



UNIVERSITY OF  
PENNSYLVANIA  
HEALTH SYSTEM

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September 22, 2016

Robert Freedman, MD  
American Journal of Psychiatry  
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RE: Nemeroff CB, Evans DL, Gyulai L, Bowden CL, Gergel IP, Oakes R, Pitts CD. "Double-Blind, Placebo-Controlled Comparison of Imipramine and Paroxetine in the Treatment of Bipolar Depression," American Journal of Psychiatry 2001; 158:906-912.

Dear Dr. Freedman:

We write to you as the editor in chief of the American Journal of Psychiatry to formally request immediate retraction of the Smith Kline Beecham, now GlaxoSmithKline (GSK), study report PAR 352 referenced above.

Study PAR 352 clearly failed to demonstrate efficacy for paroxetine in bipolar depressed patients. However, by way of GSK-sponsored ghostwriting, this study was misrepresented to the medical and scientific communities as a 'positive' study as part of a marketing scheme by GSK to have paroxetine (Paxil®) outsell other selective serotonin reuptake inhibitor antidepressants for all indications.<sup>i</sup> This strategic marketing plan by GSK included the ghostwriting of at least 50 paroxetine-related articles by medical communication companies that would 'spin' the data in favor of the sponsor's product for a variety of unapproved, but highly-sought after off-label indications.<sup>ii</sup> A key component of this sub rosa plan was for prominent academic researchers, known in industry as 'key opinion leaders,' to lend their names to these publications as authors in order to give the report an appearance of scientific objectivity.

The misleading analyses and conclusions published in the PAR 352 article have been propagated throughout the medical and scientific literature in no less than 457 publications (Google search), including three (3) major reviews on the treatment of bipolar depression in adults, children and adolescents.<sup>iii,iv,v</sup>

With the recent publication of our article "The Paroxetine 352 Bipolar Trial: "A Study in Medical ghost writing," in the International Journal of Risk & Safety in Medicine (24), 2012: 221–231, we, along with other scientists, have drawn

attention to the serious misrepresentations in the Nemeroff et al. article referenced above.

In July of 2011 you were notified of a complaint of research misconduct filed with the Office of Research Integrity (ORI case 2012) of the National Institute of Health of the U.S. Department of Health and Human Services pertaining to the Nemeroff et al. article.<sup>vi,vii</sup>

As a result, you became aware that the Nemeroff et al. manuscript was written almost exclusively by the medical communications firm, Scientific Therapeutics Information, Inc. (STI) in conjunction with GSK employees. There was no input from any of the PAR 352 study investigators or the named academic 'authors.' You also became aware that GSK identified and designated the so-called 'authors' for the Nemeroff et al. manuscript only after the second, revised draft of the manuscript had been prepared by STI and GSK.

As a result of both declassified and still classified documents from litigation and ORI whistle blower cases, the extent of industry manipulation is only just becoming clear -- well beyond what was available to the public previously. Some of this information is documented in the enclosed IJRSM paper; however, much more will be revealed as more documents are released in the public domain in the near future.

We are sure that you agree that the integrity of science depends on disinterest in hypotheses and rigorous adherence to the accurate reporting of results of experimental testing. This is particularly important in medicine where significant harms to patients have resulted from the failure to embrace the ideal of evidence-based medicine. We therefore implore you to immediately retract the Nemeroff et al. article as a serious stain on the reputation of the American Journal of Psychiatry.

We are making this letter available to interested parties and for possible posting in the public domain.

Sincerely,

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Enclosure: Amsterdam & McHenry "The Paroxetine 352 Bipolar Trial: A Study in Medical Ghostwriting. International Journal of Risk & Safety in Medicine 2011; 24:221–231.

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<sup>i</sup> [http://abcnews.go.com/images/Primetime/paxil\\_bpg.pdf](http://abcnews.go.com/images/Primetime/paxil_bpg.pdf) (Accessed May 2012)

<sup>ii</sup>C. B. Nemeroff, (ed). Advancing the treatment of mood and anxiety disorders: The first 10 years' experience with paroxetine," *Psychopharm Bul.* 2003; 37/1.

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<sup>iii</sup> British Psychological Society., National Collaborating Centre for Mental Health (Great Britain), and National Institute for Health and Clinical Excellence (Great Britain). *Bipolar Disorder: The Management of Bipolar Disorder in Adults, Children, and Adolescents, in Primary and Secondary Care*. British Psychological Society, 2006.

<sup>iv</sup> IV Ghaemi, S N, A P Wingo, M A Filkowski, and R J Baldessarini. "Long-Term Antidepressant Treatment in Bipolar Disorder: Meta-Analyses of Benefits and Risks." *Acta Psychiatrica Scandinavica* 118, no. 5 (November 2008): 347–56. doi:10.1111/j.1600-0447.2008.01257.x.

<sup>v</sup> V Zhang, Yingli, Huan Yang, Shichang Yang, Wei Liang, Ping Dai, Changhong Wang, and Yalin Zhang. "Antidepressants for Bipolar Disorder: A Meta-Analysis of Randomized, Double-Blind, Controlled Trials." *Neural Regeneration Research* 8, no. 31 (November 5, 2013): 2962–74. doi:10.3969/j.issn.1673-5374.2013.31.009.

<sup>vi</sup> ORI case 2012-33 - Complaint of Scientific Misconduct against Dwight L. Evans, Laszlo Gyulai; Charles Nemeroff, Gary S. Sachs and Charles L. Bowden.

<sup>vii</sup>(<http://psychrights.org/research/Digest/Science4Sale/110708EthicsComplaintAgainstEvansGyulaiNemeroffSachsBowdenetal.pdf>;

<http://blogs.nature.com/news/files/2012/06/Jay-Amsterdam-today-filed-a-24-page-complaint-with-the-Office-of-Research-Integrity-at-the-US-National-Institutes-of-Health.pdf>).