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

Past Chairman, C’ee on Publication Ethics (COPE) and board member, UK Research Integrity Office

Director, Council of Science Editors

Chair, GMC Fitness to Practice Panels
<table>
<thead>
<tr>
<th>Journal discipline</th>
<th>Number</th>
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<tbody>
<tr>
<td>Medicine</td>
<td>689</td>
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<tr>
<td>Life Sciences</td>
<td>420</td>
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<tr>
<td>Arts &amp; Humanities</td>
<td>385</td>
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<tr>
<td>Economics, finance, industry, business</td>
<td>288</td>
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<tr>
<td>Psychology, Social &amp; behavioural science</td>
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<td>Engineering &amp; Technical</td>
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<td>Computer Science</td>
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<td>Chemistry</td>
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<td>Education</td>
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<td>Earth Sciences &amp; Geography</td>
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<td>Dentistry, Veterinary Science, Nursing</td>
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<td>Math, Statistics</td>
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<td>Law</td>
<td>25</td>
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<tr>
<td>Astronomy, Astrophysics, Space Science</td>
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Cases discussed 1998-2008

- Duplication/redundancy 92
- No ethics approval 42
- Authorship issues 42
- Falsification/fabrication 36
- Plagiarism 36
- No or inadequate consent 33
- Unethical research or clinical malpractice 28
- Undeclared conflict of interest 22
- Reviewer misconduct 10
- Editor misconduct 7
- Other 49
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
• Private practice
• 38 publications in peer reviewed journals
• Successful bid for $10m grant 2005
• Admitted to fraud 2006
• Removed from practice/research 2007
• Reinstated in dental practice 2009
Sudbø: the investigation

- 69 of his 150 cases should have been excluded
- Duplicated data from individual patients
- Published ages not backed up by raw data
- No REC application or approval
- No patient consent
- Lancet data ‘invented’
Rogues Gallery

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

Hwang Woo-Suk, South Korea, 2005

Eric T Poehlman, Canada, 2005
(& prison 2007)

Hans Werner Gottinger
?100 plagiarised papers
Publication Ethics

• Honesty and integrity are essential if the public is to be protected and science validated

• Researchers, editors, publishers and sponsors are all responsible
Why does it happen when journals exist to enhance the academic database?

• and… enhance seniority and income

• and… increase publishers’ profits

• and (in biomedicine) … enhance pharmaceutical company profits
How frequent is research misconduct?

- 1.97% of scientists admitted fabrication/falsification
- 33.7% admitted other ‘questionable research practices (qrp)’
- 14% report fabrication/falsification by colleagues
- 72% report observing ‘qrp’ by colleagues

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
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
• Ojuawo A. Milla PJ. Lindley KJ. **Non infective colitis in infancy: evidence in favour of minor immunodeficiency in its pathogenesis.**
  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.**
  Held at BMA Library, Currently received
  **UI:** 9166029
• Dr S Dutta-Roy erased by the GMC in November 2007

• Plagiarised the work of colleagues

• Invented a co-author (Dr Kupp), whom he blamed for the plagiarism
FFP is ‘serious’

But ‘questionable research practices may have greater impact on patients or the public health’
Duplicate publication

- Impact of covert duplicate publication on meta-analysis
  Ondansetron: number needed to treat (NNT*)

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<tr>
<td>Unduplicated trials (16)</td>
<td>9.5</td>
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<tr>
<td>Duplicated trials (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>
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*A lower NNT indicates greater efficacy

Tramer et al BMJ 1997;315:635-40
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.*
Not just researchers

• Positive trials are more likely to be submitted. *(Rogue authors and sponsors)*

• Positive trials are more likely to be published. *(Rogue editors)*

• Positive trials are more likely to be published quickly. *(All three)*

Stern and Simes *BMJ* 1997;315:640-645  
*JAMA* 2002;287:2825-2828
BMJ systematic reviews: ‘Positive spin’ v funding and disclosure

Kjaergard, L. L et al. BMJ 2002;325:249
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”
Competing Interests (2)

- A review of 1534 cancer studies in 8 leading journals in 2006

- 29% declared COI; 17% declared industry COI

- Industry funded studies more likely to focus on treatment (62% v 36%)

- Randomised trials more likely to report positive survival outcome if COI present (29% v 14%)

Jagsi et al Cancer 2009;115:2783-2791
Competing interests

• Non-financial conflicts may be more common

  – Political
  – Personal likes or dislikes
  – Institutional jealousy or favouritism
  – Religious
How is fraud detected?

• Colleagues (usually junior)
• Other whistleblowers
• Reviewers
• Readers
• Regulatory bodies
• Editors (plagiarism software/photoshop)
• Statisticians
• Sponsors
• Publishers
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
Academic responses

• Not all institutions have robust systems

• UK universities and research councils have rejected a mandatory supervisory body to investigate and regulate research practices

• UKRIO procedures published 2009 are advisory only
CODE OF PRACTICE FOR RESEARCH

Promoting good practice and preventing misconduct

September 2009
Academic responses

• A Croatian government report finds a senior researcher guilty of serial plagiarism and duplication: the Univ. of Zagreb tells it to get lost.


• A senior academic is currently under GMC investigation for alleged ‘cover-up’ of research misconduct
Can we trust sponsors to prevent misconduct?
Sponsors and misconduct

• The overwhelming majority of allegations of research misconduct reported to the UK General Medical Council has come from the pharmaceutical industry.

• But.....
Can we trust publishers?

- This journal was published by Elsevier, paid for by Merck and contained only reprinted or summarised papers favourable to Merck products. No disclosure made of sponsorship.
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
(the figure did not appear in the published paper)

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. Visser†, E. Yuen†, C. Assaï†, M.L. Nessly†, B.A. Norman†, C.C. Baranak†, C.R. Lines†, S.A. Reines†, G.A. Block† on behalf of the Rofecoxib Protocol 078 study group

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

Leon J Thal†, Steven H Ferris‡, Louis Kirby‡, Gilbert A Block‡, Christopher R Lines∗‡, Eric Yuen‡, Christopher Assaï†, Michael L Nessly‡, Barbara A Norman‡, Christine C Baranak‡ and Scott A Reines‡, on behalf of the Rofecoxib Protocol 078 study group§

†University of California, San Diego, CA, USA; ‡New York University School of Medicine, New York, NY, USA; §Pivotal Research Centers, Peoria, AZ, USA; ∗Merck 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 Romaskiewicz, 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 Romaskiewicz 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: 10/20

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 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 do editors watch for?

- Authors unlikely to have sufficient resources
- Data ‘too good to be true’
- Findings hard to believe
- Paper submitted by back door
- Author puts undue pressure on editor
- Reviewer reports concern
What do (some) editors watch for?

- Blurred images
- Cloned region within an image
- ‘Blowout’ (no pixel structure)
- JPEG compression
- Use of touch-up tools for cloning & healing

Seeing is believing J Cell Biol 2006;172:9
Plagiarism detection

cross check

Sample Report

Turn it in
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
…and publishers?

• A code of conduct is in press

• Some of the largest scientific and academic publishers have joined COPE
but

- Reprints can make millions

- Journals are produced claiming to be academic but are actually promotional
Trial registration failing?

• 176/323 trials published in major journals in 2008 not properly registered

• 46/147 properly registered trials had a different primary outcome on publication.

• Of 23 evaluable, 19 had outcomes changed to reflect favourable results

JAMA 2009;302:977-84
Trial registration failing

- Of 677 trials registered and completed by 2005, only 311 traceable through Medline.

- 60% reported their primary outcomes.

- (FDA now require updating ClinicalTrials.gov with outcomes within 2 years.)

PLoS Med 2009; doi:10.1371/journal.pmed.1000144
Guidelines & Codes of Conduct

- World Association of Medical Editors [www.wame.org](http://www.wame.org)
- International Committee of Medical Journal Editors [www.icmje.org](http://www.icmje.org)
- Committee on Publication Ethics [www.publicationethics.org](http://www.publicationethics.org)
- Council of Science Editors [www.councilscienceeditors.org](http://www.councilscienceeditors.org)
Scientific Misconduct Blog

http://scientific-misconduct.blogspot.com

• About all manner of corporate pharmaceutical scientific misconduct and related curious incidents. If you're not outraged, you're not paying attention.
And it’s not just medicine
‘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