ALLIANCE FOR HUMAN RESEARCH PROTECTION

www.ahrp.org
142 West End Avenue, Suite 28P
New York, NY 10023
212-595-8974

April 25, 2008
Dr. Andrew von Eschenbach, Commissioner
Food and Drug Administration

> Re: Draft Guidance for Industry on Good Reprint Practices for the Distribution of Medical Journal Articles and Medical or Scientific Reference Publications on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices (Docket No. FDA-2008-D-0053)

Dear Dr. von Eschenbach:

The following comments update our June 7, 2007 letter of concern to which you have not yet responded. [See attached]

This follow-up letter was prompted by two reports published by the *Journal of the American Medical Association*,[1] analyzing evidence recently uncovered during Vioxx litigation; show how Merck manipulated the data, minimizing the impact of Vioxx-related deaths in ghostwritten journal reports.

Numerous other cases currently under litigation have uncovered a mountain of evidence demonstrating the insidious impact of ghostwritten journal reports—but these are under court seal.[2] Indeed, ghostwritten articles—in essence, industry propaganda--have infiltrated the scientific literature, undermining the integrity of medicine. Industry-sponsored ghostwritten reports have unduly influenced medical practice guidelines and physicians' prescribing practices, resulting in preventable harm.

We urge the FDA to take no action on this "draft guideline for industry" permitting distribution of medical journal articles on unapproved uses of approved drugs--until manufacturers are required to (a) identify ghostwritten journal reports (b) fully disclose all safety information, and (c) waive confidentiality court seals once a case is adjudicated—so that independent scientists can verify the accuracy of the information.

The Alliance for Human Research Protection has located apparently ghostwritten articles to which the name of Dr. Thomas Laughren, director of the FDA's Division of Psychiatry Products, CDER, is penned.

For example, in 2005, Dr. Laughren was named a co-author of the article, "Mood Disorders in the Medically Ill: Scientific Review and Recommendations," published by the *Journal of the Society of Biological Psychiatry*.[3] The article promotes the notion that depression accompanies practically all patients with medical illnesses—e.g., cardiovascular disease, cancer, AIDS, Alzheimer's, Parkinson's, Diabetes, Osteoporosis, Obesity, and Pain.

Antidepressants are recommended for presumed underlying depression and even "to prevent" depression:

> "[a] novel approach involves using antidepressants to prevent development of depression in patients receiving medications known to cause severe depressive symptoms."

Can one even begin to calculate the added infusion of cash from antidepressants whose use is recommended not only by "prominent" psychiatrists, but by the highest ranking FDA official authorized to approve expanded marketing licensure!!

A note states: **"Editorial support was provided by Scientific Therapeutics Information, Springfield, New Jersey."** (p. 183. Emphasis added).

According to its website, Scientific Therapeutics Information ("STI") is "a full-service medical publishing group specializing in the development of scientific literature and other resource media with direct application to clinical therapeutics. STI has been serving members of the pharmaceutical industry and medical associations since 1985." See http://www.stimedinfo.com/sti.htm.

In point of fact, ghostwriters are hired by pharmaceutical companies to subvert science ("developing scientific literature") into a marketing tool.

STI ghostwriters have crafted numerous misleading journal reports that were instrumental in turning ineffective, even lethal drugs into blockbuster sellers. For example, STI ghosted Merck's Vioxx reports,[1] Cyberonic's VNS (Vagus Nerve Stimulation) report,[4] and GlaxoSmithKline's deceptive published report about Paxil study 329,[5] which was identified as a key document in New York State Attorney General's lawsuit against GSK (2004).[6]

The GSK-STI ghostwritten report[5] mischaracterized the Paxil pediatric Study 329, falsely asserting the drug's efficacy in children. In fact, documents obtained during litigation revealed that study 329 was negative for efficacy on all 8 protocols specified outcomes and shown to be harmful. Beginning in 1998 GSK memos discussed Study 329 (and other pediatric studies) as having failed.[7] Several internal memos (2001, recently posted on a website) [8] reveal how ghostwriters "improved" the published findings failing to report that there were 8 times as many suicidal events amongst the Paxil patients compared to the placebo patients.

Of note, **Dr. Laughren was instrumental in the approval of SSRI antidepressants, including Paxil. He then actively maneuvered to prevent added label warnings—even as evidence linked SSRIs to an increased risk of suicide and suicidal behavior since 1991**.[9]

FDA officials embargoed the data analysis report by Dr. Andrew Mossholder[10] (an FDA psychopharmacology safety expert) prepared for the Feb. 2004 FDA Pediatric Drug Advisory Committee. The analysis showed a twofold increased suicide risk in children prescribed Paxil compared to placebo. **Dr. Laughren made the presentation instead.**[11]

It was later revealed at a Congressional hearing that Dr. Laughren had excluded from his PDAC presentation Dr. Mosholder's recommendations and the data supporting his disturbing findings.[12]

The disclosure attached to Dr. Laughren's name states that his "contribution to this paper was made in his private capacity; no official support or endorsement by the U.S. Food and Drug Administration is intended or should be inferred."[3]

But the issue is whether it is acceptable for a pivotal FDA official to endorse industry funded propaganda masquerading as recommendations backed by science?

FDA is an agency whose mandate is to ensure that the information disseminated to physicians and the public about drug safety meets the standards of science. By penning his name to ghostwritten industry-sponsored articles whose commercially-driven recommendations are not supported by scientific evidence, Dr. Laughren, a high ranking FDA official—whether or not he is acting in his official capacity—is contributing to the erosion of science-based medicine by undermining the integrity of the scientific literature.

Two published "Consensus Conference" reports and recommendations (2003, 2007)[13] [14] following conferences convened by the American Academy of Child and Adolescent Psychiatry, were penned by some 46 named "authors." Disclosure statements indicate they **were industry-sponsored**:

> "This conference was convened by the American Academy of Child and Adolescent Psychiatry and funded by Best Practice with partial financial support from unrestricted grants from the following companies: Abbott Pharmaceuticals, Bristol-Myers Squibb, GlaxoSmithKline, INC Research, Janssen Pharmaceutica, Johnson & Johnson Pharmaceutical Research and Development, Eli Lilly, Novartis, Pfizer, and Solvay Pharmaceuticals."[13]
>
> "The conference on which this article is based was funded by unrestricted grants from Annie E. Casey Foundation, Bristol-Myers Squibb, Forest Research Institute, Jazz Pharmaceuticals, Otsuka Pharmaceuticals, Janssen, Eli Lilly and Company, Pfizer Laboratories, and Sanofi Synthelab."
>
> "Conference participants agreed that Impulsive Aggression is a substantial public health and clinical concern, constitutes a key therapeutic target across multiple disorders, and can be measured with sufficient precision that pharmacological studies are warranted."[14]

Such industry-sponsored "Consensus Conferences" are convened to lend legitimacy to prescribing guidelines lacking scientific justification – most notably, the Texas Medication Algorithm Program (TMAP).[15]

"Impulsive Aggression" is a fabricated "symptom" concocted to legitimize the illegitimate prescribing of antipsychotics for children. Antipsychotics are the most toxic drugs in psychopharmacopaeia. A body of evidence uncovered during litigation confirmed these drugs' life-shortening risks.[16] In children the metabolic risks are even greater.[17]

The following disclosure statement is disingenuous: "Dr. Vitiello's[18] and Dr. Laughren's contributions to this article were made in their private capacity. No official support or endorsement by the National Institute of Mental Health or the U.S. Food and Drug Administration is intended nor should be inferred."

These government officials have lent their name to an industry-sponsored document promoting a commercially-driven public health policy aimed at increasing the use of highly toxic drugs that now carry Black Box warnings about death.

The professional integrity of the "authors" who penned their names to these and numerous other such articles may be questioned. In Dr. Laughren's case, the issue is especially egregious. He wielded pivotal authority in approving these drugs and in determining what the label disclosed. We believe he appears to be abusing his government position by lobbying for a commercially-driven public health policy that is aimed at increasing the use of these drugs – clearly a boon for pharmaceutical companies' profit margins. What's more, Dr. Laughren appears to be acting as a double agent—a lobbyist who lobbies the regulator, himself.

We believe that a Congressional investigation is urgently warranted.

Of note, the article, "Mood Disorders in the Medically Ill"[3] includes well-known but discredited "co-authors":

- Trey Sunderland III, MD, presented as a leading expert on Alzheimer's disease at the NIMH, invoked his Fifth Amendment privilege before a House committee, and was convicted of criminal felony for contracting with Pfizer as a paid consultant for work that overlapped his duties as a public servant. He was fined $300,000. See http://www.ahrp.org/cms/content/view/405/27/

- Charles B. Nemeroff, MD, Professor and Chairman of the Department of Psychiatry and Behavioral Sciences, Emory, is an influential promoter, dubbed the "Boss of Bosses." In 2006, the Wall Street Journal uncovered the fact that Dr. Nemeroff and seven prominent authors penned their name to a ghostwritten article published by the journal of the American College of Neuropsychopharmacology (ACNP), whose editor he was. The article promoted vagus nerve stimulation, a device manufactured by Cyberonics without disclosing his financial ties to Cyberonics. http://www.ahrp.org/cms/content/view/295/27 After this public disclosure, Dr. Nemeroff was forced to resign as editor. http://www.ahrp.org/cms/content/view/295/27; http://download.journals.elsevierhealth.com/pdfs/journals/0270-6644/PIIS0270664406717994.pdf

- Jack M. Gorman was a prominent pharmaceutical promoter of bogus "mental conditions" such as social anxiety disorder (SAD) and GAD (generalized anxiety disorder) on behalf of GlaxoSmithKline, manufacturer of the antidepressant, Paxil. He was Deputy Editor of the American Journal of Psychiatry, and served as a paid consultant to at least 13 pharmaceutical firms, including Eli Lilly, Pfizer, and Forest Laboratories. He penned his name to a pivotal (later) discredited Forest Lab. study which was used to promote Lexapro, its new antidepressant.[19] Less than six months after his appointment to president and psychiatrist in chief of McLean Hospital, Harvard's teaching hospital, in October 2005, in "an astonishing fall from grace", he was forced to resign because of sexual relations with patient. He temporarily lost his license to practice in New York, and permanently in Massachusetts. http://ahrp.blogspot.com/2007/11/cover-up-gorman-case-professional-moral.html

- Laurie Flynn is Executive Director of the Columbia University TeenScreen Program since January 2001. She clearly has a vested interest in promoting TeenScreen, which is a market expansion gimmick for increasing the rolls of children prescribed psychotropic drugs.[20]

Furthermore, pharmaceutical companies are using confidentiality stipulations and protective orders in product litigation cases to cover-up their malfeasance and misconduct. By hiding their documents behind court-sealing orders, drug companies are impeding an impartial scientific evaluation of drug safety issues. As a result, thousands of American lives have been sacrificed.

FDA, Division of Dockets Management (Docket No. FDA-2008-D-0053)

We respectfully submit that the agency needs to restore the FDA to the safety function and independence for which it was created.

Sincerely,

Vera Hassner Sharav
President
Alliance for Human Research Protection

---

[1] Joseph S. Ross, MD, MHS, Kevin P. Hill, MD, MHS, David S.Egilman, MD, MPH Harlan M. Krumholz, MD, SM. Guest Authorship and Ghostwriting in Publications Related to Rofecoxib: A Case Study of Industry Documents From Rofecoxib Litigation, *JAMA*, 2008: 299(15):1800-1812; Bruce M. Psaty MD; Richard A. Kronmal MD. Reporting Mortality Findings in Trials of Rofecoxib for Alzheimer Disease or Cognitive Impairment: A Case Study Based on Documents From Rofecoxib Litigation," *JAMA*, 2008:299(15):1813.

[2] To cite but a few:

- Re: Risperdal/Seroquel/Zyprexa Litigation, Case No. 274 (Superior Court of New Jersey, Middlesex County)
- Re: Vioxx Litigation, Case No. 619 (Superior Court of New Jersey, Atlantic County)
- Re: Bextra/Celebrex Litigation, Case No. 272 (Superior Court of New Jersey, Atlantic County)
- Re Seroquel Products Liability Litigation, MDL No. 1769 (M.D. Fla.)
- Re Zyprexa Products Liability Litigation, MDL No. 1596 (E.D.N.Y.)
- State of Louisiana, Attorney General v. Janssen Pharmaceutica, Inc., Docket no. 04,3977 (27th Judicial District Court for the Parish of St. Landry, Louisiana)

[3] Evans DL, Charney DS, Lewis L, Golden RN, Gorman JM, Krishnan KR, Nemeroff CB, Bremner JD, Carney RM, Coyne JC, Delong MR, Frasure-Smith N, Glassman AH, Gold PW, Grant I, Gwyther L, Ironson G, Johnson RL, Kanner AM, Katon WJ, Kaufmann PG, Keefe FJ, Ketter T, Laughren TP, Leserman J, Lyketsos CG, McDonald WM, McEwen BS, Miller AH, Musselman D, O'Connor C, Petitto JM, Pollock BG, Robinson RG, Roose SP, Rowland J, Sheline Y, Sheps DS, Simon G, Spiegel D, Stunkard A, Sunderland T, Tibbits P Jr, Valvo WJ. Mood disorders in the medically ill: scientific review and recommendations. *Biol Psychiatry*. 2005 Aug 1;58(3):175-89.

[4] DAVID ARMSTRONG. Medical Reviews Face Criticism Over Lapses, *Wall Street Journal* July 19, 2006; Page B1. http://www.ahrp.org/cms/content/view/295/27.pdf
[5] Keller MB, Ryan ND, Strober M, Klein RG, Kutcher SP, Birmaher B, Hagino OR, Koplewicz H, Carlson GA, Clarke GN, Emslie GJ, Feinberg D, Geller B, Kusumakar V, Papatheodorou G, Sack WH, Sweeney M, Wagner KD, Weller EB, Winters NC, Oakes R, McCafferty JP. "Efficacy of Paroxetine in the Treatment of Adolescent Major Depression: A Randomized, Controlled Trial" *J. Am. Academy Child Adolescent Psychiatry*, 2001; 40(7):762-72.
[6] See: NYS Attorney General Complaint, 2004:
http://www.oag.state.ny.us/press/2004/jun/jun2b_04_attach1.pdf
[7] See: SB Confidential. October 1998.
http://www.ahrp.org/risks/SSRI0204/GSKpaxil/pg1.html
[8] See: Study 329 documents:
http://www.healthyskepticism.org/documents/PaxilStudy329.php See: Correspondence between STI ghostwriter (Sally Laden) and principle “author” (Martin Keller, MD) of published Study 329:
http://www.healthyskepticism.org/documents/PaxilStudy329/GSKNulli.pdf
[9] In 1991, after examining the Prozac data, the chairman of FDA’s Advisory Committee declared, “yes there is a signal there” of an increased risk of suicide. But FDA officials maneuvered to steer the divided vote against changing the label to warn physicians and patients about the potential risk.
[10] Dr. Mossholder’s report: http://www.ahrp.org/infomail/04/07/26.php
[11] http://www.fda.gov/OHRMS/DOCKETS/AC/04/transcripts/4006T1.htm
[12] See: Committee on Energy and Commerce. Hearing, FDA’s role in protecting the public health: Examining fda’s review of safety and Efficacy concerns in anti-depressant use By children. September 23, 2004:
http://a257.g.akamaitech.net/7/257/2422/12jan20051100/www.access.gpo.gov/congress/house/pdf/108hrg/96099.pdf

[13] Gabrielle A. Carlson, MD, Peter S. Jensen, MD, Robert L. Findling, MD, Roger E. Meyer, MD, Joseph Calabrese, MD, Melissa P. DelBello, MD, Graham Emslie, MD, Laurie Flynn, Frederick Goodwin, MD, Martha Hellander, Robert Kowatch, MD, Vivek Kusumakar, MD, Thomas Laughren, MD1, Ellen Leibenluft, MD, James McCracken, MD, Editha Nottelmann, PhD, Daniel Pine, MD, Gary Sachs, MD, David Shaffer, MD, Renee Simar, PhD, Michael Strober, PhD, Elizabeth B. Weller, MD, Janet Wozniak, MD, and Eric A. Youngstrom, PhD. Methodological Issues and Controversies in Clinical Trials with Child and Adolescent Patients with Bipolar Disorder: Report of a Consensus Conference, J *of Child and Adolescent Psychopharmacology*, 2003:13 (1): 13-27.

[14] Jensen PS, Youngstrom EA, Steiner S, Findling RL, Meyer RE, Malone RP, Carlson GA, Coccaro EF, Aman MG, Blair J, Dougherty D, Ferris C, Flynn L, Green E, Hoagwood K, Hutchinson J, Laughren T, Leve LD, Novins DK, Vitiello B. Consensus Report on Impulsive Aggression as a Symptom across Diagnostic Categories in Child Psychiatry: Implications for Medication Studies. *J of the American Academy of Child and Adolescent Psychiatry*, 46(3):309-322, 2007.

[15] See: Allen Jones Report. http://psychrights.org/drugs/allenjonestmapjanuary20.pdf See also, Jackson P. Former state pharmacist charged, *Business Week*, June 11, 2006. http://ahrp.blogspot.com/2006/11/former-state-pharmacist-pennsylvania.html

[16] Alex Berenson. Drug Files Show Maker Promoted Unapproved Use, *NYT*, December 18, 2006, A-1.

[17] CORRELL CU. CARLSON HE. Endocrine and Metabolic Adverse Effects of Psychotropic Medications in Children and *Adolescents J. Am. Acad. Child Adolescent. Psychiatry*, 2006;45(7):771 Y 791.
[18] Dr. Benedetto Vitiello is the Chief, Child and Adolescent Treatment and Preventive Interventions Research Branch, with the NIMH.
[19] Melody Petersen. Madison Ave. Plays Growing Role in Drug Research, *NYT*, Nov. 22, 2002 p. 1.

[20] Evelyn Pringle, Evelyn J. Pringle. Meet Laurie Flynn TeenScreen's Top Pusher, *Counterpunch*, June 6, 2005. http://www.counterpunch.org/pringle06062005.html