EXHIBIT 1

BAUM, HEDLUND, ARISTEI & GOLDMAN

A Professional Corporation

Washington, D.C. Office
1250 24th Street, N.W.
Suite 300
Washington, D.C. 20037-1124
Tel (202) 466-0513
Fax (202) 466-0527

12100 Wilshire Boulevard, Suite 950
Los Angeles, California 90025-7114
Tel (310) 207-3233
Fax (310) 820-7444
www.baumhedlundlaw.com

Philadelphia Office
1500 Market Street
12th Floor East Tower
Philadelphia, PA 19102-2100
Tel (215) 665-5659
Fax (215) 569-8228

July 8, 2011

Donald Wright, MD MPH
Acting Director, Office of Research Integrity
U.S. Department of Health and Human Services
Office of Research Integrity
1101 Wootton Parkway, Suite 750
Rockville, Maryland 20852
Tel: 240-453-8200
Fax: 301-443-5351
Email: Don.Wright@hhs.gov

Re: Complaint of Scientific Misconduct against Dwight L. Evans, Laszlo Gyulai, Charles Nemeroff, Gary S. Sachs and Charles L. Bowden

Dear Dr. Wright:

On behalf of Dr. Jay D. Amsterdam, Professor of Psychiatry at the University of Pennsylvania, a charge of research misconduct is hereby submitted against Dr. Dwight L. Evans, Professor of Psychiatry and Chairman of the Department of Psychiatry at the University of Pennsylvania, Dr. Laszlo Gyulai, Associate Professor of Psychiatry at the University of Pennsylvania, Dr. Charles B. Nemeroff, Professor of Psychiatry and Chairman of the Department of Psychiatry at the University of Miami, Dr. Gary S. Sachs, Professor of Psychiatry at Harvard University, and Dr. Charles L. Bowden, Professor of Psychiatry and Chairman of the Department of Psychiatry at the University of Texas.

Dr. Amsterdam believes the individuals named above engaged in scientific misconduct by allowing their names to be appended to a manuscript that was drafted by a "medical communications company" (Scientific Therapeutics Information, "STI") hired by SmithKline Beecham (now known as GlaxoSmithKline, "GSK"), and which Dr. Amsterdam contends misrepresented information from a scientific research study (Paroxetine Study 352), which was funded by GSK and NIH. The manuscript (hereinafter "Study 352") was eventually published in the *American Journal of Psychiatry*

(158:906-912, June 2001) suggesting that Paxil may be beneficial in the treatment of bipolar depression, without acknowledging the medical communication company's contribution or the extent of GSK's involvement. The published manuscript was biased in its conclusions, made unsubstantiated efficacy claims and downplayed the adverse event profile of Paxil. (Attachment A.) Since its publication, study 352 has been cited in hundreds of medical journal articles, textbooks and practice guidelines up to 2011. (See, e.g., Attachment B and C.) Although Dr. Amsterdam was a Co-Principal Investigator of the study and possibly enrolled the largest number of patients, he was excluded from the final data review, analysis and publication. (See Attachment D.)

Dr. Amsterdam only recently became aware that two of the lead authors of Study 352, including his direct supervisor, were linked to ghostwriting through a letter from the Project On Government Oversight (POGO) to NIH Director Francis Collins in November 2010, posted on POGO's website at http://www.pogo.org/pogo-files/letters/public-health/ph-iis-20101129.html. Like the examples contained in POGO's letter to NIH, Dr. Amsterdam believes the manuscript published in the *American Journal of Psychiatry* was ghostwritten by STI, which was hired by GSK and paid with GSK funds, and that the individuals above lent their names as "authors" to the manuscript.

Based upon evidence presented in this complaint and the documents attached hereto, it appears that most, if not all, of the "guest authors" were determined by GSK in conjunction with the "medical communications" firm, STI. STI has had a long-standing history of ghostwriting scientific and medical articles and textbooks which have been attributed to prominently known academics - a practice that has been the subject of mounting criticism. See, for example, an editorial in the *Journal of the American Medical Association* regarding ghostwriting in relation to Merck's promotion and sales of VIOXX. (Attachment E.)

The acknowledgement section of the published manuscript states that Study 352 was conducted and published with support from NIMH grant MH-51761. (Attachment A.) According to a recent search of the NIH Reporter database, NIMH grant MH-51761 was part of an "infrastructure support" and "core-patient recruitment and assessment" project for NIH-funded clinical research trials. (Attachment F.) In this case, it was used to support the recruitment and assessment of research subjects for participation in this GSK-sponsored and GSK-funded clinical trial of Paxil for the treatment of patients with bipolar type I major depression.

According to a letter written by Dr. Francis Collins, Director of the NIH, ghostwriting that involves a federal grant may be cause for an investigation of plagiarism. Dr. Collins stated in his letter, which was published on POGO's website:

> [A] case of ghostwriting involving NIH-funded researchers may be appropriate for consideration as a case of plagiarism; i.e., the appropriation of another person's ideas, processes, results, or words without giving appropriate credit; or fabrication, i.e., making up data or results and recording or reporting them. Such a case would be handled by the Office of Research Integrity (ORI) of the Department of Health and Human Services (HHS), which investigates research misconduct as defined in the PHS's 42 C.F.R. Parts 50 and 93, Policies on Research Misconduct and the Final Rule.
>
> (Attachment G.)

Moreover, according to a report on ghostwriting by Senator Charles Grassley (dated June 24, 2010), the University of Pennsylvania considers ghostwriting to be equivalent to plagiarism.[1]

While this incident took place some time ago (i.e., 2001), the manuscript has been cited hundreds of times up through 2011 according to an internet search on Google Scholar. (Attachment B.) In fact, Dr. Gyulai cited the paper again in a study he published in 2007 in the *New England Journal of Medicine* (Attachment H) and Dr. Sachs cited the paper in 2011 in the *Journal of Clinical Psychiatry*. (See Attachment C, Record 1.)

Moreover, the purported "findings" of Study 352 and the published results from other studies and articles that have cited this study have been used to support the design and implementation of at least two other NIMH-funded grants to study the efficacy and safety of antidepressant drugs (like Paxil) in bipolar depression. See, e.g., MH080097, Prevention of Relapse and Recurrence of Bipolar Depression and MH060353, Treatment of Bipolar Type II Major Depression.

Dr. Amsterdam submits this complaint in the hopes that ORI will conduct an investigation, impose appropriate penalties to correct the past publication of Study 352's results, to prevent similar conduct from happening again, and hopefully prevent further use of this paper to support the dangerous prescription of Paxil to patients diagnosed with bipolar depression.

---

[1] See: http://grassley.senate.gov/about/upload/Senator-Grassley-Report.pdf

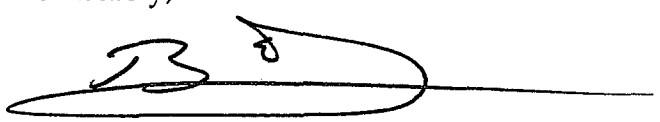
Pursuant to 42 C.F.R. Part 50.103(d)(13), Dr. Amsterdam should receive full and complete protection from retaliation and/or defamation by either the University of Pennsylvania or any other parties involved in the production and publication of Study 352. Dr. Amsterdam requests the protections described in ORI's "Handling Misconduct - Whistleblowers." (Attachment I.)

To ensure that this complaint is taken seriously, and to alert interested parties, we are providing copies of this correspondence to Senator Charles Grassley, Senator Herb Kohl, and the Chairman and Ranking members of the House Energy and Commerce, and the House Committee on Oversight and Government Reform.

In the following pages, we will lay out Dr. Amsterdam's complaint in more detail.

Thank you for your time and interest in this important matter. Please apprise me of any further help I may offer to you.

Sincerely,



Bijan Esfandiari, Esq.

BE:gb

cc:

Dr. Jay Amsterdam
Senator Charles Grassley
Senator Herb Kohl
Chairman, House Energy and Commerce, Fred Upton
Ranking Member, House Energy and Commerce, Henry Waxman
Chairman, House Committee on Oversight and Govt. Reform, Darrell E. Issa
Ranking Member, House Committee on Oversight and Govt. Reform, Elijah Cummings

DR. AMSTERDAM'S TIMELINE RE PUBLICATION OF PAXIL BIPOLAR STUDY 352 WITHOUT HIS KNOWLEDGE

In the mid-1990's, Dr. Amsterdam became a Co-Principal Investigator on a clinical trial, Paroxetine Study 352, comparing the antidepressant drugs imipramine (Tofranil®) and paroxetine (Paxil®) for the treatment of bipolar type I major depression (or manic depression). The trial was sponsored, in part, by GlaxoSmithKline which sells paroxetine under the brand names Paxil® in the US and Seroxat in other countries.

Dr. Amsterdam recruited one of the largest, if not the largest, patient samples into a study that comprised 18 other investigative-sites.

In early 2001, Dr. Amsterdam became aware that Dr. Dwight Evans and Dr. Laszlo Gyulai were attempting to publish data from the above referenced study. Although Dr. Amsterdam was a Co-Principal Investigator of Study 352 and enrolled one of the largest numbers of patients, he was excluded from the final data review, analysis and publication. (Attachment J, K, L and D.)

Dr. Amsterdam contacted his immediate supervisor and department chairman, Dr. Dwight L. Evans about the matter. In a March 22, 2001 email to Dr. Amsterdam, Dr. Evans stated that he had discussed the issue with Dr. Karl Rickels who was also a professor in the Department of Psychiatry at the University of Pennsylvania and Dr. Gyulai's direct supervisor. Dr. Evans assured Dr. Amsterdam that Dr. Rickels would be reviewing the matter and, once accomplished, he trusted there would be "an equitable outcome." (Attachment M.)

Dr. Amsterdam sent a follow-up email to Dr. Rickels on April 1, 2001 asking him what he had found during his investigation. Dr. Amsterdam explained to Dr. Rickels that, if he (Dr. Rickels) felt uncomfortable dealing with the matter, that he should let Dr. Amsterdam know so that he (Dr. Amsterdam) could "take up the issue with others at the University and/or the American Journal of Psychiatry." (Attachment J.) The American Journal of Psychiatry accepted the manuscript for publication in January 2001 (Attachment A at p. 911) and the study was eventually published in the June 2001 edition of the journal. *Id.*

On April 3, 2001, Dr. Rickels sent Dr. Amsterdam a letter discussing what he had learned during his investigation. (Attachment K.) In that letter, Dr. Rickels noted, among other things, the following information:

(1) Dr. Amsterdam was co-investigator of the trial;
(2) Dr. Amsterdam had enrolled more patients in the trial than Dr. Gyulai;
(3) The ghostwriting firm, STI, had chosen Dr. Gyulai as the paper's first author;
(4) GSK had decided to replace Dr. Gyulai as first author with Dr. Charles Nemeroff; and
(5) Academic investigators in the trial never reviewed or even saw the submitted manuscript.

On May 1, 2001, Dr. Amsterdam sent Drs. Evans and Rickels another email to explain that he was unsatisfied with the response and, since the last letter, there has been only "radio silence." As he wrote, *"Am I to assume that it is okay in this department for a junior faculty member to abscond with data from a full professor and publish it without any ramifications?"* (Attachment N.)

The following day, Dr. Rickels emailed Dr. Amsterdam and explained that Dr. Evans had tasked him (Dr. Rickels) with trying "to bring about a resolution." (Attachment O.)

On May 11, 2001, Dr. Amsterdam emailed Dr. Rickels and explained that he considered data that he (Dr. Amsterdam) accumulated in his research unit from the study "were misappropriated from me and used and published without my knowledge and without regard to the significant contribution that I made to this study." Dr. Amsterdam complained that the "theft and publication of [his] data should not go unnoticed and uncensured." He proposed that Dr. Gyulai write a letter of apology and be censured in order to ensure "this situation does not happen again." (Attachment P.)

Ten days later, Dr. Rickels emailed Dr. Amsterdam stating that he had shared Dr. Amsterdam's comments with Dr. Evans and, once he received a reply from Dr. Evans, he (Dr. Rickels) would like to meet with Dr. Amsterdam to discuss the topic. (Attachment Q.)

On Jun 13, 2001, Dr. Amsterdam again emailed Dr. Rickels to complain that there had been no resolution of the matter. Dr. Amsterdam wrote: *"Before I contact either University officials or the editorial board of [the American Journal of Psychiatry] regarding this egregious behavior, I await your last efforts at resolution of this problem."* (Attachment R.)

That same day, Dr. Rickels responded that Dr. Gyulai had been ill and that Dr. Amsterdam would be contacted soon. (Attachment S.)

On June 29, 2001, Dr. Amsterdam received a formal letter from Dr. Rickels stating that Dr. Gyulai had returned part-time from sick leave and he intended to speak with Dr. Gyulai concerning "this unfortunate situation ... today." (Attachment T.)

On July 5, 2001, Dr. Gyulai sent a letter of apology to Dr. Amsterdam. In that letter, Dr. Gyulai explained that control of the paper had been taken away from him and that GSK published the paper without circulating the draft to all the participants and only allowed him (Dr. Gyulai) to see a near-final draft "when only minor changes could be done." (Attachment L.)

Four days later, Dr. Amsterdam sent an email to Dr. Rickels stating that the apology was not sufficient in light of the "deliberate misappropriation and publication of [his] data" without his knowledge. Dr. Amsterdam was insistent that some sort of reprimand was necessary to ensure "plagiarism" of a colleague's data never happens again. (Attachment U.)

The following day, July 20, 2001, Dr. Rickels sent Dr. Amsterdam a letter stating "it is unfortunate that [GSK] did not circulate the manuscript to you and I regret that Dr. Gyulai did not share it with you. Once again, as Dr. Gyulai's Program Director, I have expressed my belief that he should have done so." (Attachment V.)

TIMELINESS OF COMPLAINT

According to Office of Research Integrity (ORI) guidelines, rules governing research misconduct only apply if such conduct occurred within six years, unless "the respondent continues or renews any incident of alleged research misconduct that occurred outside the six-year limit through the citation, republication or other use for the potential benefit of the research record that is the subject of the allegation."

With respect to this condition, although the data were published in an NIH-supported study in 2001, Dr. Gyulai cited this study just four years ago, in a study published in 2007 in the *New England Journal of Medicine*. (Attachment H, at page 3.) This is well within the six-year window for filing a complaint of research misconduct. Moreover, the report that appeared under Dr. Evans', Dr. Gyulai's and the other authors' names has had an ongoing influence on the scientific field as evidenced by its citation in hundreds of medical journal articles, textbooks and practice guidelines, up through and including 2011. (See Attachment B and C.)

EVIDENCE OF POTENTIAL GHOSTWRITING / ALLEGED PLAGIARISM

In defense of Dr. Gyulai, Dr. Rickels sent Dr. Amsterdam a letter on April 3, 2001, explaining that the "medical communications" firm, STI, had chosen Dr. Gyulai as the paper's first author. (Attachment K.)

At the time, Dr. Amsterdam was not aware of STI's involvement in ghostwriting scientific studies on behalf of prominent academics (including Dr. Evans and the other individuals named in this complaint) to promote sales of pharmaceutical agents. However, such behavior is now well understood. For instance, the *Journal of the American Medical Association* published an editorial in April 2008, excoriating Merck & Co. Inc. for using STI to publish a ghostwritten article in 2002 in JAMA to push sales of VIOXX. (Attachment E.) According to this editorial:

> Perhaps some editors, investigators, reviewers, and readers would see little or no harm in this failed disclosure because all other disclosures were made. However, if there was nothing to hide, why were the names (and affiliations) of the individuals who actually wrote at least the first draft of the manuscript omitted?

Indeed, although the spectral fingerprints of STI are readily apparent, STI's involvement was not disclosed in the manuscript draft or the final published article that appeared in the *American Journal of Psychiatry*. (Attachment A and D.)

As it turned out, Dr. Amsterdam discovered that his own supervisor, Dr. Dwight L. Evans, to whom Dr. Amsterdam had been complaining, published a scientific editorial in the prestigious journal *Biological Psychiatry* in 2003 that was ghostwritten by the very same "medical communications" firm that ghostwrote the 2001 *American Journal of Psychiatry* article (i.e., STI). Dr. Amsterdam discovered this while reviewing a letter that the Project On Government Oversight sent to NIH Director Frances Collins in November of 2010.[2]

According to documents, Sally Laden of STI ghostwrote the 2003 editorial for *Biological Psychiatry* for Dr. Dwight L. Evans and Dr. Dennis Charney. Dr. Charney was then an employee at the NIH Intramural Program and he is now Dean of Research at the Mt. Sinai School of Medicine in New York. (See e.g., Attachment W and http://www.pogo.org/pogo-files/letters/public-health/ph-iis-20101129.html.)

---

[2] See: http://www.pogo.org/pogo-files/letters/public-health/ph-iis-20101129.html

In an email to a GSK employee, Ms. Laden wrote, *"Is there a problem with my invoice for writing Dwight Evans' editorial for the [Depression and Bipolar Support Alliance]'s comorbidity issue to Biological Psychiatry?"* [See Attachment W] When the editorial was published, Drs. Evans and Charney "acknowledge[d] Sally K. Laden for editorial support." (Attachment X.)

In conclusion, it is ironic and troubling that Dr. Amsterdam brought his allegations of research misconduct to his direct supervisor and chairman, Dr. Evans, and his complaint was not only ignored by Dr. Evans (who simply handed it off to Dr. Rickels to resolve), but Dr. Evans himself was involved in the ghostwritten Study 352 article by STI and then, two years later, an editorial was also ghostwritten for him by STI.

DR. AMSTERDAM'S CRITICISMS OF THE PUBLISHED PAXIL BIPOLAR STUDY 352

First, the study failed to recruit a sufficient patient sample size to adequately test the primary efficacy outcome measure. The primary efficacy outcome measure failed to show superiority of either antidepressant drug treatment compared to placebo. This important information was not reported in the manuscript. The authors then relied on *post hoc* analyses of subsets of the data to find a favorable result for the antidepressant Paxil. Specifically, this result was accomplished by sub-dividing patient cohorts for each treatment into sub-groups of "high" (i.e., ≥8.0 mEq/L) versus "low" (i.e., <8.0 mEq/L) baseline serum lithium levels after the primary data analyses were found to be negative. This *post hoc* data presentation was then presented as the primary study finding, and gave the false impression that one group of patients with low lithium levels (who may be unable to tolerate higher lithium levels) showed superior benefit with Paxil versus placebo (compared to imipramine versus placebo).

Moreover, patients with "low" lithium levels were presented as being a distinct patient group who were somehow different from patients in the "high" lithium level group. In fact, this was a disingenuous distinction because all of the patients in the study had what were considered to be adequate and clinically therapeutic lithium levels, or they would have been discontinued from the trial. Moreover, this sub-division of treatment cohorts into "high" versus "low" lithium level groups was not clinically meaningful and these data were added to the manuscript to produce a favorable outcome finding for promoting Paxil (in a study that was otherwise negative in its findings and that recruited an insufficient patient sample size to accurately test the null hypothesis for the primary efficacy measures).

Second, the published manuscript downplayed a well-known (and potentially dangerous) adverse event profile of Paxil. For example, the manuscript did not report

any mania ratings (e.g., Young Mania Rating Scale), although the results section did note that end-point mania analyses were performed. The manuscript portrayed Paxil as being safe and producing no manic symptoms or manic episodes (in either the entire Paxil-treated patient group or in the "high" or "low" lithium level sub-groups), a finding which was not supported by available clinical or research evidence in 2001 (or subsequent to that date). As a result, the stated findings suggest that Paxil is a safe and well tolerated alternative to imipramine (the other antidepressant used in the study) which appeared to cause manic symptoms in both the "high" and "low" lithium level patient subgroups. Thus, these purported findings ran completely counter to almost all available clinical and research findings up to 2001 (and subsequent to that date), and suggested a treatment approach for bipolar depression (i.e., Paxil) which contradicted much of the available clinical and research evidence, as well as most published practice guidelines for treating bipolar type I depression.

Third, the results in the published manuscript emphasized a substantial side effect profile for imipramine while minimizing and down-playing the side effect profile of Paxil. For example, the manuscript emphasized a substantial rate of sexual side effects for imipramine (an antidepressant drug not particularly known to produce this side effect), while down-playing the sexual side effect profile of Paxil, and suggested that there were no sexual side effects encountered with Paxil in the study. This was a grossly misleading fact which was further emphasized by the authors citing the medical literature indicting only imipramine side effects while simultaneously omitting citations from the medical literature that accurately report the incidence of Paxil sexual side effects. In this regard, the published manuscript stated that *"patients treated with imipramine reported a higher incidence of abnormal ejaculation (18.8%) and impotence (25.0%) than did patients receiving paroxetine (0.0% and 6.3%, respectively) or placebo (5.0% and 0.0%, respectively)"*. Moreover, in the discussion section of the published manuscript, this "finding" is further supported by literature citing the high sexual side effect rate with imipramine while providing no citations for Paxil-induced side effects - even though Paxil's sexual side effects were well known at the time of publication. In fact, the side effect bias favoring Paxil was so supportive and contrary to the available medical literature in 2001 that it would be reasonable for a reader to wonder whether SmithKline Beecham, Inc. actually provided the side effect citations to the "authors" for publication in the published manuscript.

Alarmingly, despite the foregoing enumerated deficiencies, Study 352 and its published results have been relied upon as justification for prescribing Paxil to patients diagnosed with bipolar depression, a practice with little benefit, per the above, and substantial risk of stimulating a manic reaction with an increased risk of suicide and other dangerous adverse reactions.

* * * * *