COPE COMMITTEE ON PUBLICATION ETHICS

Chairman, Dr Harvey Marcovitch
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Board member, UK Panel for Biomedical Research Integrity

Director: Council of Science Editors

www.publicationethics.org.uk

What do the following have in common?

- DNA content as a prognostic marker in patients with oral leukoplakia. NEJM 2001;344:1270-8
- Influence of resection of aneuploidy on mortality in oral leukoplakia. NEJM 2004;350:1405-1413
- NSAIDs and risk of oral cancer: a nested case-control study. Lancet 2005;333:1359-66

- Jon Sudbø

- Dentist 1985
- Physician 1994
- PhD thesis, University of Oslo 1993-2001
- Private practice
- 38 publications in peer reviewed journals
- Successful bid for $10m grant 2005
- Admitted to fraud 2006
- Removed from practice/research 2007

Hwang Woo-Suk,
South Korea, 2005

Hendrik Schön, USA
(1 paper every 8 days in 2001)

Eric T Poehlman,
Canada, 2005

Publication Ethics

- Honesty and integrity are essential if patients are to be protected and science validated
- Researchers, editors, publishers and sponsors are all responsible

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Cases discussed 1998-2006

• Duplication/redundancy	77
• No ethics approval	34
• Authorship issues	31
• No or inadequate consent	30
• Falsification/fabrication	28
• Plagiarism	26
• Unethical research or clinical malpractice	19
• Undeclared conflict of interest	15
• Reviewer misconduct	8
• Editor misconduct	6
• Other	41

Why does it happen when journals exist to enhance the scientific database?

- and… enhance seniority and income
- and… enhance pharmaceutical company profits
- and… increase publishers' profits

- How honest are researchers?

How honest are researchers

- 0.3% admitted a major offence
- 6% failed to present data contradicting their previous research
- 12% overlooked others' use of flawed data

Martinson et al Nature 2005;435:737-8

How honest are researchers?

- 107/194 NHS consultants had observed research misconduct
- 11 admitted personal misconduct
- 35 said they might do it in future
- Geggie J Med Ethics 2002;28:207

How honest are researchers?

- N = 2212 scientists with NIH grants
- 192 (8.7%) had evidence of misconduct in 265 events in their departments, 2002-5
- Of these, 201 fulfil criteria for FFP
- 58% of incidents reported
  - Titus SL, Wells J, Rhoades LJ. Nature 2008; 453:980-2

Duplicates and plagiarisers

- 62,213 Medline citations

- 0.04% with no shared authors highly similar = plagiarism

- 1.35% with shared authors highly similar = duplication

- So there may be 3500 plagiarised and 117,500 duplicate papers

- **Déjà vu—A study of duplicate citations in Medline**
  Mounir Errami et al ***Bioinformatics 2008;24:243-9***

•Ojuawo A. Milla PJ. Lindley KJ. **Non infective colitis in infancy: evidence in favour of minor immunodeficiency in its pathogenesis.**
East African Medical Journal. 74(4):233-6, 1997
Held at BMA Library, No longer received
UI: 9299824

•Ojuawo A. St Louis D. Lindley KJ. Milla PJ. **Non-infective colitis in infancy: evidence in favour of minor immunodeficiency in its pathogenesis.**
Archives of Disease in Childhood. 76(4):345-8, 1997.
Held at BMA Library, Currently received
UI: 9166029

Duplicate publication

- Impact of covert duplicate publication on meta-analysis

  Ondansetron: number needed to treat (NNT*)

Unduplicated trials only (16)	9.5
Duplicated trials only (3)	3.9
Skewed result with duplicate data (i.e. 3 trials included twice)	4.9
True result	6.4

*A lower NNT indicates greater efficacy

Tramer MR et al BMJ 1997;314:1088

Accentuating the positive

- A systematic review shows company sponsored research less likely to be published
- Company sponsored studies more likely to have outcomes favouring the sponsor than studies with other sponsors
- None of 13 studies that analysed methods reported studies funded by industry were of poorer quality
- Where are the negative studies?

Joel Lexchin, Lisa A Bero, Benjamin Djulbegovic, and Otavio Clark
Pharmaceutical industry sponsorship and research outcome and quality: a systematic review ***BMJ* 2003; 326: 1167 - 1170**.

Competing interests

- Analysis of 789 articles from major medical journals - 1 in 3 lead authors had financial interests in their research—patents, shares, or payments for being on advisory boards or as a director

- A quarter of US researchers have received pharmaceutical funding

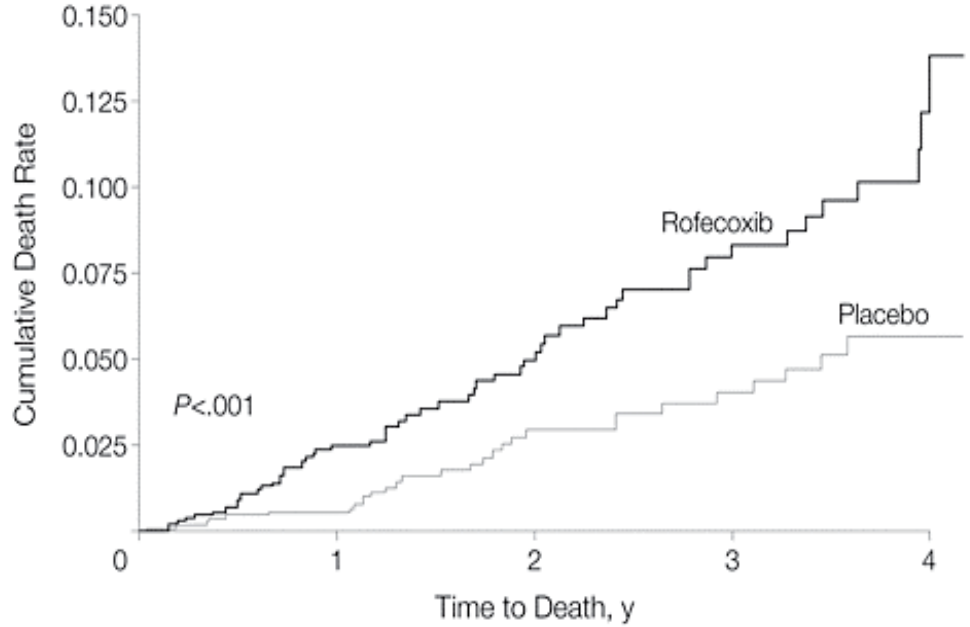
- Half have received “research related gifts”
- **Bekelman JE, Li Y, Gross CP. Scope and impact of financial conflicts of interest in biomedical research. A systematic review. JAMA 2003; 289: 454-65.**

Data manipulation

- **Reporting Mortality Findings in Trials of Rofecoxib for Alzheimer Disease or Cognitive Impairment A Case Study Based on Documents From Rofecoxib Litigation**
- **Bruce M. Psaty, MD, PhD; Richard A. Kronmal, PhD**

- *JAMA.* 2008;299(15):1813-1817.

Cumulative Mortality Rate by Treatment in the Alzheimer Disease Studies



No. at risk					
Rofecoxib	1069	845	418	260	67
Placebo	1074	909	459	309	83
No. of deaths					
Rofecoxib		24	14	11	7
Placebo		6	15	4	4

Psaty, B. M. et al. JAMA 2008;299:1813-1817.

6. Guests & ghosts

- Guest Authorship and Ghostwriting in Publications Related to Rofecoxib:
- A Case Study of Industry Documents From Rofecoxib Litigation

- Joseph S. Ross, MD, MHS; Kevin P. Hill, MD, MHS; David S. Egilman, MD, MPH; Harlan M. Krumholz, MD, SM
- *JAMA.* 2008;299(15):1800-1812.

Draft Version and Final Version of Article Describing the Results of Protocol 078

Rofecoxib does not delay the onset of Alzheimer's disease: results from a randomized, double-blind, placebo-controlled study

External author?, W.H. Visser[1], E. Yuen[1], C. Assaid[1], M.L. Nessly[1], B.A. Norman[1], C.C. Baranak[1], C.R. Lines[1], S.A. Reines[1], G.A. Block[1] on behalf of the Rofecoxib Protocol 078 study group

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A Randomized, Double-Blind, Study of Rofecoxib in Patients with Mild Cognitive Impairment

Leon J Thal[1], Steven H Ferris[2], Louis Kirby[3], Gilbert A Block[4], Christopher R Lines*[,4], Eric Yuen[4], Christopher Assaid[4], Michael L Nessly[4], Barbara A Norman[4], Christine C Baranak[4] and Scott A Reines[4], on behalf of the Rofecoxib Protocol 078 study group[5]

[1]University of California, San Diego, CA, USA; [2]New York University School of Medicine, New York, NY, USA; [3]Pivotal Research Centers, Peoria, AZ, USA; [4]Merck Research Laboratories, West Point, PA, USA

Ross, J. S. et al. JAMA 2008;299:1800-1812.

October 1999 E-mail Between Representatives of Scientific Therapeutics Information Inc and Merck Co Inc Discussing Contracted Publications Related to Rofecoxib

Dear Susan,

At the request of John Romankiewicz, I am providing you with an update on development and estimated delivery dates for various publications related to VIOXX that STI is working on.

1) Rofecoxib for the Treatment of Pain: Role of COX-2 Inhibitors for the Treatment of Nonmalignant Pain
- intended author: [redacted]
- intended journal: Analgesia
- estimated delivery of Draft 2 to Merck: 10/22

2) Clinical Implications of Drug Interactions with COX-2 Inhibitors
- intended author: [redacted]
- intended journal: Pharmacotherapy
- estimated delivery of Draft 2 to Merck: 10/22 (John Romankiewicz recently e-mailed you Draft 1 of this manuscript)

3) Overview of Clinical Pharmacology and Clinical Experience with Rofecoxib
- intended author: [redacted]
- intended journal: American Journal of Medicine or Archives of Internal Medicine
- estimated delivery of Draft 1 to Merck: 11/5

4) Review of Pharmacology and Clinical Experience with Rofecoxib for Osteoarthritis
- intended author: [redacted]
- intended journal: Journal of Rheumatology
- estimated delivery of Draft 1 to Merck: 10/29

5) Osteoarthritis in the Elderly: The Role of COX-2-Specific Inhibitors
- intended author: [redacted]
- intended journal: Geriatrics
- Draft 1 provided to Merck (C. Yarbrough) 9/27 - await comments; this manuscript cannot be sent via E-mail at this time as it is being actively edited based on additional internal comments; please call if you would like a copy FAXed to you

6) Changing Paradigm for Management of Osteoarthritis
- intended author: [redacted]
- intended journal: Journal of Osteopathic Medicine or Journal of Family Practice
- estimated delivery of Draft 1 to Merck: 11/12

7) Pharmacoeconomic Considerations in Treating Osteoarthritis: COX-2-Specific Inhibitors Versus NSAIDs
- author (confirmed): [redacted]
- intended journal: Journal of Managed Care
- extended outline provided to Merck (C. Yarbrough) and author 9/27 - copy attached for your reference. Outline approved by author; no comments received from Merck to date
- estimated delivery of Draft 1 of manuscript to Merck: 11/5

8) Managed Care Perspective on the COX-2 Inhibitors
- intended author: [redacted]
- intended journal: Managed Care
- estimated delivery of Draft 1 to Merck: 11/19

If you have any questions or require additional information at this time, please do not hesitate to contact me.

Why do researchers not detect fraud?

- Junior researchers fearful for their job
- Overwhelmed by charisma
- Bullying and threats
- Not trusting their own suspicion
- Lack of support from institution
- Turning a blind eye

Why editors detect few cases

- Normally trust authors
- Paper not within specialty knowledge
- Initial paper triage is cursory
- Lack of statistical expertise
- Effect of conflict of interest
- Hunger for high impact papers
- Cannot afford image screening or plagiarism detection software

4 | International Herald Tribune
Thursday, November 30, 2006

Panel urges tighter rules for science publications

Stem cell scandal prompted review

By Nicholas Wade

Fraudulent stem cell reports that shook the scientific world could have been prevented by extra review procedures, according to a panel appointed by Science, the journal that published the claims.

Donald Kennedy, the editor of Science, said the journal would accept the panel's major findings.

A South Korean researcher, Hwang Woo Suk, reported in Science in 2004 that he had generated embryonic stem cells from an adult human cell, the necessary first step in proposed schemes for growing replacement tissues from a patient's own cells. In a second report, in 2005, he claimed that he could perform this step routinely and efficiently, using very few human eggs.

Both reports proved to be fabrications, and the journal formally retracted the papers last January.

The fraud came to light not through any of the formal checking procedures in the scientific process, but because a whistle-blower in Hwang's lab spoke to a South Korean television station.

Science has long taken the position that its reviewing procedures work well but cannot be expected to detect deliberate fraud; therefore, no change is necessary. But the spectacular nature of the fraud prompted deeper thought on the part of leading journals.

After reviewing the paper record of how the Hwang reports were handled, a panel headed by John Brauman, a chemist at Stanford University, recommended four changes in Science's procedures on Tuesday.

A risk-assessment method should be developed to flag high-visibility papers for further review, the panel said. Also, authors should specify their individual contributions to a paper, a reform aimed at Hwang's stratagem of allowing another researcher, Gerald Schatten of the University of Pittsburgh, to be the lead author of one of the reports even though he had done none of the experiments.

The panel advised online publication of more of the raw data on which a report is based. It also suggested that Science, Nature and other leading journals establish common standards to prevent authors bent on deceit from favoring journals with laxer standards.

What should editors do? (Science investigation)

- Demand trial registration
- Risk stratify papers
- Clarify contributions/responsibilities of authors
- Make primary data available to reviewers/readers
- Act in concert with other “high-profile journals”
- Use plagiarism & data manipulation technology

JAMA proposals

- Trial registration
- Strict authorship rules
- Consider impact of funding
- For-profit sponsors subservient to academics
- Independent stats analysis
- Sanctions on miscreants
- No sponsored medical education

European Network of Research Integrity Offices (ENRIO)

- Twelve countries represented so far
- Supportive of ESF ‘Stewards of Integrity text’
- Key issues: open access to data
  informed consent
  sharing information

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‘Remember that truth alone is the matter that you are in search after; and if you have been mistaken, let not vanity seduce you to persist in your mistake.’

Henry Baker, The Microscope Made Easy, 1742