



UNIVERSITY OF
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HEALTH SYSTEM

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Maria A. Oquendo, M.D.
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RE: CIT-MD-18, Wagner *et al.*, 'A randomized, placebo-controlled trial of citalopram for the treatment of major depression in children and adolescents.' *Am J Psych* 2004; 161 (6): 1079-1083.

Dear Dr. Oquendo,

We write to you in your capacity as President of the American Psychiatric Association, and as a staunch supporter of ethics in psychiatry, about our concerns regarding gross misrepresentations made in the above referenced journal article published in the *American Journal of Psychiatry* in 2004 and reiterated recently in comments that appeared in the American Psychiatric Association's *Psychiatric News* discussing the same clinical trial in 2016.

Specifically, between January 2000 and April 2001 Forest Laboratories, Inc., conducted a multi-site clinical trial of citalopram for depression in children and adolescents, Protocol CIT-MD-18, IND Number 22,368, with the results published in 2004 by Wagner *et al.* in the *American Journal of Psychiatry*.

The article was ghostwritten by agents of the manufacturer and seriously misrepresented both the effectiveness and the safety of citalopram in treating child and adolescent depression.

While substantive problems with CIT-MD-18 and the Wagner *et al.* article have been exposed in legal actionsⁱ and in the medical literature,^{ii, iii} the article continues to be cited uncritically in the psychiatric literature as evidence of the efficacy of citalopram for treatment of adolescent depression^{iv} when, in fact, it was no better than placebo.

Our main concern is that children and adolescents are continuing to be at risk of harm unnecessarily because well-intentioned physicians have been misled.

Moreover, the misrepresentation has been compounded by the following issues:

- 1) In a letter of May 9, 2016, the *Journal's* editor, Dr. Robert Freedman, was asked by three of the undersigned, Drs. Jureidini, Amsterdam and McHenry, to retract the article, but he has curtly refused to do so.
- 2) In an email of July 11, 2016, Drs. Jureidini, Amsterdam and McHenry wrote to the former editor of the *American Journal of Psychiatry* who accepted the Wagner *et al* manuscript for publication, Dr. Nancy Andreasen, and asked her to support retraction of the article, but she did not respond.
- 3) Drs. Jureidini, Amsterdam and McHenry submitted for publication a letter to the editor of the *Psychiatric News*, Catherine F. Brown, on July 7, 2016 regarding the misrepresentations of Dr. Wagner on CIT-MD-18 and received no response.

The putative research misconduct involved in the CIT-MD-18 study reveals the pervasive influence of Forest's marketing objectives on the preparation and publication of a 'scientific' manuscript written primarily for marketing purposes and only secondarily as a peer-reviewed journal article. Forest's own internal documents disclosed in litigation show that company staff were aware that there were serious problems with the conduct of this trial but concealed the problems in advancing their commercial objectives. Procedural deviations went unreported (failure to disclose that unblinded patients were included in the final outcome analyses contrary to the study protocol in order to impart statistical significance to a non-significant primary outcome measure). An implausibly large effect size was claimed. Positive *post hoc* measures were introduced while negative primary and secondary outcomes were not reported. Adverse events were misleadingly analyzed, hiding substantial agitation in the citalopram group. Many of the de-classified Forest documents have now been posted on the Drug Industry Document Archive (DIDA) at the University of California, San Francisco, and many more documents are in the process of being released into the public domain.

We believe that the unretracted Wagner *et al.* article represents a stain on the high standard of the *American Journal of Psychiatry* (AJP) and the American Psychiatric Association (APA). Neither the AJP nor the APA can claim to be a leader in scientific research and moral integrity while failing to redress this article that negligently misrepresents scientific findings.

In bringing this matter to your attention, we also ask that you write to the current editor of the *American Journal of Psychiatry*, Dr. Robert Freedman, supporting our request for retraction of Wagner *et al.* journal article.

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

Yours sincerely

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ⁱ *United States v. Forest Pharmaceuticals, Inc.*, Cr. No. 10-10294-NG (D. Mass.); *Celexa and Lexapro Marketing and Sales Practices Litigation*: Master Docket 09-MD-2067-(NMG)

ⁱⁱ Martin A, Gilliam WS, Bostic JQ, Rey JM. Letter to the editor. Child psychopharmacology, effect sizes, and the big bang. *Am J Psych* 2005; 162 (4): 817;

ⁱⁱⁱ Jureidini J, Amsterdam J, McHenry L. The citalopram CIT-MD-18 pediatric depression trial: A deconstruction of medical ghostwriting, data manipulation and academic malfeasance," *International Journal of Risk & Safety in Medicine*, 28, 2016: 33-43

^{iv} Levin, A. Child psychiatrists look at specialty from both macro, micro perspectives. *Psychiatric News*, 51/12, June 17, 2016: 23.