

# A Sarbanes-Oxley for Science

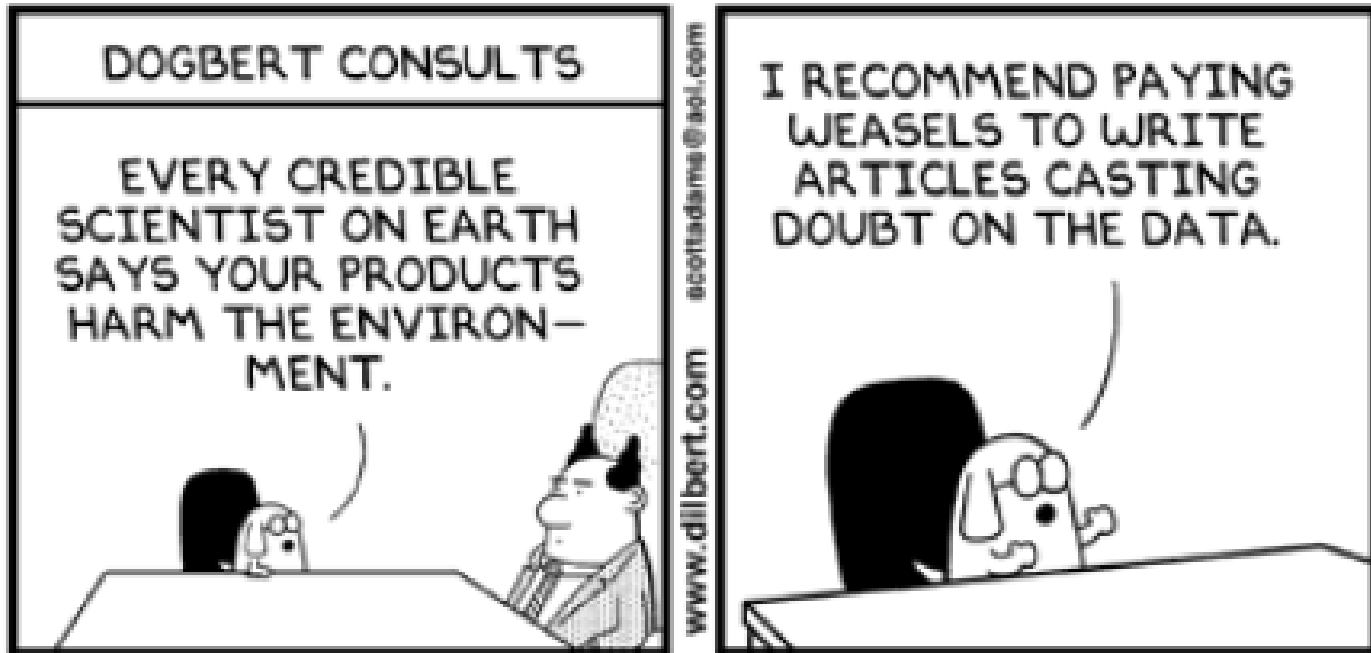
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# Why Sarbanes-Oxley?

- Enron
- WorldCom
- Tobacco Smoke
- Global Warming
  
- Vioxx?
- Bisphenol A?

# The Work of Mercenary Scientists Hurts the Credibility of All Scientists



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# How to Get the Best Science

Problems arise in:

- The production of scientific information
- The interpretation of scientific information

# Production Of Scientific Information

- Clarify and Strengthen Requirements to learn if products are hazardous
- Chemicals:
  - REACH vs. TSCA
- Drugs:
  - Clinical Trial Registry
  - Phase IV Clinical Trials

# Production of Scientific Information

- Full Disclosure of Information
  - Limit “Confidential Business Information” Claims
- Hold Real People Accountable

# The Funding Effect

- The close correlation between the results desired by a study's sponsors and the results reported

# The Funding Effect

- Secondhand Tobacco Smoke
- Drugs
- Industrial chemicals

## Commentary

# An Extensive New Literature Concerning Low-Dose Effects of Bisphenol A Shows the Need for a New Risk Assessment

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**Table 1.** Biased outcome due to source of funding in low-dose *in vivo* BPA research as of December 2004.

Source of funding	All studies		CD-SD rat studies		All studies except CD-SD rats	
	Harm	No harm	Harm	No harm	Harm	No harm
Government	94 (90.4)	10 (9.6)	0 (0%)	6 (100)	94 (96)	4 (4)
Chemical corporations	0 (0)	11 (100)	0 (0%)	3 (100)	0 (0)	8 (100)

Values shown are no. (%).

# BISPHENOL A BISPHENOL A BISPHENOL A BISPHENOL A

Volume 2 Number 1 April, 2000

A new journal of key scientific studies focused on the safety of bisphenol A, an important industrial intermediate used to manufacture polycarbonate plastics, epoxy coatings and other products.

The Bisphenol A Global Industry Group

# What Needs to be Done?

- Full Disclosure and Publication of Conflicts

Online access to disclosed information, rather than leaving it to editorial judgment

# What Else Needs to be Done?

- Scientist Control of Work Product
  - No publication of papers whose first author did not have the unfettered right to publish
- Level the Playing Field
  - Equal treatment of public and private science

**Is That Enough?**

# Medical Journals Are an Extension of the Marketing Arm of Pharmaceutical Companies

Richard Smith

**Competing Interests:** RS was an editor for the *BMJ* for 25 years. For the last 13 of those years, he was the editor and chief executive of the BMJ Publishing Group, responsible for the profits of not only the *BMJ* but of the whole group, which published some 25 other journals. He stepped down in July 2004. He is now a member of the board of the Public Library of Science, a position for which he is not paid.

**Citation:** Smith R (2005) Medical Journals Are an Extension of the Marketing Arm of Pharmaceutical Companies. *PLoS Med* 2(5): e138

## Why Do Pharmaceutical Companies Get the Results They Want?

Why are pharmaceutical companies getting the results they want? Why are the peer-review systems of journals not noticing what seem to be biased results? The systematic review of 2003 looked at the technical quality of the studies funded by the industry and found that it was as good—and often better—than that of studies funded by others [8]. This is not surprising as the companies have huge resources and are very familiar with conducting trials to the highest standards.

# Some Methods for Drug Companies Use to Get the Results they Want from Clinical Trials

- Conduct a trial of your drug against a treatment known to be inferior.
- Trial your drugs against too low a dose of a competitor drug.
- Conduct a trial of your drug against too high a dose of a competitor drug (making your drug seem less toxic).
- Conduct trials that are too small to show differences from competitor drugs.....

No matter how cynical you become,  
it's never enough to keep up.

- Lily Tomlin

# National Center for Drug (and Chemical) Testing

- Studies are paid for by manufacturer, but conducted by independent researchers
- Center selects researchers
- First proposed by Sen. Gaylord Nelson in 1971, then Sheldon Krimsky in 2003

# Product Defense Consultants

- Scientists hired to defend products in regulatory and legal arenas
- Their value is their ability to influence regulation and litigation, not to provide valid science
- Produce science of questionable value

# Marketing "Product Defense"

## **ASBESTOS, TOBACCO, PHARMACEUTICALS - WE'RE ALL NEXT!**

- ◆ Scare science
- ◆ The loss of presumptive innocence
- ◆ Where will the liability end?

**Presented by  
Mr. Joseph Huggard  
The Weinberg Group LLC  
18 June 2003**



## Case Studies

### SUPPORT TO DRUG MANUFACTURERS

The Food and Drug Administration proposed cancellation of a registered new drug. Cancellation requires an administrative hearing. THE WEINBERG GROUP was retained by two manufacturers of the drug under attack, to define strategy for the administrative hearing, identify the experts to be used in the continued support of the drug; assist in the preparation of the experts for written testimony, analysis of the testimony of experts for the Food and Drug Administration, and preparation for oral cross-examinations and preparation of the summary brief. This led to an extensive process with a written appeal from the first decision to the Commissioner and leading to 10 additional years of sales prior to the ultimate cancellation of the drug.

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# Can We Trust the Interpretation of Conflicted Scientists?



# Whose Interpretation was Correct?

- FDA approved Vioxx in May 1999
- Results of early several imperfect studies lent themselves to conflicting interpretation, with independent experts and Merck scientists in disagreement
- Eventually, the truth is reached through double blind placebo trial ("gold standard")

# What did the Independent Experts Say?

In August 2001, JAMA publishes review of Vioxx trial by three scientists not associated with Merck:

- Patients taking Vioxx had 2.4 times the risk of cardiovascular event, compared with those taking naproxen.

Mukherjee DM, Nissen SE, Topol EJ. JAMA 2001;286:954-959.

# The Response of Merck's Conflicted Scientists: "It's the Aleve, not Vioxx"

- In Oct. 2001, Merck-affiliated scientists blame Aleve: "Differences observed between rofecoxib and naproxen are likely the result of the antiplatelet effects of the latter agent."
- Dec. 2001: " We believe that the analysis of [the independent scientists] provides no substantive support for their conclusions."

Sources: Konstam MA, Weir MR, Reicin AS, et al. Circulation 2001;104:2280-2288;  
Konstam MA, Demopoulos LA. Cardiovascular events and COX-2 inhibitors JAMA  
2001;286:2809

# The High Cost of Getting it Wrong

September 2004: Merck withdraws Vioxx after a placebo trial shows that Vioxx increases risk of heart attacks.

By then, an estimated 20 million Americans had taken the drug.

FDA scientists estimate Vioxx caused between 88,000 and 140,000 heart attacks in US alone.

Graham D, Campen D, Hui R, et al. The Lancet, 2005;365:475-481.

# Eliminate Conflicts of Interest

- “Managing” Conflicts is Not Enough
- Limit participation of conflicted scientists in Advisory Panels
  - IARC does it
  - The FDA will do it

# For More Information

- The Project on Scientific Knowledge and Public Policy:

[www.DefendingScience.org](http://www.DefendingScience.org)

- The Pump Handle Blog:

<http://thepumphandle.wordpress.com>