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

Context Authorship in biomedical publication provides recognition and establishes accountability and responsibility. Recent litigation related to rofecoxib provided a unique opportunity to examine guest authorship and ghostwriting, practices that have been suspected in biomedical publication but for which there is little documentation.

Objective To characterize different types and the extent of guest authorship and ghostwriting in 1 case study.

Data Sources Court documents originally obtained during litigation related to rofecoxib against Merck & Co Inc. Documents were created predominantly between 1996 and 2004. In addition, publicly available articles related to rofecoxib identified via MEDLINE.

Data Extraction All documents were reviewed by one author, with selected review by coauthors, using an iterative process of review, discussion, and rereview of documents to identify information related to guest authorship or ghostwriting.

Data Synthesis Approximately 250 documents were relevant to our review. For the publication of clinical trials, documents were found describing Merck employees working either independently or in collaboration with medical publishing companies to prepare manuscripts and subsequently recruiting external, academically affiliated investigators to be authors. Recruited authors were frequently placed in the first and second positions of the authorship list. For the publication of scientific review papers, documents were found describing Merck marketing employees developing plans for manuscripts, contracting with medical publishing companies to ghostwrite manuscripts, and recruiting external, academically affiliated investigators to be authors. Recruited authors were commonly the sole author on the manuscript and offered honoraria for their participation. Among 96 relevant published articles, we found that 92% (22 of 24) of clinical trial articles published a disclosure of Merck's financial support, but only 50% (36 of 72) of review articles published either a disclosure of Merck sponsorship or a disclosure of whether the author had received any financial compensation from the company.

Conclusions This case-study review of industry documents demonstrates that clinical trial manuscripts related to rofecoxib were authored by sponsor employees but often attributed first authorship to academically affiliated investigators who did not always disclose industry financial support. Review manuscripts were often prepared by unacknowledged authors and subsequently attributed authorship to academically affiliated investigators who often did not disclose industry financial support.

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Author Affiliations: Department of Geriatrics and Adult Development, Mount Sinai School of Medicine, New York, New York (Dr Ross); Department of Psychiatry, Harvard Medical School, Boston, Massachusetts, and McLean Hospital, Belmont, Massachusetts (Dr Hill); Department of Community Health, Brown University School of Medicine, Providence, Rhode Island (Dr Egilman); and Robert Wood Johnson Clinical Scholars Program and Section of Cardiovascular Medicine, Department of Medicine, Section of Health Policy and Administration, School of Public Health, Yale University School of Medicine, and Center for Outcomes Research and Evaluation, Yale-New Haven Hospital, New Haven, Connecticut (Dr Krumholz).
Corresponding Author: Joseph S. Ross, MD, MHS, Mount Sinai School of Medicine, 1 Gustave L. Levy Pl, Box 1070, New York, NY 10029 (joseph.ross@mssm.edu).

AUTHORSHIP IN BIOMEDICAL publication provides recognition while establishing accountability and responsibility. Guest authorship has been defined as the designation of an individual who does not meet authorship criteria as an author.[1,2] It was identified in 16% of research articles, 26% of review articles, and 21% of editorials in a survey of 6 peer-reviewed medical journals,[3] in addition to 41% of Cochrane reviews.[4] Ghostwriting has been defined as the failure to designate an individual (as an author) who has made a substantial contribution to the research or writing of a manuscript.[1] Ghostwriting was demonstrated in 13% of research articles, 10% of review articles, 6% of editorials, and 11% of Cochrane reviews[3,4]; other research has found similar rates.[5]

Two studies have characterized the practices of guest authorship and ghostwriting using industry documents, one examining practices related to gabapentin by Pfizer Inc and Parke-Davis, Division of Warner-Lambert Company,[6] the other sertraline by Pfizer Inc.[7] However, these studies were focused on how the research and publication strat-

See also pp 1813 and 1833.

egy of the companies was used to promote and market the products. No studies have used internal documents to characterize the role of authorship in collaborations between industry and the medical profession.

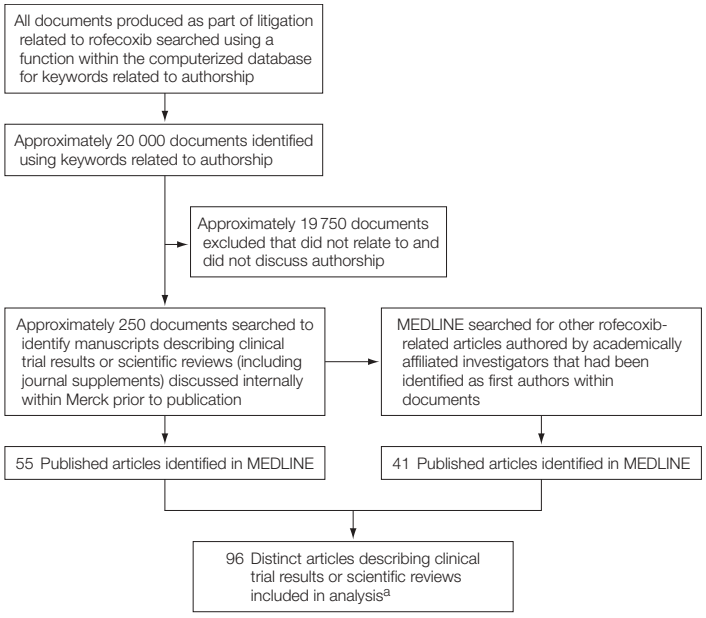
Recent litigation against Merck & Co Inc related to rofecoxib provided a unique opportunity to examine the practice of guest authorship and ghostwriting related to the research and promotion of this medication. Our objective was to provide a review using a case-study exploration of court documents, in tandem with a review of the medical literature, to describe the practice of guest authorship and ghostwriting related to rofecoxib.

Documents used for this article are posted at http://dida.library.ucsf.edu.

METHODS

In the course of the combined trials of *Cona vs Merck and Co, Inc* (No. ATL-L-3553-05, New Jersey Superior Court, Atlantic City) and *McDarby vs Merck and Co, Inc* (No. ATL-L-1296-05, New Jersey Superior Court, Atlantic City), millions of documents were made available to and archived in an integrated database maintained by the plaintiff's attorneys. These documents were created between 1996 and 2004 and included Merck internal and external correspondence, reports, and presentations. As consultants to attorneys on the behalf of plaintiffs, we had complete access to all archived documents. One investigator (J.S.R.) searched the database to extract a subset of documents related to authorship (FIGURE 1). The search was performed using the database keyword search function and included the following search terms: *clinical trial, author, authorship, review, manuscript,* and *publication*, along with terms encompassing the names of Merck scientists, the names of academically affiliated authors of clinical trials, the names and numbers of clinical trials, the names of medical publishing companies, and the names of journals. The search identified approximately 20 000 documents that included 1 or more of the keyword terms. Document numbers are an approximation because information within one document may overlap with another, making it difficult to determine the exact number of distinct documents. For example, 1 document may include a string of 2 e-mails, whereas another document may include a string of 5 e-mails, including the prior 2.

Figure 1. Document and Manuscript Identification Flowchart



See the "Methods" section for detailed descriptions of the search terms and the number of documents searched and for the definition of "related to or discussed authorship."
[a] Identification of these manuscripts does not imply that each was guest authored or ghostwritten; we examined these manuscripts because we believed their discussion within internal documents (or the discussion of specific authors) suggested that Merck was aware of the publication and perhaps had provided support for the project.

One investigator (J.S.R.) searched the documents identified using the authorship keywords to determine if each was actually related to or discussed authorship, examining the document titles and the content within the database. "Related to or discussed authorship" refers specifically to examination for authorship of manuscripts describing nonpharmacological, human participant clinical trial results or scientific reviews (or journal supplements) that included an external, academically affiliated (non-Merck employee) author. Approximately 250 documents were identified, the majority of which were Merck internal correspondence and publication reports, along with external correspondence between Merck and medical publishing companies.

Two investigators (J.S.R. and K.P.H.) reviewed these 250 documents using the principles of grounded theory, an inductive approach in which source material was used to generate ideas rather than to test a preestablished hypothesis.[8] This method has been applied to study issues at the intersection of litigation and health, particularly with tobacco,[9,10] and more recently with pharmaceutical[6] products. We first reviewed the documents to identify broad themes reflecting the practice of ghostwriting and guest authorship. Next, pertinent documents were reviewed again by all of the authors, using a negotiated consensus process to reach our final interpretation. This process ultimately generated a single agreed-upon set of themes, as well as documents and quotations to illustrate each theme.

After determining themes, 2 investigators (J.S.R. and K.P.H.) again reviewed these 250 documents to iden-

tify articles describing clinical trial results or scientific reviews (including journal supplements) discussed internally within Merck prior to publication that proposed an external, academically affiliated investigator as an author. No documents were excluded as part of this search; all documents were related to 1 or more of the identified manuscripts (most manuscripts were discussed within >1 document). The published articles were subsequently identified via MEDLINE. This search was supplemented with MEDLINE queries for other rofecoxib-related articles authored by academically affiliated investigators identified as first authors within documents, which were found by searching for the author's name and "rofecoxib" or "cyclooxygenase inhibitor." This search identified 96 published articles. Importantly, identification of these articles does not imply that each was guest authored or ghostwritten; we examined these articles because we believed their discussion within internal documents (or the discussion of specific authors) suggested that Merck was aware of the manuscript prior to publication and perhaps had provided support for the project.

All published articles were categorized as to whether a manuscript's coauthor was affiliated with Merck (ie, a Merck employee), whether the published article included any financial disclosure, whether the published article included a financial disclosure of Merck support, and whether the published article included a financial disclosure of Merck support by at least 1 of the academic authors. For articles in which there was neither a published disclosure of Merck financial support nor a published disclosure of Merck financial support by 1 of the academic authors, other articles by the academic authors published within 2 years of the relevant article were examined to determine if they had disclosed Merck financial support.

This research was deemed exempt from normal review by the Yale University Human Investigation Committee.

RESULTS

Review of internal documents and the published literature revealed 3 key findings related to guest authorship and ghostwriting: the first focused on the publication of clinical trials, the second focused on the publication of review papers, and the last was related to financial support disclosures.

Clinical Trial Manuscripts

When publishing their own clinical trials (designed, conducted, and sponsored by Merck), documents were found describing Merck scientists often working to prepare manuscripts and subsequently recruiting external, academically affiliated investigators to collaborate on the manuscript as guest authors. For instance, trial 078 (a randomized, double-blind study to investigate whether rofecoxib could delay the onset of Alzheimer disease in patients with mild cognitive impairment) was designed and conducted principally by scientists at Merck. FIGURE 2 shows the title and author list both from draft[11] and published[12] versions of the manuscript describing the trial. Both the title and the authorship were modified to attribute authorship to 3 academically affiliated investigators (first, second, and third authors) on the published article, in addition to the 8 Merck scientists who are attributed authorship on both the draft and published versions of the manuscript (1 Merck scientist is attributed authorship on the draft but not the final manuscript). Of note, only 1 of the 3 academically affiliated investigators who are attributed authorship on the published article was acknowledged in the draft version as a participating investigator in the rofecoxib 078 study group. In an internal e-mail discussing where to publish trial 078 as the draft is circulated, one of the Merck scientists states, "I think you should be the first author since you have done virtually all of the writing."[13] Although there are minor differences in language and organization between the draft and final versions of the manuscript (particularly in the abstract, as opposed to the text), the results presented are almost identical, reinforcing that the trial itself and the analyses were complete before the academically affiliated investigators were involved in the manuscript.

This same pattern occurred for the manuscript describing the Merck protocol 901 studies, which compared the efficacy of rofecoxib and naproxen in Asian and European populations. An e-mail written on behalf of members of Merck's publication committee to a Merck scientist states that the European study had been prepared as a manuscript and that a draft was shared with the European authors, in addition to describing 2 Merck employees who will prepare the manuscript describing the Asian study.[14] However, the final publication describes both trials in a single article and lists neither of them as authors.[15]

Documents were found describing other examples of Merck recruiting external, academically affiliated investigators to collaborate as guest authors on manuscripts prepared by Merck scientists. The first author of the Assessment of Differences Between Vioxx and Naproxen to Ascertain Gastrointestinal Tolerability and Effectiveness (ADVANTAGE) study[16] described to a *New York Times* reporter in 2005, "Merck designed the trial, paid for the trial, ran the trial . . . Merck came to me after the study was completed and said, 'We want your help to work on the paper.' The initial paper was written at Merck, and then was sent to me for editing."[17] The academically affiliated authors of the Vioxx GI Outcomes Research (VIGOR) study,[18] in response to an expression of concern by the *New England Journal of Medicine*,[19] make a point of asserting that no Merck employee or representative was involved in the drafting of their response, but do not discuss who drafted the manuscript and with respect to cardiovascular events allude to not developing the analysis plan, not having access to the data, and not performing the analyses.[20] Merck's performance of the analyses was confirmed by the Merck-affiliated authors.[21]

A Merck publications status report identifies several of the early clinical

trials conducted by the company that were eventually published for which data were available (or would soon be available), including Merck protocols 010, 029, 033, 034, 035, 040, 041, 044, 045, 050, 058, 068, 072, 085, 088 (VIGOR), 090, 097, 098, 102 (ADVANTAGE), 103, 120, 121, 901, and 902.[22] For each of these study protocols, a Merck employee is designated within the report as the author of the first draft of the manuscript. Examining the published articles, the first author is an external, academically affiliated investigator for 16 of 20 articles (some protocols were combined into single articles),[15,16,18,23-35] with the exception of protocols 010, 029, 058, and 072,[36-39] 3 of which had external, academically affiliated investigators listed as authors, but not in the first authorship position. Among these 16 articles, all had 2 or more external, academically affiliated investigators who were attributed authorship (median, 4.5; range, 2-10) and these authors occupied 77% of the first, second, and third authorship positions (37 of 48). Of note, the Merck employee designated to be first author in the Merck publications status report is attributed authorship in 14 of these 16 articles (88%), most often as the final author.

Not all manuscripts were prepared independently by Merck before inviting an academically affiliated author; documents also were found describing Merck contracting with medical publishing companies to have manuscripts prepared. For instance, FIGURE 3 displays a letter from representatives of Scientific Therapeutics Information to Merck employees presenting the completed draft of a contracted manuscript for rofecoxib protocol 116.[40] Scientific Therapeutics Information describes itself on its Web site as "a full-service medical publishing group specializing in the development of scientific literature and other resource media with direct application to clinical therapeutics that has been serving members of the pharmaceutical industry and medical associations since 1985."[41]

Review Papers

Documents were found describing Merck employees contracting with medical publishing companies to ghost-

Figure 2. 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

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

write review manuscripts focused on rofecoxib and subsequently recruiting external, academically affiliated investigators to be guest authors. For example, FIGURE 4 displays an e-mail from representatives of Scientific Therapeutics Information to Merck employees providing an update on the development and estimated delivery dates for

Figure 3. October 2000 Letter From Representatives of Scientific Therapeutics Information Inc (Grace E. Johnson, Una Kistner, John Romankiewicz) to Merck & Co Inc (Deborah Matzura-Wolfe, Greg Geba) Discussing the Completion of the First Draft of a Contracted Manuscript Related to Rofecoxib

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SCIENTIFIC THERAPEUTICS
INFORMATION, INC

505 Morris Avenue
Springfield, New Jersey
07081

(973) 376-3655 telephone
(973) 376-0611 fax 1
(973) 376-3567 fax 2

http://www.stimedinfo.com
E-mail: staff@stimedinfo.com

October 9, 2000

Deborah Matzura-Wolfe
Medical Program Coordinator
Clinical Development
Merck US Human Health
PO Box 4, HM-202
West Point, PA 19486

RE: VIOXX C-1 MANUSCRIPT (PROTOCOL 116)

Dear Deborah:

We are pleased to enclose Draft I of the "A Randomized, Placebo-Controlled, Parallel-Group, Double-Blind Study to Evaluate the Safety and Efficacy of Rofecoxib 25 mg and Celecoxib 200 mg in Patients with Osteoarthritis of the Knee or Hip" manuscript to be submitted to *JAMA Express*.

Please feel free to mark your revisions directly on the hard copy provided.

We look forward to receiving your comments by **October 23, 2000**. If you have any questions during your review, do not hesitate to contact me at (970) 204-4446.

Sincerely,

Grace E. Johnson, PharmD
Senior Editor

encl

cc: J Romankiewicz, U Kistner, G Geba (MER), .1617

STI0023352

8 manuscripts related to rofecoxib that the company was preparing, including intended titles, authors, and journals.[42] Review articles were identified by 7 of the 8 investigators listed in Figure 4, several with titles nearly exactly as proposed.[43-49] In addition, FIGURE 5 displays a contract for Health Science Communications Inc to provide a 20-page review manuscript with 6 figures or tables intended for a cardiology audience for Merck at a cost of $23 841.00.[50] Contracts also were identified between these 2 parties to provide review manuscripts intended for nephrology and primary care audiences,[51,52] as well as for other medical specialties. Health Science Communications Inc describes itself on its Web site as "a full-service health marketing communications company committed to the highest quality of service . . . We're there pre-launch, preparing the market for a product's introduction. At launch, we establish the foundation for product uptake."[53]

Documents were found demonstrating that medical publishing companies provided near complete drafts of review manuscripts to authors for editing, in addition to managing submissions and revisions. For instance, in preparing one manuscript, representatives from Scientific Therapeutics Information indicate in a publications status report that the first draft was sent to Merck and the company was awaiting comments, but an author needed to be invited.[54] In another e-mail that discusses an article with which the company was involved, a Scientific Therapeutics Information representative states:

"The .1439 journal article that was submitted to Pharmacotherapy by Dr. William Garnett has been accepted (I believe) with revisions. He has faxed me only the reviewers' comments, but is mailing me the entire packet that they sent to him. He would like us to make the revisions, as he is too busy at the moment to make them himself. According to the proposal (Doc # 66468) there is no mention of whether revisions are included, or can be done for an additional fee."[55]

Documents also were found demonstrating that medical publishing companies played critical roles in overseeing the development, organization, and manuscript drafting of supplemental issues focused on rofecoxib for journals.[46,49,56-75]

Figure 4. 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

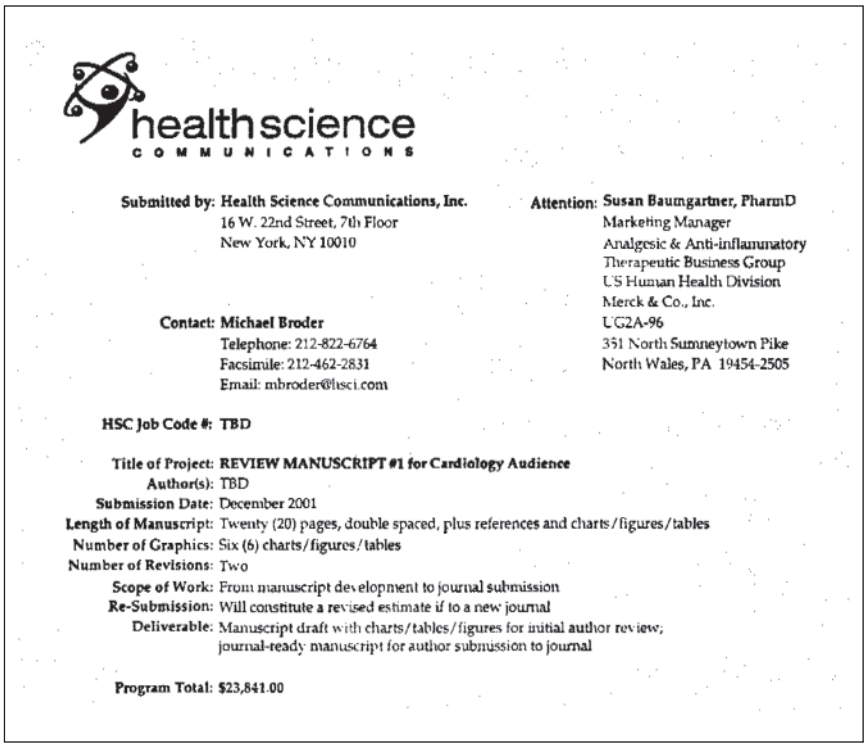
7) Pharmacoeconomic Considerations in Treating Osteoarthritis: COX-2-Specific Inhibitors Versus NSAIDs
- author (confirmed): [redacted]
- intended journal: Journal of Managed Care
- extended outline provided to Merck (C. Yarbrough) and author 9/27 - copy attached for your reference. Outline approved 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.

Review articles were identified by 7 of 8 investigators listed above, several with titles nearly exactly as proposed. Intended author names have been blacked out because articles were not identified by all named investigators.

Figure 5. Health Science Communications Inc Contract to Provide One 20-Page Review Manuscript With 6 Figures or Tables Intended for a Cardiology Audience for Merck & Co Inc at a Cost of $23 841.00



health science COMMUNICATIONS

Submitted by: Health Science Communications, Inc.
16 W. 22nd Street, 7th Floor
New York, NY 10010

Attention: Susan Baumgartner, PharmD
Marketing Manager
Analgesic & Anti-inflammatory
Therapeutic Business Group
US Human Health Division
Merck & Co., Inc.
UG2A-96
351 North Sumneytown Pike
North Wales, PA 19454-2505

Contact: Michael Broder
Telephone: 212-822-6764
Facsimile: 212-462-2831
Email: mbroder@hsci.com

HSC Job Code #: TBD

Title of Project: REVIEW MANUSCRIPT #1 for Cardiology Audience
Author(s): TBD
Submission Date: December 2001
Length of Manuscript: Twenty (20) pages, double spaced, plus references and charts/figures/tables
Number of Graphics: Six (6) charts/figures/tables
Number of Revisions: Two
Scope of Work: From manuscript development to journal submission
Re-Submission: Will constitute a revised estimate if to a new journal
Deliverable: Manuscript draft with charts/tables/figures for initial author review; journal-ready manuscript for author submission to journal

Program Total: $23,841.00

Documents were found describing Merck compensating investigators with honoraria for agreeing to serve as authors on review manuscripts ghostwritten on their behalf by medical publishing companies. Honoraria varied, ranging from $750 to $2500. One author refused his honorarium from Scientific Therapeutics Information stating, "I really do not feel it is appropriate to be paid for this type of effort."[76]

Financial Support Disclosure

There were 96 relevant published articles including 24 clinical trials and 72 reviews (TABLE). Of the 24 clinical trials, 22 (92%) published a disclosure of Merck's financial support. Of the 72 reviews (38 of which published any financial disclosures, and 34 of which either did not require or did not publish financial disclosures), 36 (50%) published either a disclosure of Merck sponsorship or a disclosure of whether the author had received any financial compensation from the company.

Among 24 nonpharmacological, human participant clinical articles, all 24 included at least one coauthor who was a Merck employee. Nearly all (n=22) published a disclosure that the trial was supported by Merck, including 7 that also published a disclosure of a financial relationship between Merck and an academic author of the article. No financial disclosure was published for the academic authors of the remaining 17 articles, which may indicate that they did not receive or that they did not disclose receiving financial compensation.

Among 72 scientific review articles, 50 (69%) were solo-authored by an academic physician and 2 (3%) included at least 1 coauthor who was a Merck employee. Of these 72, 21 (29%) published a disclosure that the review was supported by Merck, usually through an unrestricted educational grant, 14 (19%) published a disclosure of a financial relationship between Merck and an academic author of the review article, and 1 (1%) published a disclosure that the author had no financial relationship with Merck. However, for 15 of the 35 review articles (43%) that published a disclosure of Merck support, the disclosure was provided either as part of an introductory editorial describing the supplement's contents or on a separate "disclosure" page; a disclosure statement was not identified when any of the articles were individually accessed electronically [accessed by the authors on February 27, 2008].

Among the 36 of 72 review articles (50%) in which there was no published disclosure of Merck support or a financial relationship between Merck and the academic author, 24 of 36 articles (67%) were authored by at least 1 investigator who published a disclosure of a financial relationship between himself/herself and Merck within another article published within 2 years of the review article. Moreover, several others were authors of clinical trials sponsored by Merck, although no disclosure of a financial relationship between himself/herself and Merck was published. In addition, while none of the review articles from one journal's supplement disclosed financial relationships between Merck and the non-Merck employee authors of the review article, communication between representatives from Scientific Therapeutics Information describes an honorarium offered to the authors in payment for their service.[128]

COMMENT

This case-study review of industry documents related to rofecoxib demonstrates that Merck used a systematic strategy to facilitate the publication of guest authored and ghost written medical literature. Articles related to rofecoxib were frequently authored by Merck employees but attributed first authorship to external, academically affiliated investigators who did not always disclose financial support from Merck, although financial support of the study was nearly always provided.

Table. Published Financial Disclosures Among Articles Describing Clinical Trial Results or Scientific Reviews (Including Journal Supplements) Discussed Internally Within Merck Prior to Publication That Proposed an External, Academically Affiliated Investigator as an Author[a]

Type of Article and Reference No.	Coauthor Affiliated With Merck (ie, Employee)	Financial Disclosure		Academic Author(s) Disclosed Financial Support From Merck		Where Trial or Review Identified
		Any[b]	From Merck[c]	Current Article	Another Article	
Published in 1999						
Review[77]	No	No	NA	NA	No	Correspondence[d]
Trial[37]	Yes	Yes	Yes	No	Yes[18,78]	Merck publication status report[e]
Review[79]	No	Yes	No	Yes	NR	Merck publication status report[e]
Trial[23]	Yes	Yes	Yes	No	Yes[18,78]	Merck publication status report[e]
Published in 2000						
Trial[18]	Yes	Yes	Yes	Yes	NR	Merck publication status report[e]
Trial[33]	Yes	Yes	Yes	No	No	Merck publication status report[e]
Review[80]	No	No	NA	NA	No	Correspondence[d]
Review[81]	No	No	NA	NA	No	Correspondence[d]
Trial[32]	Yes	Yes	Yes	No	Yes[18]	Merck publication status report[e]
Review[82]	No	No	NA	NA	Yes[18,79]	Merck publication status report[e]
Review[83]	No	Yes	No	No	No	Merck publication status report[e]
Trial[31]	Yes	No	NA	NA	Yes[18,79]	Merck publication status report[e]
Trial[27]	Yes	Yes	Yes	No	No	Merck publication status report[e]
Trial[29]	Yes	Yes	Yes	Yes	NR	Merck publication status report[e]
Trial[35]	Yes	Yes	Yes	No	No	Merck publication status report[e]
Trial[84]	Yes	Yes	Yes	Yes	NR	Correspondence[d]
Published in 2001						
Review[85]	No	No	NA	NA	Yes[18,78]	Merck publication status report[e]
Review[86]	Yes	No	NA	NA	Yes[84]	Correspondence[d]
Review[87]	No	Yes	No	No	No	Correspondence[d]
Review[67]	No	Yes[f]	Yes[f]	No	No	Correspondence[d]
Review[68]	No	Yes[f]	Yes[f]	No	No	Correspondence[d]
Review[69]	No	Yes[f]	Yes[f]	No	No	Correspondence[d]
Review[88]	No	No	NA	NA	Yes[18]	Merck publication status report[e]
Trial[36]	Yes	Yes	Yes	All authors employed by Merck[g]	All authors employed by Merck[g]	Merck publication status report[e]
Review[89]	No	Yes	No	Yes	NR	Correspondence[d]
Review[44]	No	No	NA	NA	No	Merck publication status report[e]
Review[47]	No	No	NA	NA	No	Merck publication status report[e]
Review[90]	No	No	NA	NA	No	Correspondence[d]
Review[91]	No	No	NA	NA	Yes[84]	Correspondence[d]
Review[92]	No	Yes	No	No	No	Correspondence[d]
Trial[30]	Yes	Yes	Yes	Yes	NR	Merck publication status report[e]
Review[93]	Yes	No	NA	NA	Yes[18,79]	Merck publication status report[e]
Review[94]	No	No	NA	NA	Yes[18,79]	Merck publication status report[e]
Review[95]	No	No	NA	NA	Yes[18,79]	Merck publication status report[e]
Review[96]	No	No	NA	NA	Yes[18,79]	Merck publication status report[e]
Review[70]	No	Yes[f]	Yes[f]	No	No	Correspondence[d]
Review[97]	No	No	NA	NA	Yes[18,65]	Merck publication status report[e]
Review[71]	No	Yes	Yes	No	No	Correspondence[d]
Review[98]	No	No	NA	NA	Yes[89]	Correspondence[d]
Review[72]	No	Yes[f]	Yes[f]	No	Yes[64]	Correspondence[d]
Review[73]	No	Yes[f]	Yes[f]	No	No	Correspondence[d]
Trial[39]	Yes	Yes	Yes	No	No	Merck publication status report[e]
Review[99]	No	No	NA	NA	Yes[18,78]	Merck publication status report[e]
Review[48]	No	No	NA	NA	Yes[18,78]	Merck publication status report[e]
Review[74]	No	Yes[f]	Yes[f]	No	Yes[18,65]	Correspondence[d]

(continued)

Table. Published Financial Disclosures Among Articles Describing Clinical Trial Results or Scientific Reviews (Including Journal Supplements) Discussed Internally Within Merck Prior to Publication That Proposed an External, Academically Affiliated Investigator as an Author[a] (cont)

Type of Article and Reference No.	Coauthor Affiliated With Merck (ie, Employee)	Financial Disclosure		Academic Author(s) Disclosed Financial Support From Merck		Where Trial or Review Identified
		Any[b]	From Merck[c]	Current Article	Another Article	
Published in 2001						
Trial[38]	Yes	Yes	Yes	No	No	Merck publication status report[e]
Review[45]	No	Yes	Yes	No	Yes[78]	Merck publication status report[e]
Review[75]	No	Yes[f]	Yes[f]	No	No	Correspondence[d]
Trial[100]	Yes	Yes	Yes	No	Yes[18,79]	Merck publication status report[e]
Published in 2002						
Review[101]	No	No	NA	NA	Yes[102]	Correspondence[d]
Review[57]	No	Yes	No	Yes	NR	Correspondence[d]
Review[103]	No	Yes	Yes	No	Yes[18]	Merck publication status report[e]
Review[104]	No	No	NA	NA	Yes[84]	Correspondence[d]
Review[105]	No	Yes	Yes	No	Yes[84]	Correspondence[d]
Review[58]	No	Yes	No	Yes	NR	Correspondence[d]
Review[59]	No	Yes	No	Yes	NR	Correspondence[d]
Review[49]	No	Yes[f]	No	Yes[f]	NR	Merck publication status report[e]
Review[106]	No	No	NA	NA	No	Merck publication status report[e]
Trial[78]	Yes	Yes	Yes	Yes	NR	Correspondence[d]
Trial[26]	Yes	Yes	Yes	No	No	Merck publication status report[e]
Review[107]	No	No	NA	NA	No	Correspondence[d]
Review[108]	No	No	NA	NA	Yes[18,79]	Merck publication status report[e]
Review[46]	No	Yes[f]	No	Yes[f]	NR	Merck publication status report[e]
Review[109]	No	Yes	Yes	No	Yes[18,65]	Merck publication status report[e]
Review[60]	No	Yes	No	Yes	NR	Correspondence[d]
Review[110]	No	No	NA	NA	Yes[60]	Correspondence[d]
Review[111]	No	Yes	Yes	No	Yes[34]	Merck publication status report[e]
Review[112]	No	No	NA	NA	Yes[34]	Merck publication status report[e]
Review[61]	No	Yes	No	Yes	NR	Correspondence[d]
Review[113]	No	Yes	Yes	No	Yes[18]	Correspondence[d]
Review[114]	No	No	NA	NA	Yes[18]	Correspondence[d]
Review[62]	No	Yes	No	Yes	NR	Correspondence[d]
Trial[15]	Yes	Yes	Yes	No	No	Merck publication status report[e]
Review[63]	No	Yes	No	Yes[h]	No	Correspondence[d]
Review[115]	No	No	NA	NA	No	Correspondence[d]
Review[116]	No	Yes	Yes	No	Yes[117]	Merck publication status report[e]
Review[64]	No	Yes	No	Yes	NR	Correspondence[d]
Review[56]	No	Yes[f]	No	Yes[f]	NR	Correspondence[d]
Review[118]	No	No	NA	NA	Yes[18,78]	Correspondence[d]
Review[65]	No	Yes	No	Yes	NR	Correspondence[d]
Review[66]	No	Yes	No	Yes	NR	Correspondence[d]
Published in 2003						
Review[119]	No	No	NA	NA	No	Correspondence[d]
Review[120]	No	Yes[f]	Yes[f]	No	Yes[66]	Correspondence[d]
Review[43]	No	No	NA	NA	No	Merck publication status report[e]
Review[121]	No	No	NA	NA	No	Merck publication status report[e]
Trial[28]	Yes	No	NA	NA	Yes[18,79]	Merck publication status report[e]
Trial[34]	Yes	Yes	Yes	Yes	NR	Merck publication status report[e]
Review[122]	No	Yes[f]	Yes[f]	No	Yes[78]	Correspondence[d]
Review[123]	No	Yes[f]	Yes[f]	No	Yes[18]	Correspondence[d]
Trial[16]	Yes	Yes	Yes	Yes	NR	Merck publication status report[e]
Review[124]	No	Yes[f]	Yes[f]	No	Yes[62,117]	Correspondence[d]
Review[125]	No	No	NA	NA	Yes[64]	Correspondence[d]

(continued)

Table. Published Financial Disclosures Among Articles Describing Clinical Trial Results or Scientific Reviews (Including Journal Supplements) Discussed Internally Within Merck Prior to Publication That Proposed an External, Academically Affiliated Investigator as an Author[a] (cont)

Type of Article and Reference No.	Coauthor Affiliated With Merck (ie, Employee)	Financial Disclosure		Academic Author(s) Disclosed Financial Support From Merck		Where Trial or Review Identified
		Any[b]	From Merck[c]	Current Article	Another Article	
Published in 2004 or Later						
Trial[24]	Yes	Yes	Yes	No	No	Merck publication status report[e]
Review[126]	No	No	NA	NA	No	Merck publication status report[e]
Trial[127]	Yes	Yes	Yes	No	Yes[18,78]	Correspondence[d]
Trial[25]	Yes	Yes	Yes	No	Yes[18,78]	Merck publication status report[e]

Abbreviations: NA, not applicable, no disclosure was published; NR, not relevant, if a disclosure of the academic author's financial support from Merck was published within the article, it was not relevant whether there was a published disclosure of financial support from Merck of the author within a different, recently published article.

[a] The sample was supplemented with MEDLINE queries for rofecoxib-related articles authored by academic investigators named within internal documents. Identification of these articles does not imply that each was guest authored or ghostwritten. We examined these articles because we believed that their discussion within internal documents (or the discussion of specific authors) suggested that Merck was aware of the manuscript and perhaps had provided support for the project.

[b] No may indicate that the journal did not require or did not publish financial disclosures.

[c] No may indicate that the academic authors did not receive financial compensation or that the academic author did not disclose receiving financial compensation.

[d] Indicates either named within correspondence between Merck and a medical publishing company or written by an external, academically affiliated investigator named within the correspondence.

[e] Indicates either named within a rofecoxib publication status report or written by an external, academically affiliated investigator named within the publication status report.

[f] Financial disclosure provided in the journal's supplement overview or introduction, not in the individual article.

[g] An external, academically affiliated author was identified within internal documents but was not attributed authorship within published article.

[h] Disclosed that there was no financial relationship between Merck and the author.

Similarly, review articles related to rofecoxib were frequently prepared by unacknowledged authors employed by medical publishing companies and attributed authorship to investigators who often did not disclose financial support from Merck.

The limited nature of our source material for this case-study review prevented an exact determination of the contributions of recruited authors to the overall design and conduct of the clinical trial and/or the preparation of manuscripts. Although we reviewed in excess of 20 000 documents produced during the consolidated rofecoxib litigation, we were frequently unable to identify versions of manuscript drafts dated before and after external, academically affiliated authors had been recruited. In addition, we cannot exclude contributions by authors made by telephone or in person that would not be identified by reviewing documents obtained through litigation. However, the instances for which we did identify before and after manuscript drafts, such as for protocol 078, we found scant documentary evidence that the recruited authors were involved in the design or conduct of the study or made substantive contributions to the manuscript beyond minor editing. Participating only in minor editing does not meet authorship criteria of the International Committee of Medical Journal Editors (ICMJE).[129] In addition, we could not determine how often ghostwriting and guest authorship actually occurred, whether the contracted manuscript drafts from medical publishing companies were used, or if the proposed payments (honoraria) were provided. Nevertheless, although we cannot conclude that each of the external, academically affiliated investigators attributed authorship for their respective trial or review article made no substantive contributions to the study design or manuscript preparation, the authorship pattern observed within these documents suggests there was a widespread practice of inappropriately attributing authorship to academic authors and a failure to disclose relevant financial relationships.

Several issues should be considered in evaluating this study. Although every effort was made to present this information objectively and fairly, it is important to note that all of the authors of this article have been compensated for their work as consultants/expert witnesses at the request of plaintiffs in litigation against Merck related to rofecoxib. In addition, relevant documents may not have been identified in our review, despite our use of a systematic method with a comprehensive and exhaustive search strategy to minimize missed documents. However, we believe that while our review may not be sensitive, it was specific. We do not think that we missed documents that would negate the totality of our findings.

Finally, this case-study review is based on documents from a single company related to a single medication. We cannot determine if the authorship pattern we observed for clinical trial and review articles related to rofecoxib also would be observed in articles describing other Merck products or the products of other pharmaceutical companies. However, given the reported prevalence of guest authorship and ghostwriting among the most prestigious medical journals[3-5] and that similar authorship patterns were identified using documents produced during litigation surrounding both gabapentin and sertraline,[6,7] it is reasonable to expect that the authorship practices observed in this case study may be used by other pharmaceutical companies as well. A recent press account seems to confirm as much,[130] as does the presence of an industry specializing in medical writing.[41,53] Because Merck has traditionally characterized itself and its conduct as among the most ethically ap-

propriate of pharmaceutical companies,[131] perhaps the practices we observed are conservative in comparison with other companies within the industry. Nevertheless, access to industry documents through litigation presents a rare opportunity to explore the relationship between the medical profession and the pharmaceutical industry and has provided valuable insights and findings in the past.[132]

The medical profession must determine how to interpret and respond to these examples of guest authorship and ghostwriting, conduct that the World Association of Medical Editors has described as dishonest and unacceptable[133] and that erodes the ethical foundation of medicine and medical research.[134] Our case-study review suggests that the practice of inappropriately attributing authorship was common. However, we cannot be certain of the specific actions of individuals, both by those active in academic medicine and those employed by Merck. Perhaps academic authors just permitted themselves to be listed as authors, perhaps they did a substantial amount of editing and simply should have disclosed the actual writer as a coauthor. Moreover, we cannot be certain of the actions of journals. Each journal likely differs in its policies regarding authorship and financial disclosures; we assume that every journal expects that the primary author of an article makes substantive intellectual contributions to the paper, which may include conception of the project, design and conduct of the trial, responsibility for the data and analysis, or drafting of the manuscript, and discloses all other individuals who substantially contributed to the article.

We are hopeful that our findings encourage discussion of ways in which to improve the integrity of research. The medical profession and the pharmaceutical industry should agree that collaborations must be conducted with the highest standards.[135] We suggest that academic researchers consistently provide to the journals the author contributions for all manuscripts, including original research, meta-analyses, reviews, and commentaries, and disclose relationships and support from all industry sources, regardless of the journal's requirements. Authors who "sign-off" on or "edit" original manuscripts or reviews written explicitly by pharmaceutical industry employees or by medical publishing companies should offer full authorship disclosure, such as, "drafting of the manuscript was done by representatives from *XYZ, Inc*; the authors were responsible for critical revisions of the manuscript for important intellectual content." A coordinated oversight strategy involving academic physicians, journal editors, and industry representatives is necessary to discourage both guest authorship and ghostwriting and improve the integrity of the biomedical authorship system.

Author Contributions: Dr Ross had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Ross, Hill, Egilman, Krumholz.
Acquisition of data: Ross, Hill, Egilman, Krumholz.
Analysis and interpretation of data: Ross, Hill, Krumholz.
Drafting of the manuscript: Ross.
Critical revision of the manuscript for important intellectual content: Ross, Hill, Egilman, Krumholz.
Study supervision: Krumholz.
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Role of the Sponsor: No outside source had any role in the design or conduct of the study; collection, management, analysis or interpretation of the data; preparation, review or approval of the manuscript, or in the decision to submit the manuscript for publication.
Additional Information: All legal documents used in this article are available at http://dida.library.ucsf.edu.

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