Susan Haack
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THE INTEGRITY OF SCIENCE: WHAT IT MEANS, WHY IT MATTERS

Susan Haack

I am not fond of expecting catastrophes, but there are cracks in the universe. — Sydney Smith[1]

1. "Integrity": Its Many Meanings

The *Oxford English Dictionary* tells us that the word "integrity" derives from (the negation of) the Latin "*tangere*," suggesting the untouched, what is whole, unadulterated, sound, or pure; and lists among its current meanings the condition of being in an "undivided or unbroken state," of "material wholeness, completeness, entirety"; of "not being marred or violated" but "unimpaired or uncorrupted"; and "soundness of moral principle, esp. in relation to truth and fair dealing," i.e., "uprightness, honesty, sincerity." *Merriam-Webster's* dictionary tells us that among the current meanings of the word are "completeness," "unity," "incorruptibility," and "firm adherence to values," especially artistic or moral values; and suggests "honesty" as a synonym for the last of these. (According to *Aurelio*, in Portuguese the word "*integridade*" still bears the meaning "chastity, virginity," as the corresponding word also once did in Spanish and, long ago, in English; but this sense, though etymologically as well as sociologically interesting, need not concern us here.)[2]

1. My source is John R. Gross, *The Oxford Book of Aphorisms* (Oxford: Oxford University Press, 1983), p.8. Gross doesn't give the original source.

2. The English word "entire," which is etymologically akin to "integrity," I believe still has a specialized use in which it refers an uncastrated animal.

We may speak of the integrity of a person, such as an artist or politician; of a body of work, such as a writer's or painter's *oeuvre*; or of an institution, such as a voting system, a company, an academic discipline. So thinking about "the integrity of science" leads to a whole snarl of issues: about science *qua* body of work, about individual scientists, and about science *qua* institution; about wholeness, unity, and adherence to values; and about values of different kinds — the ethical, the aesthetic, and the epistemological — and the relations among them.

Questions about wholeness or unity, for example, seem to be best understood as questions about science *qua* body of work (or as we like to say, and as the etymology of "science" suggests, *qua* "body of knowledge"). But the integrity of science in this sense should not be understood as requiring that it be complete, that every possible scientific question have been answered; or that it include no falsehoods, no supposed "knowledge" that will eventually turn out to be mistaken; or even that it be unified, or at least unifi*able*, in the philosophically ambitious sense of the old "Unity of Science" program, reducible in its entirety to the laws of physics. What matters, rather, is that, though scientific inquiry is fallible, it is also capable of correcting earlier mistakes and refining earlier ideas as new information comes in, new concepts are devised, and new, synthesizing conjectures are articulated; and that science *qua* body of knowledge is in an important sense integrated, or at least integr*atable* — undivided, as the *Oxford English Dictionary* says.

By no means every component as yet interlocks neatly with the rest; but as we learn more, once-disjoint elements of the scientific body of knowledge come together — as, for example, revised calculations of the age of the earth, modern theories about the mechanisms of genetics (very different from the "blending" theory Darwin himself accepted), and recent observations of the emergence of new, drug-resistant strains of bacteria and viruses now harmonize with the (also much-revised) theory of evolution. To be sure, the integration of the social with the natural sciences, even in this quite modest sense, remains a long way off; but it seems reasonable to hope that eventually we will understand how the socio-historical road map of language, beliefs, goals, and actions can be superimposed on the physical contour map of the brain, the nervous-system, and the rest.[3]

Interesting and important as they are, however, in what follows I shall set these issues aside, focusing instead on integrity in the sense of "firm adherence to values," and in particular on how this concept applies to science *qua* institution. I shall begin by identifying and articulating the most relevant values — the epistemological values of evidence-sharing and respect for evidence — and sketching how they are rooted in the character of the scientific enterprise; and this will pave the way for an exploration of the circumstances that presently threaten to erode commitment to these core values. Then, looking in some detail at the disturbing saga of the arthritis drugs Vioxx and Celebrex, I will illustrate the threats to the integrity of science that result from the present dependence of much medical research, and especially of the medical journals, on the sponsorship of the pharmaceutical industry. And finally, returning to the broader concerns signaled by my subtitle, I shall try to articulate why the erosion of scientific integrity should concern us.

3. See Haack, *Defending Science — Within Reason: Between Scientism and Cynicism* (Amherst, NY: Prometheus Books, 2003), chapter 6.

2. The Integrity of Science: Core Values

If we ask about the integrity of an artist, his adherence to values, our primary concern will probably be the aesthetic or artistic; if we ask about the integrity of a politician, our primary concern will probably be matters of ethical or financial probity. When we ask about the integrity of a scientist, however, the primary concern is likely to be his adherence to *epistemological* values; for inquiry, investigation, is the defining business of a scientist. So when we ask about the integrity of science *qua* institution, the primary concern is likely to be how successfully the institution ensures that everyone involved behaves as nearly as possible in accordance with those epistemological values.

In saying this, I don't mean to deny that there are aesthetic dimensions to scientific work, or even that these may have epistemological significance.[4] And neither do I mean to deny that questions about adherence to ethical values are appropriate to scientists, as to the rest of us — of course, they are; or that adherence to epistemological values is never, also, a matter of ethical concern — of course, it is.[5] But morally acceptable behavior is neither necessary nor sufficient for good scientific work: it is not necessary, because you may do innovative, important, or solid science even though you are unkind to your laboratory animals, arrogant or inattentive in dealing with your students, or ungenerous in giving your collaborators credit; and it is not sufficient either, because you may do poor scientific work even though your behavior is in every respect morally impeccable. To put it another way: sexually harassing a research assistant, putting in a *pro forma* appearance at a conference as a way of getting your vacation subsidized, bullying your secretary, taking an unauthorized look at a colleague's work-in-progress, failing to get the informed consent of subjects, knowingly helping to make the gas that will efficiently exterminate a despised race, etc., are all objectionable, in varying degrees, on moral grounds; but they don't eat at the scientific core of scientific work, as failures of commitment to the epistemological values inherent in the enterprise do.

The core epistemological values of science are rooted in the central, defining concern of inquiry generally: finding things out. A scientific inquirer starts with a question about what might explain this or that natural or social phenomenon; makes an informed guess; and assesses how well his conjecture stands up to whatever evidence is already available, or can be obtained: i.e., how firmly it is anchored in experimental results and experiential evidence generally; how well it interlocks with the whole explanatory mesh of the body of thus-far well-warranted claims and theories; whether relevant evidence might have been overlooked; and what else could be done to get hold of evidence not presently available. So a scientist needs to take into account not only whatever evidence he can discover for himself, but also whatever evidence others have that may be relevant to the question(s) at issue; and to keep track not only of how well each new conjecture would explain the

4. See Haack, *Defending Science* (n.3), p.144.

5. See Haack, "'The Ethics of Belief' Reconsidered," in *The Philosophy of R. M. Chisholm*, ed. Lewis Hahn (La Salle, IL: Open Court, 1997), 129-44; and in *Knowledge, Truth, and Duty: Essays on Epistemic Justification, Responsibility, and Virtue*, ed. Matthias Steup (New York: Oxford University Press, 2001), 21-33.

phenomenon in question, but also of how well it fits in with already well-established claims and theories in the field.

Though nowadays this is quite rare, in the past many scientists have worked more or less alone. But even the greatest scientists of the past have stood on the shoulders of those who went before; and by now a broad and detailed background knowledge of what has already been achieved is essential even to understand what the important open questions in an area are. In short, science as we know it is a deeply and unavoidably social enterprise, the work of many people within and across generations, each with his or her strengths, each with his or her weaknesses, sometimes cooperating, sometimes competing. And it has succeeded as well as it has in part because, thus far, enough of those people have been faithful enough to the key values — the closely inter-related values, as we shall see — of *honesty* and *sharing*, understood specifically as applying to one's relation to evidence. Robert Merton writes of "disinterestedness" and "communism," but these, "communism" especially, carry unwanted connotations; and words like "cooperation" or "trust" would distract attention from the potentially productive aspects of competition and of skeptical mutual scrutiny. So despite the fact that "honesty" and "sharing" have been so debased by their currency in popular psycho-therapeutic jargon that one is almost embarrassed to use them, I shall do so without apology.[6]

In this context honesty (or as we might also say, respect for evidence) must be understood as both self- and other-related. Being honest with yourself means avoiding self-deception, both about where the evidence you have leads, and about whether you have the evidence you need to draw any conclusion at all. It doesn't require that you abandon a promising idea in the face of any and every piece of apparently contrary evidence; but it does require that, recognizing how complex and confusing evidence can be, you are ready to follow in good faith wherever it takes you. Being honest with others requires, obviously, that you not present fabricated, fraudulent, or massaged data, but also that when you report your work you include all the relevant evidence. Evidence-sharing doesn't require that you post every passing thought, every casual observation, on the Web for all the world to read; but it does require that you not withhold significant information from others in the field to advance your, or your sponsor's, interests.[7] Not every scientist is a paragon of intellectual honesty; not every scientist is cheerfully willing to share his work with others. When things go well, however, the norms of evidence-sharing and respect for evidence will be instilled in young scientists during their long apprenticeship, and reinforced by the acclaim that is the reward of success and the loss of reputation that is the penalty for cheating; and an ethos in which these norms are taken for granted will be transmitted from one generation of scientists to the next. As a result, new information and new ideas will be shared, and each scientist will be able to scrutinize the work of others in his field; making it

6. See Robert Merton, "Science and Democratic Social Structure," in *Social Theory and Social Structure* (Glencoe, IL: Free Press, 1946), 307-16. A pamphlet entitled *Honor in Science*, published in 1991 by Sigma Xi, the Scientific Research Society, intended for graduate students in the sciences, stresses honesty and "openness."

7. It is worth noting that evidence-sharing can be in tension with the desire for prestige, which is for many an important motive for undertaking the hard and often frustrating work of science; and that plagiarism is epistemologically damaging because it threatens the delicate incentive-structure of science.

more likely that flaws will be uncovered, and more likely that potentially promising developments will be spotted and worked out.

Over time the sciences have gradually developed instruments of observation which greatly amplify unaided human senses, and mathematical and statistical methods, computer programs, etc., which greatly refine unaided human powers of reasoning. And over time they have also gradually evolved complicated internal organizational structures and procedures, etc., to protect integrity, i.e., to ensure that results are honestly reported and candidly shared — and to harness grubbier motives, such as the desire for prestige or the hope of besting a rival, to epistemologically-desirable ends; including mechanisms — some formalized, some traditional and informal — for assigning resources and positions, disseminating information, training young scientists, and providing incentives to good work as well as penalties for cheating.

But of course all these scientific helps to inquiry, both the technical helps that amplify observation and reasoning and the social helps that enable evidence-sharing and sustain respect for evidence are, like everything human, fallible. Instruments may introduce distortions or artifactual effects; statistical techniques may import false assumptions; computer models may mislead. Most to the present purpose, no internal social organization can by itself guarantee that the scientific ethos will be sustained. When things go badly, the norms of evidence-sharing and respect for evidence can only too easily be undermined or eroded: arrangements that once served as incentives to succeed may come, in changing circumstances, to encourage carelessness or even misconduct; arrangements that once assigned resources in an epistemologically efficient way may, in changing circumstances, be corrupted to serve the interests of a clique or to forward a party line, or may become mired in a self-serving resistance to any exploration of less-familiar ideas; and arrangements for evidence-sharing may become so clogged or fall into such disrepair or corruption that they actually impede communication.

Science interacts in complicated ways with the rest of society — with industry, government, education, law, and so on. Its integrity requires that it be allowed to operate on its own terms; but this doesn't mean that it is either necessary or sufficient that science be wholly autonomous, in the sense of "entirely independent of every other aspect of the society in which it is conducted." It is not necessary, because the mixing of cultures is sometimes harmless, sometimes benign; and it is not sufficient, because threats to evidence-sharing and respect for evidence may come from within as well as from without. Nor is it either necessary or sufficient that science be wholly pure, in the sense of "free of any considerations of utility." It is not necessary, because the hope of finding a cure for the disease that is killing your child, for example, may be a powerful incentive to hard, honest scientific work; and it is not sufficient, because some of the threats to integrity apply no less to pure than to utility-driven science.

However, potentially highly profitable scientific work is in some ways especially vulnerable; and some of the most important threats to the integrity of science do come from the intrusion of the competing values of the larger society in which scientific work takes place. Some social and cultural environments are hospitable to good, honest scientific work; others are in varying degrees inhospitable, or even

hostile. And while good, honest scientific work may continue even in a surrounding culture which is less than perfectly hospitable, to the extent that the surrounding culture tends to undermine the norms of evidence-sharing and respect for evidence, or seriously to erode or compromise them, the integrity of science comes under threat. In an emergency — e.g., during the Great Influenza of 1918, as scientists worked desperately to figure out the cause of, and hence a way of dealing with, the worst plague in history — urgency and haste may induce carelessness and jumping to unwarranted conclusions.[8] Again, certain kinds of political regime seem to be inherently hostile environments for scientific work: theocracies are likely to fear scientific discoveries that may threaten their world-view, to deplore scientific methods that offend their moral sensibilities, and to be adamantly opposed to the very idea of investigating certain questions; and, as Merton especially emphasized, totalitarian states, aspiring to control every aspect of citizens' lives, are always ready to distort science to their own ends.[9]

3. Threats to Scientific Integrity Today

Today, some hear echoes of theocratic resistance to scientific advance in President Bush's moral objections to funding human embryonic stem-cell research; others hear echoes of such disturbing concepts as "bourgeois genetics" and "Jewish physics" in some recent radical-feminist talk of "masculinist science" and in radical post-colonialist talk of "Western science."[10] But the most troubling threats to the integrity of science are of another, subtler kind.

In 1946, writing of "Science, Faith and Society" — "faith" referring to the commitment to intellectual honesty, respect for evidence — Michael Polanyi observed that "[i]f each scientist set to work each morning with the intention of doing the best bit of safe charlatanry which would just get him into a good post, there would soon exist no effective standards by which such deception could be detected." After all, he continues: "[a] community of scientists in which each would act only with an eye to please scientific opinion would find no scientific opinion to please."[11] This is wonderfully vivid (and disturbingly close to the uncomfortable truth about too much of the "research and scholarship" that goes on in some areas of the humanities). But it doesn't quite fully capture how insidious the dangers may be; for Polanyi puts categorically what is really a matter of degree.

The more willing the more scientists are to cut corners, to fudge, to obfuscate, to plagiarize, to fake, to conceal unfavorable results, to put their own or their sponsors' interests above discovering the truth, the less effective the internal social mechanisms sustaining the core values of science will be. And today, though the technical helps to inquiry have clearly got better and better, the social helps — al-

8. See John M. Berry, *The Great Influenza: The Epic Story of the Deadliest Plague in History* (New York: Penguin Books, 2004).

9. Robert Merton, "Science and the Social Order," *Philosophy of Science*, 5, July 1938: 321-37; reprinted in *Social Theory and Social Structure* (n.6), 295-306.

10. See Haack, *Defending Science* (n.3), chapter 11.

11. Michael Polanyi, *Science, Faith and Society* (London: Geoffrey Cumberledge; Oxford University Press, 1946), p.40

ways more fragile, more susceptible to failure — are under considerable strain. We don't yet face Polanyi's nightmare scenario in which every scientist sets out each morning to perpetrate whatever charlatanry he can get away with; the danger is, rather, that scientists' commitment to evidence-sharing and respect for evidence will suffer a kind of creeping erosion, that too many will find themselves able to tolerate small dishonesties and small concealments: a little "improvement" of the truth here, a little reticence about inconvenient evidence there, a little corner-cutting to ensure priority, a little compromise about whom to acknowledge, and in what terms, to cultivate a potentially useful contact; and that too many even of those who would not compromise the integrity of their own work will manage to tolerate those who do. Russian mathematician Grigory Perelman comments: "[many] are more or less honest, but they tolerate those who are not honest."[12]

Why so? As science progresses, it tends to get more expensive; in part because many, if not most, of the easily- and cheaply-obtainable results have been obtained already, and in part because, as the work becomes more complex, it also becomes more costly (especially in fundamental physics, where new knowledge requires observing smaller and smaller particles moving faster and faster).[13] As scientific work becomes more expensive, it must rely more and more on governments and large industrial concerns for support; and these, obviously, are apt to give priority to quite other values than the epistemological norms at the heart of the scientific enterprise. At the very least, it is likely that such sponsors will want answers to some questions more urgently than they want answers to others — even if the latter are of more true scientific importance, or more readily tackled given present knowledge; and it is likely that they will want palatable answers to the questions they want tackled rather than unpalatable ones — sometimes so much so that they find it easy to ignore the risk of coming to believe the palatable answers on the basis of seriously inadequate evidence. So, for example, a government will be reluctant to fund work, however important intellectually, that might prove offensive to some constituency on which it relies; a pharmaceutical company will prefer to fund studies designed to bring out the benefits of its products, and may even try to suppress publication of studies that cast doubt on their effectiveness or safety.

Nor, at this point, are universities unambiguously enough committed to the culture of inquiry to serve as bulwark against the pressures from elsewhere. As Thorstein Veblen predicted nearly a century ago, universities have become increasingly entangled with the ethos of business, and increasingly bureaucratized;[14] and so even in the academy values of other kinds increasingly pull against evidence-sharing and respect for evidence. Profit is a very different thing from truth; and a bureaucratic culture is deeply inimical to serious intellectual work. The bureaucratized university inevitably stresses money-raising, rankings, numbers of publications, the number and size of grants, volumes added to the library — and bureaucratic administrators strongly prefer conveniently manageable, fungible faculty; while serious intellectual work (whether in the sciences or in history, philos-

12. Quoted in Sylvia Nasar and David Gruber, "Manifold Destiny: A legendary problem and the battle over who solved it," *The New Yorker*, August 28, 2006, 44-57, p.57.

13. According to Donald Kennedy, this "implacable law of the economics of knowledge" was first stated by Max Planck. See Kennedy, *Academic Duty* (Cambridge: Harvard University Press, 1997), p.11.

14. Thorstein Veblen, *The Higher Learning in America* (1919; Stanford, CA: Academic Reprints, 1954).

ophy, or *any* field) is by its very nature unpredictable and ragged, and requires that those with the talent, originality, patience, penetration, and ingenuity to make real intellectual progress — precisely the least fungible, often the least conformist and manageable — be allowed time, peace of mind, scope for experiment, exploration, mature reflection.[15]

There was a time when a fine scientist like Oswald Avery — who throughout the 1918 epidemic had quietly insisted that the evidence many medical scientists then took to show that influenza was caused by a bacterium was inconclusive — published nothing for almost a decade, and steadfastly refused to put his name on any paper unless he had actually conducted one of the experiments described. ("Disappointment is my daily bread," he averred; "I thrive on it.")[16] We now know, of course, that he was correct in suspecting that influenza is viral, not bacterial; and that in 1944, after his long dry spell, he would publish the pioneering work that led to the identification of DNA, rather than protein, as the genetic material.[17] But sadly, it is hard to imagine how a scientist of such sterling intellectual integrity could survive, let alone thrive, in today's academy.

For academic scientists are now under considerable pressure from their universities to get grants, to publish, to come up with something patentable; and may also find themselves also under pressure from their sponsors, or lured by the hope of lucrative patents, large stockholdings, or fat fees as expert witnesses. Nor are scientific journals immune; for as these journals have become serious money-making enterprises, their commitment to scientific values has sometimes come into conflict with their commercial interests. The dangers seem to be greater in the life sciences than in physics, etc.; and especially so in biomedical science. The role of the big pharmaceutical companies in biomedical research in universities, and in medical journals' dissemination of results, is especially disturbing.

4. Erosion of Integrity in Biomedical Research

According to a recent headline in *The Wall Street Journal*, "Gates Won't Fund AIDS Researchers Unless They Pool Data": Mr. Gates will give $587 million in funding to researchers working on a vaccine for AIDS, but only on condition that they pool their data promptly and without reservation.[18] Shortly thereafter, another headline read, "A Nonscientist Pushes Sharing Bird-Flu Data": with a group of scientists, businessman Peter Bogner has "stitched together a network of the world's top flu

15. See also Haack, "Preposterism and Its Consequences" (1996) in Haack, *Manifesto of a Passionate Moderate: Unfashionable Essays* (Chicago: University of Chicago Press, 1998), 188-208; Pat Duffy Hutcheon, *Building Character and Culture* (Westport, CT: Praeger, 1999), 37 and 139 ff..

16. Quoted in Berry, *The Great Influenza* (n.8), p.423.

17. Oswald Avery, Colin MacCleod, and Maclyn McCarty, "Studies of the Chemical Nature of the Substance Inducing Transformation in Pneumococcal Types," *Journal of Experimental Medicine*, 79, 1944: 137-58; reprinted in *Conceptual Foundations of Genetics*, ed. Harry A. Corwin and John B. Jenkins, (Boston: Houghton-Mifflin, 1976), 13-27. The story is told briefly in Haack, *Defending Science* (n.3), pp.102-3.

18. Marilyn Chase, "Gates Won't Fund AIDS Researchers Unless They Pool Data," *The Wall Street Journal*, July 20, 2006, B1, B4.

scientists… to share data that could speed research."[19] Apparently, scientists' commitment to evidence-sharing can no longer be taken for granted. According to another headline, there is a "Worrisome Ailment in Medicine: Misleading Journal Articles":[20] a study finds that in 65% of papers surveyed, harmful effects were not completely reported.[21] Apparently, scientists' commitment to honest reporting of their findings cannot be taken for granted either.

Even some editors of major medical journals have expressed concern. The *American Journal of Hypertension* recently split away from the American Society of Hypertension when the editor of the journal concluded that the society had become, in effect, a tool for drug company marketing.[22] An online article by Richard Smith — for 25 years an editor of the *British Medical Journal*, and for 13 of those 25 years editor and chief executive of BMJ publishing — is entitled: "Medical Journals Are an Extension of the Marketing Arm of the Pharmaceutical Companies."[23] Richard Horton, editor of *The Lancet*, and Marcia Angell and Jerome Kassirer, both former editors of the *New England Journal of Medicine* [NEJM], all sound the same theme.[24]

What has gone wrong? Rather than a simple chain of cause-and-effect, many factors contribute to the erosion of integrity. Mechanisms for evidence-sharing that once worked, if not perfectly, well enough, are falling into disrepair as the burdens placed on them has grown. One factor is the increased pressure on scientists to publish. Once, a handful of good papers was enough to secure a scientist's reputation; now, a constant flow of publications is expected. In 1992 a survey showed that over the previous decade the 20 most "productive" scientists in the world published an article at least once every 11.3 days; at the head of the list was Yury Struchov of the Institute for Organoelemental Chemistry in Moscow, who published a paper every 3.9 days.[25] And that was then — by now the pressure to publish is even more severe; as I can testify from service on university committees, the *curriculum vitae* of a senior medical faculty member will likely list hundreds of papers.

Understandably, some people publish essentially the same material over and over in slightly different forms; and many split their work into shorter papers that can be published separately — a practice so common that scientists themselves talk wryly of "salami publishing," and "minimal publishable units" ("MPUS"). Unfortunately, multiple publications can impede communication; and fragmentation into MPUS may affect study design, e.g., by leading to a focus on intermediate out-

19. Nicholas Zamiska, "A Nonscientist Pushes Sharing Bird-Flu Data," *The Wall Street Journal*, August 21, 2006, B1, B7 (the quotation is from p.B1).

20. Anna Wilde Matthews, "Worrisome New Ailment in Medicine: Misleading Journal Articles," *The Wall Street Journal*, June 10, 2005, A1. A9.

21. An-Wen Chan *et al.*, "Empirical Evidence for Selective Reporting of outcomes in Randomized Trials," *Journal of the American Medical Association*, 291.20 (May 26, 2004): 2457-2465.

22. Robert L. Goodman and Olveen Carrasquillo, "The Corporate Co-author, The Ghost Writer, and the Medical Society," *Journal of General Internal Medicine*, 20 (2005): 102.

23. Richard Smith, "Medical Journals Are an Extension of the Marketing Arm of the Pharmaceutical Companies," Plos Medicine, 2.5, e138: 03646, available at <www.plosmedicine.org>.

24. Richard Horton, "The Dawn of McScience," *New York Review of Books*, 51.4, 2004: 7-9. Marcia Angell, *The Truth About Drug Companies: How They Deceive Us and What to Do About It* (New York: Random House, 2005); Jerome Kassirer, *On the Take: How America's Complicity With Big Business Can Endanger Your Health* (Oxford: Oxford University Press, 2005).

25. Christopher Anderson, "Writer's Cramp," *Nature*, 355 (1992): 101.

comes rather than meaningful endpoints, to controlled trials run over too short a period, to studies that compare a target drug with placebo rather than with proven therapies.[26]

The same pressure to publish has also contributed to the ever-increasing numbers of authors listed on each paper, some of whom may have made only the most minimal contributions to the work reported — or none at all. In 1993 the editor of the NEJM accepted the Ig Nobel Prize for Literature on behalf of the 972 scientists listed as coauthors of a ten-page paper — i.e., just 2 words per author![27] Heads of laboratories or teams may insist on having their name on every paper that the team produces. In 1992, ten geologists at the Russian Institute of Volcanic Geology and Geochemistry went on hunger-strike in protest against an "autocratic" director who forced them to put his name on all their work.[28] Sometimes a senior professor will put his name on a study to which he has contributed little or nothing in hopes of helping a junior colleague get it published. Sometimes, after papers have been discovered to be fraudulent, co-authors have denied all knowledge of the perpetrator's fabrications.[29] Even after some major medical journals adopted policies to discourage "honorific" author listings, a study found that many first authors said co-authors had really made little or no contribution;[30] and when all the members of a research team applied for grant money, "their total participation came to 300%."[31]

Along with the ever-swelling flood of submissions, there has been a steady increase in the number, and the size, of journals. A search of PubMed turned up 19,355 journals, and 734,858 articles published between January 1st 2005 and January 1st 2006. Many medical journals now carry not only articles but news sections, short summaries, and even summaries of summaries, as well as lots of glossy illustrations; the price of these journals rose, on average, almost 11% a year in a period, 1984-2001, in which inflation generally was around 3%;[32] and now that these journals are serious money-making enterprises, some editors are trying to improve their citation-rate, and thus their journal's library sales, by putting pressure on authors to cite other papers that appeared in their pages.[33]

The peer-review process is severely strained by the enormous number of submissions. Reviewers are estimated to spend an average of only 2.4 hours reading a manuscript and making their recommendations (and more of the reviewers, naturally, are more junior than in the early days, when enough relatively senior sci-

26. Jerome P. Kassirer, "Reflections on Medical Journals: Has Progress Made Them Better?", *Annals of Internal Medicine*, 137.1 (July 2, 2003): 46-8, p.46.

27. Steve Nadis, "Ig Nobel Prizes reward fruits of unique labor," *Nature*, 365 (1993): 599. The paper in question was "An International Trial Comparing Four Thrombolytic Strategies for Acute Myocardial Infarction," *The New England Journal of Medicine*, 329.10 (September 2, 1993): 673-82.

28. Anderson, "Writer's Cramp" (n.24 above).

29. Arnold Relman, "Lessons from the Darsee Affair," *New England Journal of Medicine*, 308 (1983): 1417.

30. D. W. Shapiro, *et al*., "The contributions of authors to multiauthor biomedical research papers," *Journal of the American Medical Association*, 271 (1994): 438-42.

31. William J. Broad, "The Publishing Game: Getting More for Less," *Science*, new series, 211.4487 (March 13, 1981): 1137-1139, p.1137.

32. Kassirer, "Reflections on Medical Journals" (n.25 above), p.47.

33. Sharon Begley, "Science Journals Artfully Try to Boost Their Rankings," *The Wall Street Journal*, June 5, 2006, B1, B5.

entists could be found to carry the load); most journals make no independent check of the statistical calculations crucial to the conclusions of many papers. And because there are now so many journals, eventually almost everything submitted gets published somewhere — perhaps after having been turned down numerous times.[34]

So perhaps it is no wonder that honesty as well as evidence-sharing is under threat. According to a study published in *Nature* in 2005, more than 10% of 3,247 scientists polled admitted that they had withheld details of methodology or results from papers or research proposals, more than 15% that they had dropped inconvenient observations or data points, and more than 27% that they had kept inadequate records of research work;[35] according to a study published the same year in the *Journal of the American Medical Association* [JAMA], of 45 highly-cited studies claiming effective medical interventions, published in the most prestigious journals, 15 were later contradicted in whole or part by other studies.[36]

Another factor contributing to the erosion both of sharing and of honesty is the role of industrial sponsors, especially the pharmaceutical companies. At a time when government funding is not keeping pace, increasing pressure on faculty to get grants, and increasing collaboration of universities with industry (usually politely described as "technology transfer") has meant that a larger proportion of scientific, and especially medical, research in the universities is funded by industry. This often means that information deemed proprietary must be kept confidential, and that results will be withheld from publication for a time to protect sponsors' business interests; and it sometimes means that sponsors are allowed to vet, or even control, the publication of results.[37]

The situation is especially severe in the case of medical faculty, who are often obliged, in effect, to raise their own salaries in grant money.[38] At the same time, there are especially attractive financial opportunities for medical scientists who are successful in attracting corporate sponsorship: fees for speaking at company-sponsored conferences, lucrative consultancies, stock holdings, etc.. Other faculty are themselves involved in (sometimes enormously profitable) biotech companies. Universities generally have some kind of conflict-of-interest rules; but there is no uniform standard, in many cases the guidelines are pretty generous or flexible, and often enough policies are not energetically enforced (probably because faculty

34. See Brief Amici Curiae for Daryl E. Chubin, Edward J. Hackett, David Michael Ozonoff, and Richard Clapp in Support of Petitioners, *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993), 11-19; Haack, "Peer Review and Publication: Lessons for Lawyers," forthcoming in *Stetson Law Review* (2007).

35. Brian C. Martinson *et al*., "Scientists behaving badly," *Nature*, 435.9 (June 2005): 737-8.

36. John Ionnadis, "Contradicted and Initially Stronger Effects in highly Cited Clinical Research," *Journal of the American Medical Association*, 294.2 (July 7, 2005): 218-28.

37. See Joshua A. Newberg and Richard L. Dunn, "Keeping Secrets in the Campus Lab: Law, Values and Rules of Engagement for Industry-University R&D Partnerships," *American Business Law Journal*, 39 (2002): 187-240.

38. "[E]specially in the health sciences but also in the basic sciences, faculty are often recruited with the understanding that they will have to generate part or all of their salaries through external funding for the duration of their careers at the university": Donald G. Stein (formerly a working scientist, now a senior academic administrator), "A Personal Perspective," in Stein, ed. *Buying In or Selling Out? The Commercialization of the American Research University* (New Brunswick, NJ: Rutgers University Press, 2004), 1-16, p.3.

serving on the relevant committees are reluctant to oblige a colleague to decline a grant).[39]

Though most of the medical societies that run them claim "editorial independence," many journals receive large revenues from drug-company advertising. After the *Annals of Internal Medicine* published a study critical of drug-company advertisements, the American College of Physicians, which runs the journal, is estimated to have lost between a million and a million-and-a-half dollars of advertising revenue.[40] There is evidence, moreover, that those advertisements are quite often misleading; in particular, the scientific studies cited don't always show what the advertisement claims, usually because "the [advertising] slogan recommended the drug [for] a patient group other than that assessed in the study."[41]

Many medical journals publish symposia organized by pharmaceutical companies, a privilege for which they often charge significant fees; some suspend the peer-review process for such publications. Many receive large revenues from the sale to such companies of thousands, sometimes hundreds of thousands, of offprints of articles favorable to their products. According to a study published in 1992, between 1975 and 1988 the proportion of pharmaceutical companies' marketing budgets spent on sponsoring symposia rose from $6 million to $86 million; editors reported charges for publishing the proceedings of such symposia ranging from between $400 and $1,000 a page to a flat fee of $100,000; and journals charged an average of $15 per reprint, of which they sold, on average, 25,000. Eight editors reported that their review procedures were affected by pressure of various kinds from the organizers of the symposia.[42] Once again, it seems likely that by now these problems are not better, but worse.

Most journals require that authors disclose the sources from which they have received support for their work; but disclosure is at best a weak precaution against undue credulity on the part of readers, and few journals impose any real sanctions when disclosure rules are flouted. Jerome Kassirer, former editor of the NEJM, writes that in the 1990s it became harder and harder to find people without conflicting drug-industry connections to write review articles, as journal policy required; in 2002, the new editor, Jeffrey Drazen, simply gave up the policy as unworkable. The same year, the journal published an article on the anti-depression drug nefazodone, listing 29 authors; the editor noted that "all but 1… of the 12 principal authors have had financial associations with Bristol-Myers Squibb — which also sponsored the study… 2 [other authors] are employees of Bristol-Myers Squibb."[43] In 2006, just days after the editor of JAMA, Dr. Catherine DeAngelis, had announced more stringent disclosure rules, she ruefully acknowledged — the

39. See e.g., Sheldon Krimsky, *Science in the Private Interest: Has the Lure of Profits Corrupted Biomedical Research?* (Lanham, MD: Rowman and Littlefield, 2003), chapter 3.

40. Goodman and Carrasquillo, "The Corporate Co-author, the Ghost Writer, and the Medical Society" (n.21).

41. P. Villanueva *et al*., "Accuracy of pharmaceutical advertisements in medical journals," *The Lancet*, 361 (2003): 27-32. The quotation is from p.27.

42. Lisa Bero, Alison Galbraith, and Drummond Rennie, "The Publication of Sponsored Symposiums in Medical Journals," *The New England Journal of Medicine*, 327.16 (October 15, 1992): 1135-40. See also M.K. Cho and Lisa Bero, "The quality of drug studies published in symposium proceedings," *Annals of Internal Medicine*, 124 (1996): 485-9.

43. Jerome P. Kassirer, *On the Take* (n.26), p.23.

third such rueful acknowledgment in two months[44] — that the journal had just learned that all six authors of a just-published study linking severe hearts attacks to migraines in women had received funding from the manufactures of medicines for migraine or heart-related illnesses.[45] The following week, at the tail end of a press report of a new study of Lipitor, we read not only that all 11 authors of the study, which was funded by Pfizer, but even the doctor recruited by the NEJM to write an opinion piece on the study, had financial connections to the company.[46] The week after that, we learned that the editor of *Neuropsychopharmacology* was stepping down after a controversy over his having written a favorable review of a new device for the treatment of depression without disclosing that he, like all the other eight authors of the article, had financial ties to the manufacturer.[47]

Moreover, the evidence is that company sponsorship has a significant effect on the results reported: reports of work supported by a manufacturer are significantly more likely to be favorable to its products than reports of work not so supported (perhaps the result of a study design more likely to lead to the desired result, perhaps of economy with the truth in reporting, perhaps of simple, optimistic self-deception). As early as 1986, a study found that "in no case was a therapeutic agent manufactured by a sponsoring company found to be inferior to an alternative manufactured by another company";[48] a 1994 study of 56 company-sponsored trials of non-steroidal anti-inflammatory drugs [NSAIDS] found that not one of them presented results unfavorable to the sponsoring company;[49] and a study published in 2004 reported that authors with financial ties to drug companies were between ten and twenty times less likely to report negative findings than authors without such ties.[50]

There is also disturbing evidence of pharmaceutical companies' recruiting academic scientists, in return for listing as senior author, to "edit" reports actually produced in-house but submitted to peer-reviewed journals under the supposed senior author's name. Adriane Fugh-Berman describes how it works: on August 24th, 2004 she received, from a "medical education company" sponsored by a drug manufacturer, a draft article on warfarin-herb interactions, complete with her name as author and her institutional affiliation; and was asked to review this and suggest any "amends" [*sic*] needed before it was submitted to a peer-reviewed journal — preferably by September 1st. (She didn't "make amends," but declined the offer.) As Fugh-Berman observes, this practice is especially hard for readers to detect

44. "Periscope," *Newsweek*, August 7, 2006: 8.

45. Lindsay Tanner, "JAMA says docs misled over industry ties," July 18, 2006, available at http://www.chron.com/disp/story.mpl/ap/health/4055561.html.

46. Thomas M. Burton, "Lipitor Shows Limited Benefit for Stroke," *The Wall Street journal*, August 10, 2006, D1, D4.

47. David Armstrong, "Medical Journal Editor Nemeroff Steps Down Over Undisclosed Ties," *The Wall Street Journal*, August 28th, 2006, B7.

48. Richard A. Davidson, "Source of Funding and Outcome of Clinical Trials," *Journal of General Internal Medicine*, 1.1 (January/February 1986): 155-8, p.155.

49. Paula Rochon *et al.*, "A study of manufacturer-supported trials of nonsteroidal anti-inflammatory drugs in the treatment of arthritis," *Archives of Internal Medicine*, 154 (1994): 157-63.

50. Lee S. Friedman and Elihu D. Richter, "Relationship Between Conflict of Interest and Research Results," *Journal of General Internal Medicine*, 19 (January 2004): 51-6, p.54.

when, as in this case, the article doesn't specifically mention the company's product, but is designed to increase the perceived need for some drug of theirs.[51]

Moreover, we know that drug companies sometimes put pressure on scientists to withhold findings unfavorable to their products. In 2006, for example, Bausch and Lomb recalled its contact-lens solution Renu with MoistureLoc after it was linked to a recent outbreak of fungal eye infections; shortly thereafter, we learned that the problem (which I was intrigued to see described as a threat to "the integrity of the cornea") had been known since 1999, and that the company had tried to get studies unfavorable to its product suppressed.[52]

It only makes matters worse, of course, that the process of cleaning up the literature after fraud has been discovered, or even after work has been retracted or a journal has published an "expression of concern," is slow and far from thorough. After admitting that they had fabricated data, Friedreich Herrmann and Marion Brach, both with the Max Delbrück Center for Molecular Medicine in Berlin, retracted 11 papers published between 1991 and 1999; but according to Ulf Rapp, who led an investigation of the case for the funding agency, the fabricated data actually appeared in 94 papers, 83 of which were *not* retracted.[53] And even retracted papers often continue to be cited over and over. A year after the Office of Research Integrity informed ten journals that they had published papers co-authored by Dr. Eric Poehlman based on fraudulent data, only 8 had been retracted; and even after *The Annals of Internal Medicine* had retracted one of these papers, other authors went on innocently referring to it.[54]

5. Trials and Tribulations: Troubling Tales of Vioxx and Celebrex

In *Defending Science*, discussing the tensions between the epistemological values of science and the commercial values of pharmaceutical companies that sponsor scientific work, I mentioned in passing the efforts of the Immune Response Corporation to suppress publication of the unfavorable results of a large clinical trial conducted by a medical scientist at the University of California, San Francisco, and of Merck and Pfizer to suppress evidence that the blockbuster drugs Vioxx and Celebrex might cause heart-related problems.[55] I have explored the Remune story in detail elsewhere;[56] here, I want to look more closely at the story of Vioxx and Celebrex, and especially at the role of the journals where this research was published — for this is a story that illustrates just about all the problems that flow from

51. Adriane Fugh-Berman, "The Corporate Coauthor," *Journal of General Internal Medicine*, 20.6 (June 2006): 546-8.

52. Sylvia Pagan Westphal, "Bausch and Lomb Solution Recall Exposes Risks for Eye Infection," *The Wall Street Journal*, July 26, 2006, A1, A12.

53. Laura Bonito, "The Aftermath of Scientific Fraud," *Cell*, 124 (March 10, 2006): 873-5.

54. Harold C. Sox and Drummond Rennie, "Research Misconduct, Retraction, and Cleansing the Medical Literature,: Lessons from the Poehlman Case," *Annals of Internal Medicine*, 144 (March 6, 2006): 609-613; Jennifer Couzin and Katherine Unger, "Cleaning Up the Paper Trail," *Science*, 38 (April 7, 2006): 38-43.

55. Haack, *Defending Science* (n.3), p.320.

56. Haack, "On Scientific Secrecy and 'Spin': The Sad, Sleazy Saga of the Trials of Remune," *Law and Contemporary Problems*, 69 (2006): 47-67.

the relation of the medical journals to the pharmaceutical industry: studies designed to produce the desired results, published in prestigious journals whose reviewers didn't notice flaws in their design; large revenues for the sale of offprints of such articles; misleading attribution of drug-company papers to academic supposed lead authors; company efforts to suppress criticism or prevent publication of unfavorable evidence.

For more than forty years, conventional NSAIDs were used for the control of chronic pain; but these drugs carry increased risk of bleeding ulcers in susceptible patients. So it seemed a big advance when new NSAIDs were developed to inhibit the Cox-2 enzyme, which causes inflammation, without affecting the Cox-1 enzyme, which protects against the adverse gastro-intestinal effects. These included Vioxx [rofecoxib] and Celebrex [celecoxib], approved for sale by the U.S. Food and Drug Administration [FDA] in 1999.[57]

While Vioxx was on the U.S. market, Merck spent more than $100 million a year on direct-to-consumer advertising; more than 80 million people took the drug; and annual sales exceeded $2.5 billion.[58] But in September 2004 Merck withdrew Vioxx because of concerns over cardiovascular risks; and by late October 2006 there were around 24,000 Vioxx lawsuits pending against the company. When Merck withdrew Vioxx, Pfizer suspended its huge advertising campaign, but continued to maintain that no studies showed that Celebrex carried cardiovascular risks. Now, however, advertisements for Celebrex warn in bold letters that the drug "may increase the chance of a heart attack or stroke that can cause death." The first Celebrex suit against Pfizer, postponed from its originally scheduled date of June 2006, is still pending.[59]

Merck's first large clinical trial, the VIGOR study, showed that Vioxx carried a lower risk of adverse gastro-intestinal effects than the rival drug naproxen (Aleve); as did the company's subsequent, smaller ADVANTAGE study. The FDA approved Vioxx in less than a year, before the VIGOR trial was completed; after FDA approval a report of the VIGOR study was submitted to the NEJM, where it appeared in November 2000.[60] This study indicated the gastro-intestinal benefits; but it also suggested a significantly higher rate of myocardial infarction, among patients given one or the other drug for more than 18 months, in those taking Vioxx than in those tak-

57. "Cox-2 Nonsteroidal Anti-inflammatory Medication," <www.clevelandclinic.org.org/arthritis/treat/facts/cox2/htm>, visited March 3, 2006; "Vioxx, Celebrex: Concerns over popular arthritis drugs," <www.cbc.ca/printablestory.jsp>, visited March 3, 2006. According to a market research report dated April 2004, "Commercial Services Portugal foresees" that the ten drugs "with the highest market potential will be… 3. Vioxx… 6.Celebrex." <http://strategis.ic.gc.ca/epic/internet/inimr-ri.nsf/ed/gr111846 3e.html>. Though this prediction was still unchanged on the website on 8.1.06, I understand that Vioxx was withdrawn from the market in Portugal, as it was in the U.S., in September 2004.

58. David J. Graham et al., "Risk of acute myocardial infarction and sudden cardiac death in patients treated with cyclo-oxygenase 2 selective and non-selective non-steroidal anti-inflammatory drugs: nested case-control study," *The Lancet*, 365 (February 5, 2005): 475-81, 480.

59. Heather Won Tesoriero, "First Celebrex Trial Date is Set," *Wall Street Journal*, February 28, 2006, D4. "Celebrex Trial is Delayed," *Los Angeles Times*, June 6, 2006, Part C, p.3.

60. Claire Bombadier *et al.*, "Comparison of Upper Gastrointestinal Toxicity of Rofecoxib and Naproxen in Patients With Rheumatoid Arthritis," *The New England Journal of Medicine*, 343.21 (November 23, 2000): 1520-28.

ing naproxen.[61] Merck attributed this to a cardio-protective effect of naproxen;[62] but by early 2001 an FDA review concluded that "it is mandatory to conduct a trial specifically assessing the cardiovascular risk of [Cox-2 inhibitors]."[63] No such trial was conducted; but in 2002 Merck was required to add a warning label to the package insert. And in 2004 the drug was taken off the market after Merck's third major clinical trial, the APPROVe study — designed to show that Vioxx lowered the risk of colon polyps — was halted by the data monitoring safety board when it emerged that patients given 25 mg. of Vioxx for more than 18 months had a fourfold greater incidence of serious thromboembolic events.[64]

In April 2005 the *New York Times* reported that the published account of the ADVANTAGE trial had omitted three cardiac deaths among the patients given Vioxx. The purported lead author explained that Merck scientists had designed, paid for, and run the study, and written the report; his role was only to give editorial help after the paper was written, and he hadn't known about the additional deaths.[65] In December of that year the NEJM published an "Expression of Concern" about "inaccuracies and deletions" in the report of the VIGOR trial: three heart attacks among patients taking Vioxx had been omitted. These adverse events had been included in the data on the FDA website since February 2001; and two of the three authors had known of them well in advance of the publication of the paper. Their inclusion raised the rate of heart attacks among those taking Vioxx from 0.4% to 0.5% (compared with 0.1% among those taking naproxen); and contradicted the claim in the paper that only those already at risk showed an increase in heart attacks with Vioxx. On behalf of the NEJM Dr. Drazen explained to reporters that the study had been "misleading," designed to be more sensitive to gastrointestinal benefits than to cardiovascular risks by continuing to track gastrointestinal effects after it stopped tracking cardiovascular events.

But there is more to the story. We now know that in June 2001 the editors of the NEJM had received a letter from pharmacist Jennifer Hrachovec asking that the article be corrected in light of the information on the FDA website, but had declined to publish it on the grounds that "the journal can't be in the business of policing every bit of data we put out." (The same year Merck officials had pressured a leading cardiologist, Dr. Eric Topol, not to publish an article critical of Merck's claim that the reason for the disparity in the rate of heart attacks wasn't that Vioxx in-

61. Some critics suspected that the trial showed no adverse cardiovascular effects in patients taking Vioxx for less than 18 months because it had too little statistical power to detect such effects. Graham et al. (n.58), p.479. A Canadian study published in 2006 indicated an increased risk of heart attack within 6-13 days after Vioxx therapy began. Linda E. Levesque, James M. Brophy, and Bin Zhang, "Time variations in the risk of myocardial infarction among elderly users of COX-2 inhibitors," published electronically at <www.cmaj.ca>, May 2, 2006 (an abridged version is published in *Canadian Medical Association Journal*, 174.11 (May 23, 2006).)

62. Susan Okie, "Raising the Safety Bar — The FDA's Coxib Meeting," *New England Journal of Medicine*, 352.13 (March 31, 2005): 1283-5, p.1284.

63. Eric Topol, "Failing the Public Health — Rofecoxib, Merck, and the FDA," *New England Journal of Medicine*, 351.17 (October 21, 2004): 1707-9, p.1707.

64. "COX-2 selective inhibitors — important lessons learned," *The Lancet*, 365 (February 5, 2005): 449-51, p.449.

65. Alex Berenson, "Evidence in Vioxx Suit Shows Intervention by Merck Officials," *New York Times*, April 24, 2005, section 1.

creased the risk, but that naproxen lowered it.)[66] What changed the minds of the editors of the NEJM and prompted them to post that "expression of concern" — four and a half years after they were made aware of the problem — was an urgent e-mail from public-relations specialist Edward Cafasso that testimony to be presented the next day in a Vioxx case in which executive editor Dr. Gregory Curfman had been deposed made it essential to post something right away, to "drive the media away from the NEJM and toward the authors, Merck, and plaintiff attorneys." We also now know that the NEJM — which listed $88 million in total publishing revenue for the year ending May 31st, 2005 — had sold 929,000 offprints of the article, most of them to Merck, for revenue estimated to be between $679,000 and $836,000.[67]

As if this weren't bad enough, in July 2006 the journal posted a correction to the report it had earlier published of the APPROVe study: key results claimed in the article had not in fact been arrived at by the statistical method the authors said they used; and, had they used it, the results would have undermined the claim in the article that cardiovascular risks increased only after 18 months.[68]

What about Celebrex? The CLASS study, completed and published in the JAMA in 2000,[69] indicated that Celebrex carried a significantly lower risk of adverse gastrointestinal effects than conventional NSAIDs. Subsequently, however, letters to the journal (including one from Dr. Hrachovec) pointed out that the article reported only data from the first 6 months of the 12-month trial, while the more complete information available on the FDA website revealed that "[f]or upper GI safety, and also global safety, there does not appear to be any meaningful advantage for Celebrex"; and that patients with pre-existing cardiovascular disease had been excluded from the study.[70] In December 2004, a study published on-line suggested that Celebrex offered some protection against non-fatal myocardial infarction; the same month, however, the National Cancer Institute halted both the Adenoma Protection with Celebrex (APC) trial, and a second trial, the PreSAP study, because of a 2.5-fold increased risk of acute MI and stroke in patients given 400 mg. of Celebrex a day, and a 3.4-fold increase in patients given 800 mg..[71] This led to the warning added to the package insert and advertisements for Celebrex.

Then, a twist in the tale: analysis of the results of the two halted studies, reported at the annual meeting of the American Association for Cancer Research in April

66. Anne Belli and Bill Hensel, Jr., "Doctor: Merck tried to influence article: Company urged him not to publish warnings against Vioxx use," *Houston Chronicle*, December 4, 2005, section B.

67. David Armstrong, "How the New England Journal Missed Warning Signs on Vioxx: Medical Weekly Waited Years to Report Flaws in Article that Praised Pain Drug," *The Wall Street Journal*, May 15, 2006, A1, A10.

68. Heather Won Tesoriero, "Vioxx Correction May Add Pressure to Merck's Defense," *The Wall Street Journal*, June 27, 2006, A2.

69. Fred E. Silverstein *et al*., "Gastrointestinal Toxicity With Celecoxib vs Nonsteroidal Anti-Inflammatory Drugs for Osteoarthritis and Rheumatoid Arthritis: The CLASS Study," *Journal of the American Medical Association*, 284.10 (September 13, 2000): 1247-55.

70. Letters, *Journal of the American Medical Association*, 286.19 (November 21, 2001): 2398-400. The quotation from the FDA website appears on p.2398.

71. David J. Graham *et al*. (note 57 above), p.480, citing M. Kaufman, "Celebrex trial halted after finding of heart risk: FDA chief urges patients to ask about alternatives," *Washington Post*, December 18, 2004, A1.

2006, showed a dramatic reduction in risk of colon cancer in patients given Celebrex.[72]

Even after the withdrawal of Vioxx, Merck remains a player in the Cox-2 inhibitor market. In October 2004, after reviewing Merck's application for approval of a new Cox-2 inhibitor, Arcoxia [etoricoxib], the FDA had asked for further data; in August 2006 Merck released preliminary results of the first large-scale trial, the MEDAL study, concluding that Arcoxia has gastrointestinal advantages over the older, widely prescribed NSAID diclofenac [Voltaren, Cataflam], while its heart risks are comparable. But critics noted that the data Merck supplied was very limited; and expressed disappointment at the choice of diclofenac as a comparison treatment, pointing out that this drug "works in the body more like Cox-2 inhibitors than painkillers like naproxen." Only a few weeks later, two analyses of previous clinical trials found that even short-term Vioxx use increased cardiovascular risk — and that the cardiovascular risks of diclofenac (marketed by Novartis) are such as to merit the regulatory status of the drug.[73] Arcoxia was already on sale in Europe and Latin America.[74]

6. And Why The Erosion of Integrity Matters

In the words of H. L. Mencken, "there is always a well-known solution to every human problem — neat, plausible, and wrong."[75] Even if I had one, a neat, plausible solution to the thicket of problems explored here surely would be wrong. But anyway, having no such solution to offer, I will end instead by trying to articulate briefly why, as my subtitle says, the integrity of science matters, why the creeping corruption I have described should concern us.

For some people, the commitment to finding out — the "scientific attitude," as C. S. Peirce called it, "the Will to Learn"[76] — is both firm and deep; as Percy Bridgman puts it, some feel the emotional pull of the ideal of intellectual honesty almost as the religious man feels the call to serve Something much more significant than himself.[77] But for many people intellectual honesty flourishes only with the right

72. Press Release, American Association for Cancer Research, "Studies Confirm Celecoxib May Help Prevent Colorectal Cancer in High Risk Patients" (April 3, 2006), available at <www.aacr.org?Default.aspx?p=1066&d=608>. Scott Hensley, "Drug Cuts Risks of Colon Cancer in Two Studies," *Wall Street Journal*, April 14, 2006, D6.

73. Peter Loftus, "Merck's Vioxx Tied to New Threat: Heart Risks Early in Study," *Wall Street Journal*, September 13, 2006, A12.

74. Heather Won Tesoriero, "Merck's Possible Vioxx Successor Draws Mixed Results in Study," *The Wall Street journal*, August 14th, 2006, D6. See also press release, <http://www.merck.com/newsroom/press_releases/research_and_development/2006_0823.h…> (visited 8.24.2006). Note added in June 2007: the FDA has recently denied approval to market Arcoxia in the U.S.

75. H. L. Mencken, "The Divine Afflatus," in *Prejudices: Second Series* (New York: Alfred Knopf, Borzoi Books, 1926), 155-71, p.158.

76. Charles Sanders Peirce, *Collected Papers*, eds. Charles Hartshorne, Paul Weiss and (vols. 7 and 8), Arthur Burks (Cambridge: Harvard University Press, 1931-58); references are by volume and paragraph number. Peirce describes the "scientific attitude" as "a craving to know how things really are" (1.34), "an intense desire to find things out" (1.14), and the "Will to Learn" (5.583). See also Haack, "As for that phrase 'studying in a literary spirit'… " (1996), in Haack, *Manifesto of a Passionate Moderate* (n.15), 48-68.

77. Percy Bridgman, "Science, Materialism, and the Human Spirit" (1949), in Bridgman, *Reflections of a Physicist* (New York: Philosophical Library, 1955), 452-72, pp.456-7.

kind of encouragement and incentives, and with good example; in an inhospitable environment it wilts and withers. So the erosion of integrity feeds on itself: senior scientists whose commitment to the norms of science is weak or ambivalent won't transmit those norms to young colleagues or to students; and the more commitment to those norms becomes professionally disadvantageous, the more ambivalent and the shakier the more scientists' commitment to them will become.[78]

The erosion of commitment to these norms matters, first, because it is apt to impede the progress of science; as a result of which we don't know things we could have known by now, and we lose out on the benefits that knowledge would have provided had we had it. Once again, the saga of Vioxx and Celebrex makes the point vivid. Between 1999 (when Vioxx was approved by the FDA) and 2004 (when it was taken off the market) it is estimated that there were between 88,000 and 140,000 excess cases of serious coronary heart disease in the U.S..[79] In late 2004 we learned that Celebrex may protect against colon cancer; and in late 2005 the Cleveland Clinic announced that it will direct a world-wide clinical trial of around 20,000 patients to assess the relative safety of ibuprofen, naproxen, and celecoxib.[80] Think about it: if sponsors' interests hadn't got in the way, mightn't we have known much more, years ago, about which patients which NSAIDs could most benefit, and which patients which NSAIDs were likely to do more harm than good?

Second, and almost as obviously, the erosion of the integrity of science matters because when the public reads, day after day, week after week, one story after another of scientific dishonesty and corruption — Dr. Hwang Woo Suk's fraudulent work on stem-cell cloning; that laughable Columbia "Prayer Study"; the amateurishly fabricated data in Jon Sudbø's oral-cancer study[81] — its confidence in the sciences will inevitably be damaged. Indeed, public trust in science may well be damaged more than the erosion of integrity, thus far, really warrants; especially when, as now, the press takes a particularly keen interest in stories of scientific fraud and misconduct. As a result, the public is likely to become more reluctant to support government funding of an institution they come to perceive as corrupt and untrustworthy; and again we lose out on knowledge we might otherwise have had, and on the benefits such knowledge might have brought.

And third, less obviously but perhaps most consequentially, the erosion of the integrity of science matters because it feeds the anti-intellectualism, the cynicism

78. The week I wrote this paragraph, a press report on plagiarism problems in the department of mechanical engineering at Ohio University illustrated it: graduate students had copied chunks from earlier dissertations, and faculty, some of whom had supervised more than a hundred theses, hadn't read carefully enough to notice. The report quotes Michael Kalichman, Director of Research Ethics at the University of California, San Diego: "What is going to happen as these [students] become the next generation of faculty members?" Robert Tomsho, "Student Plagiarism Stirs Controversy at Ohio University," *The Wall Street Journal*, August 18 2006, A1, A10.

79. Graham *et al*., "Risk of acute myocardial infarction and sudden cardiac death in patients treated with cyclo-oxygenase 2 selective and non-selective non-steroidal anti-inflammatory drugs" (n.57), p.480.

80. Sarah Treffinger, "Cardiologist at Clinic to lead study of painkillers," *Plain Dealer* (Cleveland), December 14, 2005, A1.

81. Nicholas Wade and Choe Sang-Hun, "Human Cloning Was All Faked, Koreans Report," *The New York Times*, January 10th, 2006, Section A. Bruce Flamm, "The Columbia University 'Miracle' Study," 28.5 *Skeptical Inquirer* (September/October 2004), 25-31. Richard Horton, "Retraction: Non-Steroidal Drugs and the Risk of Oral Cancer: a nested case-control study", *The Lancet*, 367 (February 4-10, 2006): 382.

about the very possibility of discovering how things are, even about the very idea of truth, that lies not far beneath the surface even of supposedly "civilized" societies. Our capacity to figure things out is one of the best talents human beings have: we aren't especially fast; we aren't especially strong; but if we really want to, if we are willing to work and think hard, if we have enough patience, enough persistence, if we are ready to fail and try again, perhaps over and over, we can find out something of how the world is. But this is hard work, often painful and frustrating; and there is another, less admirable, side of human nature, a side that really doesn't want to go to all the trouble of finding out, that prefers to believe things are as we would like them to be, and that loves the mysterious and the impressively incomprehensible.

Almost four centuries ago, Francis Bacon wrote that "the inquiry of truth, which is the love-making or wooing of it, the knowledge of truth, which is the presence of it, and the belief of truth, which is the enjoying of it, is the sovereign good of human nature."[82] Splendid as this is, perhaps a more muted statement would be in order. Scientific inquiry is not the only kind of inquiry, but it has undeniably been an extraordinarily successful human enterprise. And so the erosion of evidence-sharing and respect for evidence matters, also, because allowing the integrity of science to languish — like human beings' allowing their talent for music, for dancing, or for story-telling to languish — would be a real tragedy for the human race. •

82. Francis Bacon, "Of Truth" (1625) in *Francis Bacon's Essays*, ed. Oliphant Smeaton (London: Dent, and New York: Dutton, Everyman's Library, 1906), 1-3, p.2.