

15 May 2006

Dr. Nancy Beck
Office of Information and Regulatory Affairs
Office of Management and Budget
725 17th Street, NW
New Executive Office Building, Room 10201
Washington, DC 20503

Re: Proposed Risk Assessment Bulletin

Dear Dr. Beck,

I write in response to the Office of Management and Budget (OMB) 17 Jan 2006 Federal Register notice requesting comments on a Proposed Risk Assessment Bulletin (http://www.whitehouse.gov/omb/infoereg/proposed_risk_assessment_bulletin_010906.pdf). This comment is my own professional opinion based on years of pertinent education and experience, including five years as a mathematical statistician in the Division of Hazard Analysis at the U.S. Consumer Product Safety Commission. I left the CPSC over four years ago to work as a mathematical statistician in another federal agency that shall remain unnamed. The following comment is solely my own opinion and does not necessarily reflect the official position of any agency or staff. My comment consists of a brief overview, six specific comments, a conclusion, and references.

Overview

Though intended to reduce the risk of poor federal risk assessments, OMB's proposed bulletin neglects scientific bias due to financial conflict of interest and would increase the risk of obstruction, delay, and suppression of federal risk analysis by special interests – a foreseeable and unacceptable risk tradeoff. As Graham and Wiener (1995) emphasized in *Confronting Risk Tradeoffs*:

Paradoxically, some of the most well-intentioned efforts to reduce identified risks can turn out to increase other risks. Though the term “risk tradeoff” may not be familiar to many people, the phenomenon is commonplace in human decision making, reflected in such familiar adages as “out of the frying pan and into the fire” and “the cure is worse than the disease.” ... Unless decision makers consider the full set of outcomes associated with each effort to reduce risk, they will systematically invite such risk tradeoffs. (pp. 2-3)

Specific Comments on OMB's Proposed Risk Assessment Bulletin

1. Unfortunately, OMB's proposed risk assessment bulletin neglects the serious concern in scientific communities about scientific bias due to financial conflict of interest and even waives the proposed bulletin's requirements for the kind of industry-sponsored research most likely to involve such bias:

This Bulletin does not apply to risk assessments that arise in the course of individual agency adjudications or permit proceedings, unless the agency determines that: (1) compliance with the Bulletin is practical and appropriate and (2) the risk assessment is scientifically or technically novel or likely to have precedent-setting influence on future adjudications and/or permit proceedings. This exclusion is meant to cover, among other things, licensing, approval and registration processes for specific product development activities...

This Bulletin also does not apply to any risk assessment performed with respect to an individual product label, or any risk characterization appearing on any such label, if the individual product label is required by law to be approved by a Federal agency prior to use. An example of this type of risk assessment includes risk assessments performed for labeling of individual pharmaceutical products. This Bulletin does not apply to risk assessments performed with respect to classes of products. An example of this type of risk assessment is the risk assessment performed by FDA in their evaluation of the labeling for products containing trans-fatty acids. (p. 10)

Scientific bias due to financial conflict of interest is widely acknowledged in scientific communities (cf., American Association of Universities Task Force on Research Accountability, 2001; Department of Health and Human Services, 1995; National Science Foundation, 1995). According to the American Association of Universities Task Force on Research Accountability (2001):

Research universities are concerned about financial conflict of interest because it strikes to the heart of the integrity of the institution and the public's confidence in that integrity. (p. i)

The term individual financial conflict of interest in science refers to situations in which financial considerations may compromise, or have the appearance of compromising, an investigator's professional judgment in conducting or reporting research. The bias such conflicts may conceivably impart not only affects collection, analysis, and interpretation of data, but also the hiring of staff, procurement of materials, sharing of results, choice of protocol, involvement of human participants, and the use of statistical methods. (p. 2)

Risk assessment often has financial ramifications for special interests, potentially affecting product sales, manufacturing costs, regulatory compliance costs, lawsuits, etc. And financial ramifications create bias that can influence scientific research. For example, an experimenter's expectations and desires can influence subjects and how the experimenter records, analyzes, and interprets data. And subjects who believe they have received an effective treatment, but have not,

often improve (Kirk, 1995, pp 20-21). The double-blind control method strives to mitigate such biases by preventing experimenters and subjects from knowing which treatment or placebo condition each subject is in. But researcher bias can also act in other ways: designing biased experiments or sampling plans that favor a desired outcome; ignoring literature inconsistent with desired conclusions; minimizing, explaining away, or withholding negative findings; exaggerating positive findings; ignoring or downplaying side effects; setting post hoc follow-up-period cutoffs that exclude negative results and favor desired conclusions; faking data; etc. Evidence of scientific bias due to financial conflict of interest appears regularly in the U.S. media and is taken seriously in scientific communities (cf., Angell, 2004; Avorn, 2004; Carson, 1962; Colborn et al., 1997; Curfman et al., 2005, 2006; Fagin et al., 1999; Goozer, 2004; Goozer & DelViscio, 2004; Kassirer, 2005; McDaniel et al., 2005; Michaels & Wagner, 2003; Smith, 2003; Washington Post, 2005; 2006). Much evidence reveals that scientific bias due to financial conflict of interest often involves U.S. regulatory agencies. **Appendix A** presents some of this evidence in detail to better define the term “scientific bias due to financial conflict” in a regulatory context.

The proposed bulletin’s neglect of scientific bias due to financial conflict of interest is inconsistent with recommendations of the Carnegie Commission on Science, Technology, and Government (1993), which stated in their report on innovation in regulatory decision making:

We believe that the regulatory system must be strongly inclined toward expanding the data base on risk: more information is better than less, as long as a framework for organizing it exists. ... We also call for a reevaluation of the confidential business information statutes that too often keep important health and safety information from the eyes of the regulators and the public. (p. 118)

2. OMB’s proposed guidelines for federal risk assessments would provide a legal instrument for special interests to petition agencies, regardless of merit, for administrative and judicial reviews challenging compliance with various parts of the guidelines in order to obstruct, delay, and suppress federal risk assessments whose conclusions, no matter how rigorous and exigent, might adversely affect the special interests. Since enactment of what OMB terms the Information Quality Act (IQA) by appropriations rider, without discussion or debate, in 2001 (Noe et al., 2003), and its broad interpretation and expansion in successive OMB actions (OMB, 2001; 2002; 2004; 2005), powerful industry representatives have filed petitions, appeals of denied petitions, and court challenges under the IQA seeking to suppress adverse information in federal risk analyses, and in some cases, the full reports (McGarity et al., 2005; Shapiro, 2005; Shapiro et al., 2006).

McGarity et al. (2005) document many cases of special interests using the IQA to file an agency petition that was denied, then an agency appeal that was denied, then a petition to the court that was denied, then a pending petition for appellate review of the lower court’s decision, in well-funded efforts to suppress federal risk analyses examining potentially adverse human health and/or environmental consequences of products sold or used industrially by the special interests. Many of the petitions and appeals, with agency responses, that McGarity et al. cite are publicly available on agency websites. For example, the Environmental Protection Agency (EPA) currently lists 35 requests for corrections or appeals under the IQA, with EPA responses, illustrating the complexity of the petitions and appeals, EPA’s review and decision making process, and the agency resources required to review and respond to each petition and appeal regardless of merit (EPA, 2006).

McGarity et al. (2005) document that petitioners citing the IQA have sought to obstruct or suppress federal studies of human health and environment involving: global climate change related to greenhouse gases associated with fossil fuels, warning automobile mechanics about the hazards of asbestos from worn brake linings, warning consumers about the link between salt and high blood pressure, useful information to prevent clothes dryer fires, warning that smokeless tobacco products are not safer than cigarettes, possible endocrine disruption effects of an herbicide containing atrazine, a notice announcing review of atrazine and 20 other substances for possible listing as a known or reasonably anticipated human carcinogen in the Annual Report on Carcinogens of the National Toxicology Program of the Department of Health and Human Services, and others.

If the challenges raised by special interests using the IQA as described above had merit, then the petitions and appeals would not have been rejected by agencies and courts after extensive review. But they were. This shows that the IQA is misused as a legal tool by special interests to obstruct, delay, and suppress federal risk analysis, thereby impeding the mission of federal agencies to protect human health and environment.

3. The unfunded resource demands of the proposed guidelines would reduce the quantity, scope, and timeliness of federal risk assessments. While the proposed risk assessment bulletin neglects the resource demands of the proposed guidelines, substantial demands are foreseeable, e.g., in calling for, reviewing and responding to public comments on draft risk assessment documents, and in reviewing and responding to the inevitable administrative and judicial challenges that the assessment is not compliant with the new OMB guidelines. Resources would be diverted from agency activities essential to the entire spectrum of human health and environment missions. It would take longer to publish final risk assessments, and the number and scope of risk assessments would shrink inversely with the increased resource demands. The quality of federal risk assessments cannot be improved by guidelines that reduce their quantity, scope, and timeliness. There already exists an appropriate opportunity for peer review and public comment, and detailed agency responses to such comments, in cases of proposed regulatory action.

4. The proposed guidelines requiring an executive summary with emphasis on uncertainties in the risk analysis, and comparison of the subject risk to supposedly more familiar risks, would introduce unnecessary complexity and controversy, e.g., about how and whether risks from different domains truly are either comparable or familiar (i.e., in an unbiased sense). Requiring an executive summary emphasizing uncertainties and comparisons to other risks dictates questionable content and style at the beginning of every federal risk assessment report, thereby inviting skepticism, controversy, and challenge before the report is even read – if it is read at all. This requirement would contradict recommendations in the literature on improving regulatory risk assessment. For example, the Committee on the Institutional Means for Assessment of Risks to Public Health of the National Research Council's Commission on Life Sciences (1983) recommended that:

Before an agency decides whether a substance should or should not be regulated as a health hazard, a detailed and comprehensive written risk assessment should be prepared and made publicly accessible. This written assessment should clearly distinguish between the scientific basis and the policy basis for the agency's conclusions. (p. 153, original underlined)

It is important, however, that the format and scope of written assessments not become an independent basis for legal attack. (p. 154)

5. The proposed guidelines requiring submission of “influential” risk assessment reports in draft form for public comment, and publication of the agency’s written responses to all “significant” or “scientific” comments in the final risk assessment reports, would increase the opportunity for special interests to obstruct, delay, and suppress federal risk analysis. The terms “influential,” “significant,” and “scientific” are open to such broad interpretation that they are meaningless. To avoid challenges that risk assessments deemed non-influential, or that comments deemed non-significant, actually were, agencies would have to regard all risk assessments as “influential” and all comments as “significant.” In addition, in combination with the requirement for an executive summary emphasizing controversial uncertainties and risk comparisons, this requirement would invite special interest challenges based on the controversial uncertainties and risk comparisons mandated in the required executive summary. Challenges, no matter how frivolous or unfounded, would manifest themselves in public comments requiring lengthy review and written response, then administrative challenges and appeals, then court challenges and appeals. There already exists a well-established and effective process by which agency proposals to establish or change federal regulations must be subjected to public comment and written response to those comments.

6. The analysts, statisticians, scientists, engineers, and other professionals engaged in federal risk assessments are well educated in diverse scientific fields, many with terminal degrees and/or extensive experience, and routinely meet the risk assessment standards identified in the proposed bulletin insofar as possible along with many venerable professional standards defined by the peer-reviewed literature and philosophical paradigms in their diverse and growing scientific fields. The proposed bulletin asserts a need for improved federal risk assessment, but provides no evidence of poor risk assessment by any federal government staff or contractors. But even if there were evidence of poor federal risk assessments, a scientifically defensible approach would be to qualify and/or improve those assessments and, if truly indicated, to improve the risk assessment processes of the responsible organizations. Given the record of federal agencies in conducting scientific risk assessments that have been repeatedly upheld upon administrative and judicial reviews allowed by the IQA, but at the cost of substantial delay and waste of taxpayer dollars, the proposed risk assessment bulletin would not improve federal risk assessment enough to justify the increased cost. Conversely, it would invite special interests to obstruct, delay, and suppress risk analysis in federal agencies whose primary mission is to protect human health and environment. Finally, the proposed OMB guidelines are inconsistent with recommendations of the Carnegie Commission on Science, Technology, and Government (1993), which stated in their report on innovation in regulatory decision making:

In developing environmental and risk-reduction policies, the Executive Office should rely, whenever possible, on the analytical capabilities of departments and agencies. It should help the President to define the broad contours of the Administration’s environmental and risk-related policy, but must take care to leave implementation details and day-to-day regulatory decisions to the regulatory agencies. (p. 43)

Conclusion

If OMB does publish a risk assessment bulletin, then I respectfully recommend: (1) guidelines that suggest, but explicitly do not mandate, particular ways that risk analysts may be able to improve their work; (2) omission of the requirements for solicitation, analysis, and review of public comments; (3) omission of the requirements for an executive summary and its controversial contents; (4) omission of the exclusions for the kind of risk assessment research discussed in comment 1 above; and (5) guidelines promoting scientific integrity and objectivity, e.g., discouraging staff and advisors with strong financial or other commitments to an industry or concern from participating in federal risk assessment research involving that industry or concern.

Sincerely,

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Appendix A

Describing a “classic” example of egregious scientific bias in their book, *Toxic Deception: How the Chemical Industry Manipulates Science, Bends the Law, and Endangers Your Health*, Fagin et al. (1999) observed that:

The U.S. regulatory system for chemical products is tailor-made for fraud. The subjects are arcane, the results subjective, the regulators overmatched, and the real work conducted by – or for – the manufacturers themselves.

Those elements all came together in the scandal surrounding what was in the mid-1970s the nation’s largest toxicology laboratory. Industrial Bio-Test Laboratories conducted 35 to 40 percent of all toxicology testing in the United States at the time, including the industry-financed tests that manufacturers submitted to the EPA and the FDA as evidence of the safety of thousands of consumer products, pesticides, and drugs.

The lab was exposed as a fraud in April 1976 when Adrian Gross, an alert FDA pathologist, started asking questions after he saw a rat study of the arthritis drug Naprosyn that looked too good to be true. In the ensuing months, federal regulators found evidence that dozens of its studies had been faked. Among other transgressions, sick animals were listed as healthy or were not included in order to achieve favorable test results. Some reports were total fabrications based on no study at all. Ultimately, hundreds of studies were declared invalid.

But until a team of federal investigators arrived at IBT’s satellite lab in Decatur, Illinois, in January 1978 for a top-to-bottom inspection there was no evidence that the fraud extended beyond the walls of IBT. Its employees may have thought they were doing what their clients wanted by faking results, but there was no evidence that the chemical companies actually knew what was going on.

That changed when the six-man team began interviewing employees and combing through whatever records had not already been shredded at IBT. In the report they wrote about the inspection, members of the team said they uncovered evidence that Monsanto, the manufacturer of alachlor and many other toxic chemicals, may have known about the fakery. (Original footnote citing source memorandum omitted)

“IBT is the worst anyone’s ever seen,” says Dowell Davis, an FDA pharmacologist who was part of the investigative team. “They were hell-bent on providing their clients with favorable reports. They did not care about good science. It was about money. They really had what was almost an assembly line for acceptable studies.”

Paul Wright had been a research chemist at Monsanto before he went to work for IBT in 1971 as its chief rat toxicologist. Wright stayed at the lab for only 18 months before he returned to Monsanto with a new title: manager of toxicology in the company’s department of medicine and environmental health. But that was long enough, the government investigators concluded, for him to be in the middle of a series of apparently fraudulent studies that benefited Monsanto products.

The investigators said that in one of the studies – for Machete, a rice and sugarcane herbicide – extra lab mice were added to skew the sample, a bit of trickery that was left out of the final report to the EPA. Even more serious accusations involved two rodent studies of monosodium cyanurate, an ingredient in a swimming-pool chlorinator, in which inspectors found evidence that missing raw data had been replaced by after-the-fact invented records, that animal deaths had been deliberately concealed, and that the final reports included claims about procedures and observations that never happened.

In all three cases, the investigators wrote in an internal memo, there was evidence that Monsanto executives knew that the studies were faked but sent them to the FDA and the EPA anyway. Wright's protocols for the three studies were riddled with mistakes. He had signed off on the completed studies after he returned to Monsanto as a supervising toxicologist. ...

Wright was indicted, tried, and sentenced to six months in jail and two years' probation for his role in the IBT scandals, and he was fired by Monsanto on conviction. The three tests were not part of the indictments. Instead, Wright was tried for fraud in connection with another Monsanto product: TCC, an anti-bacterial agent used in deodorants. (pp. 33-35)

In their 2003 commentary *Disclosure in Regulatory Science* published in the prestigious journal *Science*, Michaels and Wagner noted growing professional concern about scientific bias due to financial conflict of interest:¹

The biomedical community's concern about potential conflicts of interest is addressed in the widespread (1, 2) policy of journals to require that authors of submitted articles disclose financial relationships so that editors and readers can judge whether conclusions might have been influenced by those financial ties. The editors of 13 leading biomedical journals have gone further and declared that they will no longer publish articles based on studies done under contracts in which the investigators did not have the unfettered right to publish the findings (1). (p. 2073)

Goozer (2004) showed that financial conflicts of interest are still not fully disclosed in scientific journal articles due to lax disclosure criteria or noncompliance with such criteria. But whether or not financial conflicts are disclosed, they may influence scientific objectivity. Furthermore, published results may be a misleading subset of all pertinent results known to researchers (cf., Curfman et al., 2005, 2006; Goozer & DelViscio, 2004). Goozer and DelViscio (2004) surveyed the published literature on use of serotonin reuptake inhibitors (SSRIs), a class of drugs used mainly to treat childhood depression but also a few other psychiatric disorders in over a million children each year. They found 61 published studies of clinical trials in children, of which almost 4 out of 5 (80%) reported a positive outcome. But, they reported, when Dr. Thomas Laughren, a Food and Drug Administration (FDA) reviewer, surveyed 15 placebo-controlled clinical trials evaluating SSRIs for treatment of childhood depression (submitted to the FDA to secure a patent extension for the drugs), many of which trials had not been published in academic journals, Dr. Laughren found

¹ Michaels and Wagner's (2003) references 1 and 2 were as follows: (1) *Uniform Requirements for Manuscripts Submitted to Biomedical Journals*, www.JCMJE.org (October 2001); (2) F. Davidoff et al., *JAMA* **286**, 1232 (2001).

that only 3 of the 15 trials (20%) yielded positive results, with the other 12 no better than placebo, leading him to conclude: “These are sobering findings and certainly raise a question about the benefits of these drugs in pediatric depression.” Such findings suggest that studies with null or negative findings are systematically withheld from publication, while studies with positive findings are not.

Furthermore, in his 2005 book, *On the Take: How Medicine’s Complicity with Big Business Can Endanger Your Health*, Jerome Kassierer, past Editor-in-Chief of the prestigious *New England Journal of Medicine* for more than eight years, observed that:

Some investigators for industry intentionally compare their new drugs to placebo controls when the appropriate control is the best available treatment. Comparisons can also be staged between the new drug and a drug that is not a perfect fit with the symptoms in question. Doses of comparison drugs can be rigged to favor a new drug, and duration of treatment can be carefully selected to favor a new drug. Some studies narrow the range of side effects. Often the principal investigator simply has little role in a study’s design, and just receives prepackaged instructions from the company. (p. 167)

And, in his 2004 book, *Powerful Medicines: The Benefits, Risks, and Costs of Prescription Drugs*, Jerry Avorn, professor of medicine at Harvard Medical School and chief of the Division of Pharmacoepidemiology and Pharmacoeconomics at Brigham and Womens’ Hospital in Boston, observed that:

Since 1990, more major drugs have been withdrawn for substantial unexpected safety problems than ever before in such rapid succession. Sometimes this has been the result of premarketing studies that were too small to detect important but rare side effects. Some of the problems may have stemmed from the FDA’s attempts to speed up its approval process. But as we saw with Pondimin and Redux, in some instances the disaster was brought on by willful underestimation of a drug’s known risks. This also seems to be what happened with Rezulin, the first in a new class of diabetes medications first marketed in March of 1997. ... Not astonishingly, the new drug lowered blood sugar more than placebo did. Its initial approval hinged on premarketing studies involving only about 2,500 patients. ... Based on this evidence, an FDA advisory committee met in December 1996 to decide whether the drug should be approved for sale. In summarizing the product’s safety profile at that meeting, a doctor representing the manufacturer, Parke-Davis, reported that its clinical trials showed that the drug’s risk of liver toxicity was “comparable to placebo.” The company also had collected additional safety data from other studies, but these were not presented at that meeting. Instead, the Parke-Davis physician said that the rate of liver damage in those other analyses was “very, very similar” to what was reported at the approval hearing, and that he would provide that data to the FDA later on. Based on the data presented that day, the advisory committee voted to allow the drug onto the market. ... The company did provide the FDA with the promised data from the additional trials a week after the approval. It revealed a rate of liver abnormalities that was not at all “very, very similar” in the patients who got the new drug; it was substantially greater. But the drug had already been approved and the new information didn’t receive widespread attention.

... The committee finally recommended in March 2000 that the drug be taken off the market. More than two years after the same decision was made in England, over \$2 billion in sales and ninety-four cases of acute liver failure (sixty-six of them fatal) after its introduction, Rezulin ended its blockbuster career in the United States. (pp. 85-94).

The courts are still considering how much of the Rezulin tragedy was produced by willful malfeasance versus what could be called passive-aggressive surveillance: foot-dragging in following up on signals of a potential hazard. As scores of cases approached trial, the manufacturer's zeal to protect its molecule instead of patients followed what could be called the FDA defense, a gambit seen in many drug product liability suits. In that strategy, a company maintains a bare-bones adverse-events reporting department, staffed on the front lines by people with little or no training in epidemiology or clinical matters. Once its drug is approved for marketing, the company doesn't proactively investigate how appropriately it is being used, or what side effects occur in patients who take it. When reports of those adverse events are nonetheless sent in spontaneously by doctors or patients, the company passes them along to the FDA as required by law, with minimal or no further scrutiny. It's widely known that the FDA division on the receiving end of these reports has traditionally been underpopulated and overworked, partly because of earlier industry opposition to allocating any of its user-fee funds to support those activities. Eventually, if an important side effect does surface, company officials can respond as many have in court, saying, in effect: "We didn't notice a worrisome pattern. We obeyed the regulations and sent FDA all the reports we received. They never made us do a study, or send out a warning, or take the drug off the market. So it's not our fault if anyone got hurt." (p. 94)

In her 2004 book, *The Truth About the Drug Companies: How They Deceive Us and What to Do About It*, Marcia Angell, another past Editor-in-Chief of the *New England Journal of Medicine*, observed that:

In 1992, [Congress] enacted the Prescription Drug User Fee Act, which authorized drug companies to pay user fees to the FDA. These were to be employed only to expedite approval of drugs. Fees...soon accounted for about half the budget of the agency's drug evaluation center. That makes the FDA dependent on an agency it regulates. (p. 208) ... If the FDA were to displease industry, the user fees might even be discontinued, and many agency employees would probably lose their jobs. (p. 210) ...

Furthermore, the FDA is subject to industry pressures through its eighteen standing advisory committees on drug approvals. These committees, which consist of outside experts in various specialties, are charged with reviewing new drug applications and making recommendations to the agency about approval. The FDA almost always takes their advice. Many members of these committees have financial connections to interested companies. Although there are conflict of interest rules that prohibit participation in such cases, the agency regularly waives them on the unlikely grounds that someone's advice is indispensable. *USA Today* examined FDA hearing records in 2000 and found that "at 92 percent of the

meetings at least one member had a financial conflict of interest,” and “at 55 percent of meetings, half or more of the FDA advisors had conflicts of interest.” (citation footnote in original omitted) (p. 210)

A 24 April 2006 *Washington Post* article reporting on a recently released federal study revealed several germane issues at the FDA:

The Food and Drug Administration is sometimes too slow in picking up safety problems once drugs are on the market and in responding to emerging danger signals, a federal study concluded in a report to be released today.

The review by the Government Accountability Office found that the FDA does not have clear policies for addressing drug safety issues and that it sometimes excludes its best safety experts from important meetings. ...

The GAO inquiry was requested by Congress in 2004 after the sudden withdrawal of the blockbuster painkiller Vioxx, which was found to increase the risk of heart attacks and strokes in long-term users. ...

The report found that the Office of Drug Safety, which monitors reports of emerging safety risks, at times made recommendations that were ignored by the larger and more influential Office of New Drugs. The GAO also criticized the way experts in the Office of Drug Safety were kept from speaking at important advisory committee meetings on drugs they were studying. The drug safety office has seen considerable turnover, with eight directors in the past 10 years. ...

Caroline Loew, senior vice president of the Pharmaceutical Research and Manufacturers of America, said the industry group “believes that the FDA takes the post-market surveillance of prescription drugs seriously and has taken additional steps over the past couple of years to help ensure that patient safety cannot be compromised.” She added that only 3 percent of all approved drugs were later withdrawn.

In the aftermath of the Vioxx withdrawal, the FDA created the Drug Safety Oversight Board, with expanded ability to act on emerging safety issues. The GAO report makes clear, however, that its reviewers consider FDA’s actions insufficient. The new board may help provide greater oversight of high-level safety decisions, the report said, but “it does not address the lack of systematic tracking of ongoing safety issues.” ...

Since the Vioxx controversy, the FDA has begun posting previously withheld preliminary information about possible drug safety problems and has been quicker to highlight potential risks. But the GAO said the information available to the FDA on potential problems is still limited.

Its system for collecting reports of “adverse events,” for instance, is a voluntary one that does not require doctors to report drug-related problems they encounter. Experts estimate that only about 10 percent are reported. (pp. 1-2)

Finally, a March 2005 *Washington Post* article revealed how a U.S. regulatory agency can ignore the latest science, and its own scientific staff, to produce an inflated “cost-benefit” regulatory analysis favoring a particular industry:

When the Environmental Protection Agency unveiled a rule last week to limit mercury emissions from U.S. power plants, officials emphasized that the controls could not be more aggressive because the cost to industry already far exceeded the public health payoff.

What they did not reveal is that a Harvard University study paid for by the EPA, co-authored by an EPA scientist and peer-reviewed by two other EPA scientists had reached the opposite conclusion.

That analysis estimated health benefits 100 times as great as the EPA did, but top agency officials ordered the finding stripped from public documents, said a staff member who helped develop the rule. ...

Asked about the Harvard analysis, Al McGartland, director of the EPA’s National Center for Environmental Economics, said it was submitted too late to be factored into the agency’s calculations. He added that crucial elements of the analysis were flawed.

Interviews and documents, however, show that the EPA received the study results by the Jan. 3 deadline, and that officials had been briefed about its methodology as early as last August. EPA officials referred to some aspects of the Harvard study in a briefing for *The Washington Post* on Feb. 2.

The Harvard study concluded that mercury controls similar to those the EPA proposed could save nearly \$5 billion a year through reduced neurological and cardiac harm. Last Tuesday, however, officials said the health benefits were worth no more than \$50 million a year while the cost to industry would be \$750 million a year.

“They are saying if they fail to regulate mercury from power plants at all, it really wouldn’t make a difference,” said John Walke, clean air director with the Natural Resources Defense Council, an environmental advocacy group. “To acknowledge the real benefits would be to raise the next question: Why didn’t you go further?”

James Hammitt, director of the Harvard Center for Risk Analysis and co-author of the study, agreed. “If you have a larger effect of the benefits, that would suggest more aggressive controls were justified.”

In most cases, mercury toxicity results from eating fish: Industrial emissions fall from the air into water and are taken up by fish. Because the metal does not break down, it moves steadily up the food chain to species that people consume. A major reason for the dramatic difference in the health benefit estimates was that the EPA looked only at the effects of reducing mercury levels in freshwater fish,

but most of the fish Americans eat comes from oceans. ...

Hammitt's analysis also factored in recent evidence that mercury causes heart attacks among adults. The EPA said other studies contradicted that finding and therefore it quantified only the impact of mercury's better-known neurological hazards. Spokeswoman Cynthia Bergman called Hammitt's cardiac analysis "flawed." ...

The Harvard study was commissioned through EPA grants to an independent nonprofit organization of northeastern-state governments that works on regional environmental issues. Praveen Amar, director of science and policy at the Northeast States for Coordinated Air Use Management, said the EPA provided about \$270,000 in funding for the project. Amar said that scientist Glen Rice, Hammitt's coauthor, is an EPA employee who had been given time to work on a doctoral thesis at the Harvard center.

"Are you saving the industry a billion dollars but taking away \$10 billion worth of benefits for the general public?" Amar asked.

(p. 1-3)

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