

# United States Senate

COMMITTEE ON FINANCE

WASHINGTON, DC 20510-6200

June 4, 2008

## Via Electronic Transmission

Dr. Drew Gilpin Faust  
President  
Harvard University  
Massachusetts Hall  
Cambridge, MA 02138

Dr. Peter L. Slavin  
President  
Massachusetts General Hospital (Partners Healthcare)  
55 Fruit Street  
Boston, MA 02114

Dear Drs. Faust and Slavin:

The United States Senate Committee on Finance (Committee) has jurisdiction over the Medicare and Medicaid programs and, accordingly, a responsibility to the more than 80 million Americans who receive health care coverage under these programs. As Ranking Member of the Committee, I have a duty to protect the health of Medicare and Medicaid beneficiaries and safeguard taxpayer dollars appropriated for these programs. The actions taken by thought leaders, like those at Harvard Medical School who are discussed throughout this letter, often have a profound impact upon the decisions made by taxpayer funded programs like Medicare and Medicaid and the way that patients are treated and funds expended.

Moreover, and as has been detailed in several studies and news reports, funding by pharmaceutical companies can influence scientific studies, continuing medical education, and the prescribing patterns of doctors. Because I am concerned that there has been little transparency on this matter, I have sent letters to almost two dozen research universities across the United States. In these letters, I asked questions about the conflict of interest disclosure forms signed by some of their faculty. Universities require doctors to report their related outside income, but I am concerned that these requirements are disregarded sometimes.

I have also been taking a keen interest in the almost \$24 billion annually appropriated to the National Institutes of Health to fund grants at various institutions such as yours. As you know, institutions are required to manage a grantee's conflicts of interest.<sup>[1]</sup> But I am learning that this task is made difficult because physicians do not consistently report all the payments received from drug companies.

To bring some greater transparency to this issue, Senator Kohl and I introduced the Physician Payments Sunshine Act (Act). This Act will require drug companies to report publicly any payments that they make to doctors, within certain parameters.

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<sup>[1]</sup> Responsibility of Applicants for Promoting Objectivity in Research for Which PHS Funding is Sought, 42 C.F.R. 50 (1995).

I am writing to try and assess the implementation of financial disclosure policies of Harvard University (Harvard) and Massachusetts General Hospital (MGH/Partners), (the Institutions). In response to my letters of June 29, October 25, and October 26, 2007, your Institutions provided me with the financial disclosure reports that Drs. Joseph Biederman, Thomas Spencer, and Timothy Wilens (Physicians) filed during the period of January 2000 through June 2007.

My staff investigators carefully reviewed each of the Physicians' disclosure forms and detailed the payments disclosed. I then asked that your Institutions confirm the accuracy of the information. In March 2008, your Institutions then requested additional information from the Physicians pursuant to my inquiry. That information was subsequently provided to me.<sup>[2]</sup>

In their second disclosures to your Institutions, the Physicians revealed different information than they had disclosed initially to your respective Institutions. On April 29, 2008, I received notification from Harvard Medical School's Dean for Faculty and Research Integrity that he has referred the cases of these Physicians to the Standing Committee on Conflicts of Interest and Commitment ("Standing Committee"). The Chief Academic Officer (CAO), Partners HealthCare System, also wrote me that Partners will look to the Standing Committee to conduct the initial factual review of potential non-compliance that are contained in both the Harvard Medical School Policy and the Partners Policy. In addition, the CAO stated that, in addition to the Standing Committee's review process, Partners will conduct its own independent review of conflicts of interest disclosures these Physicians submitted separately to Partners in connection with publicly funded research and other aspects of Partners Policy. I look forward to being updated on these reviews in the near future.

In addition, I contacted executives at several major pharmaceutical companies and asked them to list the payments that they made to Drs. Biederman, Spencer, and Wilens during the years 2000 through 2007. These companies voluntarily and cooperatively reported additional payments that the Physicians do not appear to have disclosed to your Institutions.

Because these disclosures do not match, I am attaching a chart intended to provide a few examples of the data that have been reported me. This chart contains three columns: payments disclosed in the forms the physicians filed at your Institutions, payments revealed in March 2008, and amounts reported by some drug companies.

I would appreciate further information to see if the problems I have found with these three Physicians are systemic within your Institutions.

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<sup>[2]</sup> Letters from Harvard/Mass General Hospital to Drs. Joseph Biederman, Thomas Spencer, and Timothy Wilens, dated March 4, 2008. ("[W]e have been reviewing your conflicts of interest disclosure forms and have a number of questions regarding your compliance with Harvard Medical School's conflict of interest policies.")

## **INSTITUTIONAL AND NIH POLICIES**

Both Harvard and MGH/Partners have established an income *de minimus* limit. This policy forbids researchers working at your Institutions from conducting clinical trials with a drug or technology if they receive payments over \$20,000 from the company that manufactures that drug or technology. Prior to 2004, the income *de minimus* limit established by your institutions was \$10,000.

Further, federal regulations place several requirements on a university/hospital when its researchers apply for NIH grants.<sup>[3]</sup> These regulations are intended to ensure a level of objectivity in publicly funded research, and state in pertinent part that NIH investigators must disclose to their institution any “significant financial interest”<sup>[4]</sup> that may appear to affect the results of a study. NIH interprets “significant financial interest” to mean at least \$10,000 in value or 5 percent ownership in a single entity.

Based upon information available to me, it appears that each of the Physicians identified above received grants to conduct studies involving atomoxetine, a drug that sells under the brand name Strattera.<sup>[5]</sup> For example:

- In 2000, the NIH awarded Dr. Biederman a grant to study atomoxetine in children.<sup>[6]</sup> At that time, Dr. Biederman disclosed that he received less than \$10,000 in payments from Eli Lilly & Company (Eli Lilly). But Eli Lilly reported that it paid Dr. Biederman more than \$14,000 for advisory services that year—a difference of at least \$4,000.
- In 2004, the NIH awarded Dr. Wilens a 5-year grant to study atomoxetine.<sup>[7]</sup> In his second disclosure to your Institutions, Dr. Wilens revealed that he received \$7,500 from Eli Lilly in 2004. But Eli Lilly reported to me that it paid Dr. Wilens \$27,500 for advisory services and speaking fees in 2004—a difference of about \$20,000.

It is my understanding that Dr. Wilens’ NIH-funded study of atomoxetine is still ongoing. According to Eli Lilly, it paid Dr. Wilens almost \$65,000 during the period January 2004 through June 2007. However, as of March 2008, and based upon the

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<sup>[3]</sup> Id.; see also <http://grants.nih.gov/grants/partners/0706NIHExtramuralNexus.pdf>.

<sup>[4]</sup> “Significant Financial Interest” is defined by the regulation as anything of monetary value, including but not limited to: salary or other payments for services (e.g., consulting fees or honoraria); equity interests (e.g., stocks, stock options or other ownership interests); intellectual property rights (e.g., patents, copyrights and royalties from such rights).

<sup>[5]</sup> Atomoxetine is approved for children, adolescents, and adults, although it was determined to increase the risk of suicidal thoughts among children. On September 29, 2005, FDA required a black box on the label for an increased risk of suicidal thinking in children and adolescents being treated with this drug.

<sup>[6]</sup> NIH grant, “Safety & Pharmacokinetic Study of Tomoxetine Hydrochloride in Pediatrics,” to study Attention Deficit Hyperactivity Disorder (ADHD) in children using atomoxetine. (Grant No. 3M01RR001066-23S10328).

<sup>[7]</sup> National Institutes of Health, grant number 1K24DA016264. Study of Atomoxetine in Adolescents with ADHD and Substance Use Disorder (SUD).

documents provided to us to date, Dr. Wilens disclosed payments of about half of the amount reported by Eli Lilly for this period. Dr. Wilens also did three other studies of atomoxetine in 2006 and 2007.<sup>[8]</sup>

I have also found several instances where these Physicians apparently received income above your institutions' income *de minimus* limit. For instance, in 2003, Dr. Spencer conducted a study of atomoxetine in adolescents.<sup>[9]</sup> At the time, he disclosed no significant financial interests related to this study. But Eli Lilly reported paying Dr. Spencer over \$25,000 that year.

In 2001, Dr. Biederman disclosed plans to begin a study sponsored by Cephalon, Inc.<sup>[10]</sup> At the time; Dr. Biederman disclosed that he had no financial relationship with the sponsor of this study. Yet, on his conflict of interest disclosure, he acknowledged receiving research support and speaking fees from Cephalon, Inc., but did not provide any information on the amounts paid. In March 2008, Dr. Biederman revealed that Cephalon, Inc. paid him \$13,000 in 2001.

In 2005, Dr. Biederman began another clinical trial sponsored by Cephalon, Inc., which was scheduled to start in September 2005 and end in September 2006.<sup>[11]</sup> Initially, Dr. Biederman disclosed that he had no financial relationship with the sponsor of this study. But in March 2008, Dr. Biederman revealed that Cephalon, Inc. paid him \$11,000 for honoraria in 2005 and an additional \$24,750 in 2006.

In light of the information set forth above, I ask your continued cooperation in examining conflicts of interest. In my opinion, institutions across the United States must be able to rely on the representations of its faculty to ensure the integrity of medicine, academia, and the grant-making process. At the same time, should the Physician Payments Sunshine Act become law, institutions like yours will be able to access a database that will set forth the payments made to all doctors, including your faculty members. Indeed at this time there are several pharmaceutical and device companies that are looking favorably upon the Physician Payments Sunshine Bill and for that I am gratified.

Accordingly, I request that your respective institutions respond to the following questions and requests for information. For each response, please repeat the enumerated request and follow with the appropriate answer.

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<sup>[8]</sup> Atomoxetine and Methylphenidate (MPH) in ADHD (2006); Atomoxetine in Adolescents with Marijuana Use Disorders and ADHD (2006); and A Controlled Study of Adjunct Atomoxetine with Methylphenidate in Pediatric ADHD (2007).

<sup>[9]</sup> Atomoxetine in Adolescents with ADHD and SUD.

<sup>[10]</sup> Protocol C1538a/213/AD/US.

<sup>[11]</sup> A Phase II Study to Assess the Safety, Tolerability, and Efficacy of SPD503 Administered to Children and Adolescents aged 6-17 with ADHD.

1. For each of the NIH grants received by the Physicians, please confirm that the Physicians reported to Harvard and MGH/Partners' designated official "the existence of [his] conflicting interest." Please provide separate responses for each grant received for the period from January 1, 2000 to the present, and provide any supporting documentation for each grant identified.
2. For each grant identified above, please explain how Harvard and MGH/Partners ensured "that the interest has been managed, reduced, or eliminated?" Please provide an individual response for each grant that each doctor received from January 2000 to the present, and provide any documentation to support each claim.
3. Please report on the status of the Harvard Standing Committee and additional Partners reviews of the discrepancies in disclosures by Drs. Biederman, Spencer and Wilens, including what action, if any, will be considered.
4. For Drs. Biederman, Spencer, and Wilens, please report whether a determination can be made as to whether or not any doctor violated guidelines governing clinical trials and the need to report conflicts of interest to an institutional review board (IRB). Please respond by naming each clinical trial for which the doctor was the principal investigator, along with confirmation that conflicts of interest were reported, if possible.
5. Please provide a total dollar figure for all NIH monies annually received by Harvard and MGH/Partners, respectively. This request covers the period of 2000 through 2007.
6. Please provide a list of all NIH grants received by Harvard and MGH/Partners. This request covers the period of 2000 through 2007. For each grant please provide the following:
  - a. Primary Investigator;
  - b. Grant Title;
  - c. Grant number;
  - d. Brief description; and
  - e. Amount of Award.

Thank you again for your continued cooperation and assistance in this matter. As you know, in cooperating with the Committee's review, no documents, records, data or information related to these matters shall be destroyed, modified, removed or otherwise made inaccessible to the Committee.

I look forward to hearing from you by no later than June 18, 2008. All documents responsive to this request should be sent electronically in PDF format to [Brian\\_Downey@finance-rep.senate.gov](mailto:Brian_Downey@finance-rep.senate.gov). If you have any questions, please do not hesitate to contact Paul Thacker at (202) 224-4515.

Sincerely,



Charles E. Grassley  
Ranking Member

Attachment

**Selected Disclosures by Dr. Biederman and Related Information Reported by  
Pharmaceutical Companies**

<b>Year</b>	<b>Company</b>	<b>Disclosure Filed with Institution</b>	<b>Payments Revealed in March 2008</b>	<b>Amount Company Reported</b>
2000	GlaxoSmithKline	Not reported	\$2,000	\$3,328
	Eli Lilly & Company	<\$10,000	\$3,500	\$14,105
	Pfizer Inc.	Not reported	\$7,000	\$7,000
2001	Cephalon	No amount provided	\$13,000	n/a
	GlaxoSmithKline	No amount provided	\$5,500	\$4,428
	Eli Lilly & Company	No amount provided	\$6,000	\$14,339
	Johnson & Johnson	Not reported	\$3,500	\$58,169
	Medical Education Systems	Not reported	\$21,000	n/a
	Pfizer Inc.	No amount provided	\$5,625	\$5,625
2002	Bristol-Myers Squibb	No amount provided	\$2,000	\$2,000
	Cephalon	No amount provided	\$3,000	n/a
	Colwood	Not reported	\$14,000	n/a
	Eli Lilly & Company	No amount provided	\$11,000	\$2,289
	Johnson & Johnson	Not reported	Not reported	\$706
	Pfizer Inc.	No amount provided	\$4,000	\$2,000
2003	Bristol-Myers Squibb	No amount provided	\$500	\$250
	Cephalon	<\$10,000	\$4,000	n/a
	Eli Lilly & Company	<\$10,000	\$8,250	\$18,347
	Johnson & Johnson	<\$10,000	\$2,000	\$2,889
	Medlearning	Not reported	\$26,500	n/a
	Pfizer Inc.	<\$10,000	\$1,000	\$1,000
2004	Bristol-Myers	No amount provided	\$6,266	\$6,266

<b>Year</b>	<b>Company</b>	<b>Disclosure Filed with Institution</b>	<b>Payments Revealed in March 2008</b>	<b>Amount Company Reported</b>
	Squibb			
	Cephalon	Not reported	\$4,000	n/a
	Eli Lilly & Company	No amount provided	\$8,000	\$15,686
	Johnson & Johnson	Not reported	Not reported	\$902
	Medlearning	Not reported	\$26,000	n/a
2004 (Con't.)	Pfizer Inc.	Not reported	\$3,000	\$4,000
2005	Cephalon	Not reported	\$11,000	n/a
	Eli Lilly & Company	<\$20,000	\$12,500	\$7,500
	Johnson & Johnson	Not reported	Not reported	\$962
	Pfizer Inc.	Not reported	\$3,000	\$3,000
	Medlearning	Not reported	\$34,000	n/a
2006	Cephalon	Not reported	\$24,750	n/a
	Johnson & Johnson	Not reported	Not reported	\$750
	Primedia	Not reported	\$56,000	n/a
2007	Primedia	Not reported	\$30,000	n/a

Note 1: Dr. Biederman revealed in March 2008 that his outside income totaled about \$1.6 million during the period January 2000 through June 2007. Information reported by the pharmaceutical companies indicate that they made additional payments that are not reflected in Dr. Biederman's disclosures.

Note 2: When a Physician named a company in a disclosure but did not provide an amount, the text reads "no amount reported." When a Physician did not list the company in the disclosure, the column reads "not reported." The Committee contacted several companies for payment information and the notation n/a (not available) reflects that a company was not contacted.

**Selected Disclosures by Dr. Spencer and Related Information Reported by  
Pharmaceutical Companies**

<b>Year</b>	<b>Company</b>	<b>Disclosure Filed with Institution</b>	<b>Payments Revealed in March 2008</b>	<b>Amount Company Reported</b>
2000	GlaxoSmithKline	Not reported	\$3,000	\$1,500
	Eli Lilly & Company	Not reported	\$12,345	\$11,463
2001	GlaxoSmithKline	Not reported	\$4,000	\$1,000
	Eli Lilly & Company	Not reported	\$8,500	\$10,859
	Strategic Implications	Not reported	\$16,800	n/a
2002	GlaxoSmithKline	Not reported	\$3,000	\$3,369
	Eli Lilly & Company	Not reported	\$14,000	\$14,016
	Strategic Implications	Not reported	\$29,000	n/a
2003	Eli Lilly & Company	Not reported	\$6,000	\$25,500
	Johnson & Johnson	Not reported	\$1,250	\$0
	Thomson Physicians World	Not reported	\$46,500	n/a
2004	Eli Lilly & Company	Not reported	Not reported	\$23,000
	Pfizer Inc.	Not reported	\$3,500	\$3,500
2005	Eli Lilly & Company	<\$20,000	\$6,000	\$7,500
	Johnson & Johnson	Not reported	\$1,500	\$227
	Medlearning	Not reported	\$28,250	n/a
2006	Eli Lilly & Company	No amount provided	\$15,688	\$8,188
	Johnson & Johnson	Not reported	\$5,500	\$0
	Primedia	Not reported	\$44,000	n/a
2007	Eli Lilly & Company	No amount provided	\$6,000	\$16,188

Note 1: Dr. Spencer revealed in March 2008 that his outside income totaled about \$1 million during the period January 2000 through June 2007. Information reported by the pharmaceutical companies indicate that they made additional payments that are not reflected in Dr. Spencer's disclosures.

Note 2: When a Physician named a company in a disclosure but did not provide an amount, the text reads “no amount reported.” When a Physician did not list the company in the disclosure, the column reads “not reported.” The Committee contacted several companies for payment information and the notation n/a (not available) reflects that a company was not contacted.

**Selected Disclosures by Dr. Wilens and Related Information Reported by  
Pharmaceutical Companies**

<b>Year</b>	<b>Company</b>	<b>Disclosure Filed with Institution</b>	<b>Payments Revealed in March 2008</b>	<b>Amount Company Reported</b>
2000	GlaxoSmithKline	Not reported	\$5,250	\$12,009
	Eli Lilly & Company	Not reported	\$2,000	\$2,057
	Pfizer Inc.	Not reported	\$1,250	\$2,250
	TVG	Not reported	\$11,000	n/a
2001	GlaxoSmithKline	<\$10,000	n/a	\$2,269
	Eli Lilly & Company	No amount provided	\$3,952	\$952
	J.B. Ashtin	Not reported	\$14,500	n/a
2002	GlaxoSmithKline	Not reported	\$7,500	\$10,764
	Eli Lilly & Company	Not reported	\$4,500	\$3,000
	Pfizer Inc.	Not reported	\$1,500	\$1,500
	Phase 5	Not reported	\$20,000	n/a
2003	Eli Lilly & Company	Not reported	\$12,000	\$0
	Phase 5	Not reported	\$90,500	n/a
	TVG	Not reported	\$31,000	n/a
	Medlearning	Not reported	\$24,000	n/a
2004	Eli Lilly & Company	Not reported	\$7,500	\$27,500
	Phase 5	Not reported	\$84,250	n/a
	Medlearning	Not reported	\$46,000	n/a
2005	Eli Lilly & Company	<\$20,000	\$9,500	\$9,500
	Promedix	Not reported	\$70,000	n/a
	Advanced Health Media	Not reported	\$37,750	n/a
2006	Eli Lilly and Physician World (Lilly)	No amount provided	\$5,963	\$12,798
	Advanced Health Media	Not reported	\$56,000	n/a
	Primedia	Not reported	\$32,000	n/a

2007	Eli Lilly & Company	Not reported	\$9,000	\$14,969
	Veritas	Not reported	\$25,388	n/a

Note 1: Dr. Wilens revealed in March 2008 that his outside income totaled about \$1.6 million during the period January 2000 through June 2007. Information reported by the pharmaceutical companies indicate that they made additional payments that are not reflected in Dr. Spencer's disclosures.

Note 2: When a Physician named a company in a disclosure but did not provide an amount, the text reads "no amount reported." When a Physician did not list the company in the disclosure, the column reads "not reported." The Committee contacted several companies for payment information and the notation n/a (not available) reflects that a company was not contacted.