note 69.

72. *Id.*

73. Gottlieb, *supra* note 61.

74. Russell, *supra* note 59.

75. Carol Cruzan Morton, *Company, Researchers Battle Over Data Access*, 290 SCIENCE 1063 (2000).

76. *Id.*

77. Russell, *supra* note 59.

78. Cheryl Clark, *A Medical and Ethical Quandary; Fallout Over Vaccine*, SAN DIEGO UNION-TRIB., Nov. 4, 2000, at A1.

79. *Id.*

80. Crabtree, *supra* note 68.

81. Eric Niiler, *Company, Academics Argue over Data*, 18 NATURE BIOTECHNOLOGY 1235, 1235 (2000).

82. *Id.*

The sponsors' contract with Dr. Kahn's university called for binding arbitration in the event of a dispute.⁸³ In September 2000, IRC had filed an action with the American Arbitration Association to block publication.⁸⁴ Shortly after Dr. Kahn's paper appeared, the company filed an action accusing him of omitting favorable data and of violating an agreement to keep certain findings confidential, demanding \$7–\$10 million in damages. The university filed a counterclaim alleging that the company wrongfully withheld data from researchers.⁸⁵

In March 2000, while the company was disputing with Dr. Kahn over whether his results should be published, IRC stock had risen forty-three percent on news that doctors testing Remune in Thailand—where the drug-approval process is “very informal”—would seek authorization to market the drug from the Thai Minister of Public Health.⁸⁶ On March 10, 2000, Agouron sold 166,000 shares in IRC for proceeds of \$2.5 million.⁸⁷ In April 2001, the subset analysis that IRC had wanted included in Dr. Kahn's article was published, under the authorship of Dr. Turner (but referring readers to Dr. Moss, at IRC's address, for correspondence), in the European journal *HIV Medicine*.⁸⁸ This article concluded that “a beneficial effect of [Remune] was observed on viral load, CD4+ T cells, and HIV-specific immunity”;⁸⁹ IRC stock rose 115%.⁹⁰ In May 2001, IRC issued preliminary results of a subset of sixty-six patients in a Spanish Phase II trial, stating that Remune “appeared to enhance allo-immune response along with HIV specific immune responses,” and announced positive results from another, fifteen-patient study.⁹¹

But in June 2001, IRC acknowledged that the Spanish DSMB had determined that Remune failed to slow the growth of the HIV virus in patients. The company's stock price dropped around sixty percent.⁹² In July 2001, a multi-party suit was filed against IRC and Agouron Pharmaceutical for violation of the Securities Exchange Act of 1934, alleging that the defendants

83. The Immune Response Corporation & The Regents of the University of California, Research Agreement (executed Sept. 25, 1995) [hereinafter Research Agreement] (on file with Law and Contemporary Problems).

84. Clark & Crabtree, *supra* note 69. The American Arbitration Association (AAA) is a nonprofit group offering binding settlements of disputes in many professional areas without the cost, but also without some of the safeguards, of a court case. Proceedings are private, conducted without a jury, and cannot be appealed. Mangan, *supra* note 53, at A50.

85. Clark & Crabtree, *supra* note 69.

86. Rhonda L. Rundle, *Immune Response Shares Soar 43% as Thai Doctors Back AIDS Drug*, WALL ST. J., Mar. 24, 2000, at B6.

87. Hirschfeld Complaint, *supra* note 30, at 7.

88. J. L. Turner et al., *The Effects of an HIV-1 Immunogen (Remune) on Viral Load, CD4 Cell Counts and HIV-Specific Immunity in a Double-Blind, Randomized, Adjuvant-Controlled Subset Study in HIV Infected Subjects Regardless of Concomitant Antiviral Drugs*, 2 HIV MED. 68 (2001).

89. *Id.* at 68.

90. Penni Crabtree, *Analysis Boosts Carlsbad Biotech; Immune Response Stock Surges with AIDS Drug Results*, SAN DIEGO UNION-TRIB., Apr. 24, 2001, at C1.

91. Hirschfeld Complaint, *supra* note 30, at 14.

92. *Id.* at 15.

withheld and misrepresented the results of clinical trials of Remune, “to artificially inflate the price of Immune stock,” so as to enable IRC to complete a public offering of its shares.⁹³ The same month, Agouron dropped out of the development of Remune. Shares in IRC dropped another forty-four percent.⁹⁴ On September 11, the result of the arbitration proceedings against Dr. Kahn and UCSF was reported: IRC had settled “without collecting a cent.”⁹⁵ A year later, IRC had laid off more than half the workers at its headquarters “under a plan to cut costs and narrow its focus to what it sees as its most promising product,” Remune; and Mr. Carlo had resigned as President and CEO.⁹⁶ By November 2002, the company was reported to be “close to going out of business.”⁹⁷

As of late August 2005, however—with the securities case against IRC still pending, now with a number of new plaintiffs, and the drug still not approved by FDA—press releases on the IRC website reported that the company had entered a “Standby Equity Distribution Agreement” with Cornell Capital Partners, LP, which had committed to provide up to \$15 million of funding for development of its products;⁹⁸ that at the July 2005 meeting of the International AIDS Society in Rio de Janeiro, the company had presented two posters about the REMIT study, a continuation of the earlier Spanish trial, involving thirty-nine patients;⁹⁹ and that Remune is to be included in a new NIH trial, involving ninety-two patients, of the effects of various therapies in early stages of HIV infection. One press release averred: “The Company believes that results of previous clinical trials demonstrate that REMUNE boosts HIV-specific immune responses and has the potential to slow the progression of HIV infection when used alone or in conjunction with antiretroviral therapy.”¹⁰⁰ However, acknowledging that its press release about the NIH trial included “forward-looking statements,” as signaled by such terms as “could,” “will,” “might,” “plan,” “projection,” and such, the company conceded that “[a]ctual results could vary materially from those expected due to a variety of risk factors, including whether the [c]ompany will continue as a going concern,”

93. *Id.* at 2.

94. *Immune Response Stock Falls After Pfizer Ends Deal*, N.Y. TIMES, July 7, 2001, at C3.

95. *Zilch for Maker in AIDS Drug Suit*, S.F. CHRON., Sept. 11, 2001, at A10.

96. *Immune Response Corp.: Company Lays Off Workers, Shuffles Senior Management*, WALL ST. J., Sept. 10, 2002.

97. *Morning Edition: Company Founded by the Late Dr. Jonas Salk Close to Going out of Business* (NPR radio broadcast Nov. 22, 2002) (transcript on file with Law and Contemporary Problems).

98. Press Release, Immune Response Corporation, The Immune Response Corporation Signs a \$15 Million Financing Agreement (July 18, 2005), available at <http://www.imnr.com/news/2005/2005Jul18.htm>.

99. Press Release, Immune Response Corporation, The Immune Response Corporation Presents REMUNE Data at The International AIDS Society Meeting in Rio (July 27, 2005), available at <http://www.imnr.com/news/2005/2005Jul27.htm>.

100. Press Release, Immune Response Corporation, *supra* note 9.

given, among other things, that it “has not succeeded in commercializing any drug.”¹⁰¹

Does Remune work? In a telephone conversation on December 18, 2004, Dr. Kahn told me that he had no doubt that his study established decisively that it does not.¹⁰² Of course, even if I had all the available evidence, I would hardly be competent to judge; still, if I had to bet, I would certainly bet against it.

IV

THE MORALS OF THE STORY

The clinical trials of Remune vividly illustrate the complexities of the structure of evidence and the pitfalls of experimental design described earlier in an abstract, theoretical way. It should come as no surprise if, in the early stages, the evidence regarding the effectiveness or otherwise of a new drug is ambiguous or confusing; for the design of a large-scale, long-term, multi-center drug study, which inevitably relies on a whole mesh of background assumptions—penciled-in crossword entries—any of which *may* be mistaken, is a complicated matter in the best of circumstances. And in the present case the inevitable difficulties were compounded, epistemologically, practically, and morally, by the FDA decision, shortly after the inception of the trial, to allow tests of “surrogate markers,” and by the introduction of new therapies significantly lowering death rates from AIDS. Looked at strictly from an epistemological point of view, one possibility might have been to consider starting again with a new design and a larger sample; but in Dr. Kahn’s opinion, the sample was “more than big enough.”¹⁰³ Another possibility might have been to leave the trial design unchanged, not allowing subjects to use other drugs; but of course moral considerations spoke against forbidding subjects to use the promising new therapies.

Again, the unhappy interaction between the researchers and their sponsors vividly illustrates the points made earlier in an abstract, theoretical way about the difference between inquiry and advocacy, and about how scientific inquiry can be hampered or perverted by pressure to transform it into boosterism for a product (or a policy); for such pressure damages the fragile social mechanisms that sustain the scientific ethos of honest investigation and encourage the free exchange of ideas and information. Getting at the truth about Remune would have been hard enough if everyone involved had been trying his best to do just that; but IRC’s efforts to prevent publication and to put its own spin on the

101. *Id.* As of August 1, 2006, IRC was still a going concern; the stock price was two cents a share. The same day, IRC announced that it had received approval for expansion of a phase II trial of IR103, described as “a more potent formulation” based on Remune. <http://www.marketwatch.com> (last visited Aug. 1, 2006) and <http://www.imnr.com/news/2006/2006AUG01.htm> (last visited Aug. 1, 2006) [And as of that date, the securities case was still pending, and Remune still not approved by FDA.]

102. Telephone Interview with James O. Kahn, Professor of Clinical Medicine, UCSF, in San Francisco, Cal. (Dec. 18, 2004).

103. *Id.*

results cannot have failed to make an already scientifically hard task exponentially harder in other ways. Even though the company failed to prevent publication of the Kahn study, it certainly managed to muddy the waters, and (very likely) wasted resources on new trials.

Of course, it is impossible to know for sure how exceptional, or how typical, the pressure exerted by IRC might be; as Marcia Angell observed, it is “common for companies that sponsor research to assert control over data,” but because researchers so seldom stand up to their sponsors as Dr. Kahn did, “there is no way to know how many negative studies have been suppressed—or worse, how many negative studies were converted to positives.”¹⁰⁴ But almost every day there is more reason to believe that the iceberg of corruption is sizable: Congress launches an investigation into financial connections between industry and the NIH;¹⁰⁵ Pfizer is fined almost a half-billion dollars for paying physicians to promote its anti-seizure drug Neurontin;¹⁰⁶ Eliot Spitzer, Attorney General of the State of New York, accuses GlaxoSmithKline of hiding evidence that Paxil can trigger suicide;¹⁰⁷ it is revealed that Merck may have known the dangers of Vioxx well before they pulled the drug from the market;¹⁰⁸ and so on.

Entanglement with business interests undoubtedly poses a threat to the scientific ethos, and in consequence to the advancement of science. And the advancement of science is undoubtedly of value: because the sciences have revealed so much about the world; because they represent such a remarkable amplification and refinement of the human talent for inquiry; and because of the practical benefits they may bring. This does not mean, and I have been careful not to say, that the advancement of science is an overriding value: for example, some ways of procuring evidence, desirable as that evidence might be from a scientific point of view, are unacceptable morally;¹⁰⁹ and regulation of

104. Mangan, *supra* note 84, at A50 (quoting Marcia Angell, Editor-in-Chief of the New England Journal of Medicine).

105. Shannon Brownlee, *Bitter Medicine*, MOTHER JONES, Sept.–Oct. 2004, at 83, 83 (reviewing MARCIA ANGELL, *THE TRUTH ABOUT DRUG COMPANIES: HOW THEY DECEIVE US AND WHAT TO DO ABOUT IT* (2004) and JEROME KASSIRER, *ON THE TAKE: HOW BIG BUSINESS IS CORRUPTING AMERICAN MEDICINE* (2004)). See also Anna Wilde Mathews, *House Panel Grills FDA, Drug Firms*, WALL ST. J., Sept. 10, 2004, at B5 (describing House panel questioning of FDA and drug companies about disclosure of negative research findings).

106. Brownlee, *supra* note 105.

107. *Id.*

108. Well before the present brouhaha, I had noted manufacturers' efforts to play down possible risks of Vioxx and Celebrex. See HAACK, *DEFENDING SCIENCE*, *supra* note 10, at 320 (citing Thomas M. Burton and Gardiner Harris, *Note of Caution: Study Raises Specter of Cardiovascular Risk for Hot Arthritis Pills*, WALL ST. J., Aug. 22, 2001, at A1). As of August 17, 2006, there are around 14,200 Vioxx lawsuits pending against Merck; of the nine tried so far, Merck has won three, with a split verdict in a fourth. See John Carreyrou & Greg Edwards, *Merck's Net Soars on Strong Sales*, WALL ST. J., July 25, 2006, at A2; *Merck Wins Vioxx Case in New Jersey*, N.Y. TIMES, July 14, 2006, at C4; Andrew Simons & Heather Won Tesoriero, *Merck Wins California Vioxx Case, Widening Edge on Trial Score Card*, WALL ST. J., Aug. 3, 2006, at A8; Heather Won Tesoriero, *Merck Suffers Vioxx-Case Setback*, WALL ST. J., Aug. 18, 2006, at A2.

109. For example, and quite to the present purpose, testing an unproven AIDS vaccine on healthy patients who are then deliberately exposed to AIDS.

potentially dangerous scientific work is prudentially justified if the benefits outweigh the costs. It *does* mean, however, that the progress of science is not something to be lightly compromised or surrendered.

But how, specifically, is such compromise or surrender to be resisted? Acutely conscious of F.H. Bradley's stern warning that "the man of mere theory is in the practical sphere an useless and dangerous pedant,"¹¹⁰ I venture my brief concluding thoughts with more than a little trepidation.

V

CONCLUSION: THE PERILS OF UNIVERSITY-INDUSTRY COLLABORATION

Since issues about the FDA and patent law are far beyond my competence, I shall set them aside; as I will issues about legal sequestering, since the fact that scientific findings are held secret is not the only problem posed by legal sequestering, and legal sequestering is not the only, or the most fundamental, reason for scientific findings being kept secret; I shall also set aside questions about journals' financial-disclosure policies, since, desirable as they are, such policies cannot by themselves prevent industry sponsors from delaying or impeding publication. Of the great tangle of issues raised by the Remune story, I shall comment on just one: university-industry collaborations.

Much attention has been focused on universities' conflict-of-interest policies, their guidelines about collaborative research contracts, and so forth. Dr. DeAngelis mentions specifically the potentially distorting effects of sponsors' gifts and the speaking and consulting fees that sponsors offer researchers.¹¹¹ David Korn, senior vice-president for biomedical and health sciences at the Association of American Medical Colleges, suggests that medical centers negotiate for control over the data when they accept sponsors' business; Ronald Collins, director of the "Integrity in Science" project at the Center for Science in the Public Interest, focuses on the threat posed by agreements specifying that any disputes go to arbitration.¹¹²

However, an editorial in *Nature Immunology* comments that though "clinical trials sponsored by a product's developer are inherently conflicted[,] . . . industry funding is necessary, as public funding for clinical research is inadequate";¹¹³ an editorial in *Nature Biotechnology* asks, "When is it reasonable for academics to expect total freedom over the data they have gathered on a company's behalf, especially if they have signed a confidentiality agreement?";¹¹⁴ and Dr. DeAngelis observes that "[b]alance must be maintained between the need for research projects to be reasonably funded and performed

110. F. H. BRADLEY, *ETHICAL STUDIES* 226 (2d ed. 1927).

111. DeAngelis, *supra* note 60, at 2237.

112. Mangan, *supra* note 84, at A50.

113. Editorial, *Collaborative Conflicts*, 1 *NATURE IMMUNOLOGY* 449 (2000).

114. Editorial, *Knee-Jerk Response*, 18 *NATURE BIOTECHNOLOGY* 1223 (2000).

by the best possible investigators and the relative paucity of public funds for clinical research.”¹¹⁵

The stress has been on “managing” the problem; and the result has been a patchwork of compromises. Yale University will not accept any restriction on publication except for short delays to allow a sponsor to apply for a patent or license;¹¹⁶ Harvard University will not allow a scientist who owns more than \$20,000 in publicly traded stock to serve as a principal investigator on research grants funded by the same company, nor to receive more than \$10,000 annually in consulting fees or honoraria from companies that sponsor his research.¹¹⁷ Stanford University sets no fixed limits on stock ownership or royalties, but requires that faculty who own more than \$100,000 of stock or 0.5% of a company notify the university, which then decides case-by-case whether any restrictions are needed; and MIT regulations focus on whether a faculty member’s holdings are large enough to influence stock price, rather than on the dollar amount.¹¹⁸

A study of a hundred institutions from August 1998 to February 2000 found that fifty-five percent required disclosure of financial interests from all faculty, and forty-five percent only from principal investigators; only nineteen percent set explicit limits on faculty financial interests in corporate-sponsored research; only twelve percent specified what delay in publication was permissible; and only four percent prohibited student involvement in work sponsored by a company in which a faculty member had a financial interest.¹¹⁹ Management of conflict and penalties for non-disclosure are invariably discretionary; and it seems that universities rarely ask researchers to forgo financial interests: for example, the University of Washington “required researchers to give up all financial interests only eight times in 321 cases reviewed It approved conflicts of interest in most cases, including 113 cases involving clinical trials.¹²⁰ The authors of a national survey concluded that “academic institutions rarely ensure that their investigators have full participation in the design of the trials, unimpeded access to trial data, and the right to publish their findings.”¹²¹

UCSF’s agreement with IRC *did*, in fact, ensure Dr. Kahn’s right to publish his findings, subject only to his not disclosing confidential information provided by the company.¹²² “Protocol 806” of the Research Agreement between UCSF

115. DeAngelis, *supra* note 60, at 2237.

116. Yale University, Yale University Faculty Handbook 112 (2002), available at http://www.yale.edu/provost/handbook/faculty_handbook.pdf.

117. KRIMSKY, *supra* note 24, at 130.

118. *Id.* at 48.

119. Mildred K. Cho, Ryo Shohara, Anna Schissel & Drummond Rennie, *Policies on Faculty Conflicts of Interest at U.S. Universities*, 284 J. AM. MED. ASS’N 2203, 2203 (2000).

120. David Wickert, *UW Seldom Cuts Researcher, Corporate Ties*, NEWS TRIB. (Tacoma, Wash.), Oct. 14, 2002, at A10.

121. Kevin A. Schulman et al., *A National Survey of Provisions in Clinical-Trial Agreements Between Medical Schools and Industry Sponsors*, 374 NEW ENG. J. OF MED. 1335, 1339 (2002).

122. See Research Agreement, *supra* note 83, at 3-6. At Kahn’s suggestion, see *supra* note 102, I requested from UCSF copies of the contract with IRC and of the template contract in effect at that

and IRC provides that IRC should have at least four weeks' advance notice before the submission of any results for publication or presentation "[t]o permit The Immune Response Corporation to delete any proprietary information contained therein" and that "[p]ublication of the results of this trial is the responsibility of the Steering and Publication Committee," one member of which was to be the Medical Director of IRC.¹²³ "[I]s the responsibility of" is not amplified in any way; however, the same paragraph continues: "Approval by the Sponsor otherwise [that is, other than with respect to disclosure of proprietary material supplied by the Sponsor] is not required prior to publication."¹²⁴

All the same, a study of UCSF faculty financial relationships with industry published in *JAMA* alongside Dr. Kahn's paper concluded that—even though UCSF is subject to relatively stringent state and campus policies—the university committee on relations with industry (which since 1980 has reviewed cases of possible conflict of interest) works "to accommodate all but the most overtly conflicting relationships in the interest of encouraging its faculty and, presumably, encouraging future outside investment in the university."¹²⁵

If they had the will, universities could significantly mitigate the threat to the scientific ethos; but only if—recognizing that the money offered by private sponsors can be a Trojan horse—they are prepared to refuse such money when the terms on which it is offered pose unacceptable restrictions on freedom of inquiry or sharing of evidence.¹²⁶ But it is not clear they *do* have the will: academic scientists, aware that their professional survival depends on their ability to obtain grants, are likely to be reluctant to hamper colleagues' efforts

time. Eventually I obtained, from the Office of the Chancellor, copies of UCSF's template agreement; the preliminary Research Agreement between UCSF and IRC, "effective 1/1/95," executed September 25, 1995; the "Investigational Site Agreement," effective May 24, 1996, superseding the earlier agreement; and a document entitled "Clinical Endpoint Study, Protocol Number 806" (apparently incorporated into the Investigational Site Agreement as "Exhibit A").

I first asked for these documents in January 2005; receiving no response; in February I asked again, this time referring to my rights "pursuant to the California Public Records Act, Government Code sections 6254 et seq., and the California Constitution, as amended by passage of Prop. 59 on November 3, 2004." After several more (increasingly urgent and strongly-worded) requests, I finally received the documents in late August 2005. My colleague William Widen helped me sort through the material and tentatively identify, from internal clues, the relation between the preliminary and the revised (and superseding) agreement, et cetera.

123. CLINICAL ENDPOINT STUDY, PROTOCOL NUMBER 806: A MULTICENTER, DOUBLE-BLIND, PHASE III, ADJUVANT-CONTROLLED STUDY OF THE EFFECT OF 10 UNITS OF HIV-1 IMMUNOGEN COMPARED TO IFA ALONE EVERY 12 WEEKS ON AIDS-FREE SURVIVAL IN SUBJECTS WITH HIV INFECTION AND CD4 T LYMPHOCYTES BETWEEN 300 AND 549 CELLS/UL REGARDLESS OF CONCOMITANT HIV THERAPIES 55 (signed Feb. 15, 1996) (on file with Law & Contemporary Problems) [hereinafter *Protocol 806*].

124. *Id.*

125. Elizabeth A. Boyd & Lisa A. Bero, *Assessing Faculty Financial Relationships With Industry: A Case Study*, 284 J. AM. MED. ASS'N 2209, 2213–14 (2000).

126. This is not intended to suggest that *only* private funding poses such problems; that, unfortunately, would be over-optimistic to say the least. See, e.g., Bernard Wysocki, Jr., *Cash Injection: As Universities Get Billions in Grants, Some See Abuses: Cornell Director Blows Whistle Over Use of Federal Funds, Alleging Phantom Studies; Defending a Star Professor*, WALL ST. J., Aug. 16, 2005, at A1 (reporting numerous instances of alleged misuse of federal grant money).

to secure research funds; more fundamentally, universities are likely to be reluctant to risk putting lucrative opportunities for collaboration with industry in serious jeopardy.¹²⁷

Sheldon Krinsky tells us that Jean Mayer, former President of Tufts University, used to joke that “[t]he only thing wrong with tainted money is there t’aint enough of it.”¹²⁸ It’s a nice pun; all the same, it brings Thorstein Veblen’s dryly devastating analysis of “the higher learning in America” nearly irresistibly to mind: “[T]he intrusion of business principles in the universities goes to weaken and retard the pursuit of learning, and therefore to defeat the ends for which a university is maintained.”¹²⁹ And: “The run of the facts is, in effect, a compromise between the scholar’s ideals and those of business, in such a way that the ideals of scholarship are yielding ground, in an uncertain and varying degree, before the pressure of businesslike exigencies.”¹³⁰

I am sorry to say that our universities’ disturbing drift to the culture of money shows no signs of abating; and that their present preoccupation with grantsmanship over real achievement, and their eagerness to indulge in boosterism and spin on their own behalf, leave me far from optimistic that they can be relied on to hold the line.

127. Current UCSF guidelines aver that “[i]n pursuing relationships with industry, the University must keep the public trust and maintain institutional independence and integrity to permit faculty and students to pursue learning and research freely,” and preclude “assigning to extramural sources the right to keep or make final decisions about what may be published,” or allowing a sponsor to “exercise any editorial control.” Memo Operating Guidance, University of California, Guidelines on University-Industry Relations (June 6, 1989) [hereinafter Guidelines], available at <http://www.ucop.edu/raohome/cgmemos/89-20.html>; University of California, San Francisco, Frequently Asked Questions, <http://www.research.ucsf.edu/icd/icdFAQ.asp> (on file with Law and Contemporary Problems). The Guidelines also describe the university as “exploring innovative . . . approaches to assure support of worthy research . . . that provide[s] significant contributions to . . . scholarship . . . [and] that [is] responsive to industry interests.” Guidelines, *supra* (emphasis added).

128. KRINSKY, *supra* note 24, at 47.

129. THORSTEIN VEBLÉN, THE HIGHER LEARNING IN AMERICA 224 (1919).

130. *Id.* at 190.