Chairman, Dr Harvey Marcovitch
(h.marcovitch@btinternet.com)

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

• Jon Sudbø

• Dentist 1985
• Physician 1994
• Private practice
• 38 publications in peer reviewed journals
• Successful bid for $10m grant 2005
• Admitted to fraud 2006
• Removed from practice/research 2007
Hendrik Schön, USA
(1 paper every 8 days in 2001)

Hwang Woo-Suk, South Korea, 2005

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
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
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
Held at BMA Library, No longer received
UI: 9299824

Held at BMA Library, Currently received
UI: 9166029
Duplicate publication

- Impact of covert duplicate publication on meta-analysis

Ondansetron: number needed to treat (NNT*)

<table>
<thead>
<tr>
<th>Description</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unduplicated trials only (16)</td>
<td>9.5</td>
</tr>
<tr>
<td>Duplicated trials only (3)</td>
<td>3.9</td>
</tr>
<tr>
<td>Skewed result with duplicate data (i.e. 3 trials included twice)</td>
<td>4.9</td>
</tr>
<tr>
<td>True result</td>
<td>6.4</td>
</tr>
</tbody>
</table>

*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

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”
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

Cumulative Mortality Rate by Treatment in the Alzheimer Disease Studies

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

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. Visser¹, E. Yuen¹, C. Assaid¹, M.L. Nessly¹, B.A. Norman¹, C.C. Baranak¹, C.R. Lines¹, S.A. Reines¹, G.A. Block¹ on behalf of the Rofecoxib Protocol 078 study group

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

Leon J Thal¹, Steven H Ferris², Louis Kirby³, Gilbert A Block⁴, Christopher R Lines⁺⁴, Eric Yuen⁴, Christopher Assaid⁴, Michael L Nessly⁴, Barbara A Norman⁴, Christine C Baranak⁴ and Scott A Reines⁴, on behalf of the Rofecoxib Protocol 078 study group⁵

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

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 Romankiwicz, 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: Anesthesia
   - 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 Romankiwicz 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 (G. Yardbrough) 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 (G. Yardbrough) 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
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
‘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