

Mr. GRASSLEY. Mr. President, starting last year, I started looking at the financial relationships between physicians and drug companies. I first began this inquiry by examining payments from Astra Zeneca to Dr. Melissa DelBello, a professor of psychiatry at the University of Cincinnati.

In 2002, Dr. DelBello published a study that found that Seroquel worked for kids with bipolar disorder. The study was paid for by Astra Zeneca, and the following year that company paid Dr. DelBello around \$100,000 for speaking fees and honoraria. In 2004, Astra Zeneca paid Dr. DelBello over \$80,000.

Today, I would like to talk about three physicians at Harvard Medical School--Drs. Joseph Biederman, Thomas Spencer, and Timothy Wilens. They are some of the top psychiatrists in the country, and their research is some of the most important in the field. They have also taken millions of dollars from the drug companies.

Out of concern about the relationship between this money and their research, I asked Harvard and Mass General Hospital last October to send me the conflict of interest forms that these doctors had submitted to their institutions. Universities often require faculty to fill these forms out so that we can know if the doctors have a conflict of interest.

The forms I received were from the year 2000 to the present. Basically, these forms were a mess. My staff had a hard time figuring out which companies the doctors were consulting for and how much money they were making. But by looking at them, anyone would be led to believe that these doctors were not taking much money. Over the last 7 years, it looked like they had taken a couple hundred thousand dollars.

But last March, Harvard and Mass General asked these doctors to take a second look at the money they had received from the drug companies. And this is when things got interesting. Dr. Biederman suddenly admitted to over \$1.6 million dollars from the drug companies. And Dr. Spencer also admitted to over \$1 million. Meanwhile, Dr. Wilens also reported over \$1.6 million in payments from the drug companies.

The question you might ask is: Why weren't Harvard and Mass General watching over these doctors? The answer is simple: They trusted these physicians to honestly report this money.

Based on reports from just a handful of drug companies, we know that even these millions do not account for all of the money. In a few cases, the doctors disclosed more money than the drug companies reported. But in most cases, the doctors reported less money.

For instance, Eli Lilly has reported to me that they paid tens of thousands of dollars to Dr. Biederman that he still has not accounted for. And the same goes for Drs. Spencer and Wilens.

What makes all of this even more interesting is that Drs. Biederman and Wilens were awarded grants from the National Institutes of Health to study the drug Strattera.

Obviously, if a researcher is taking money from a drug company while also receiving Federal dollars to research that company's product, then there is a conflict of interest. That is why I am asking the National Institutes of Health to take a closer look at the grants they give to researchers. Every year, the NIH hands out almost \$24 billion in grants. But nobody is watching

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to ensure that the conflicts of interest are being monitored.

That is why Senator Kohl and I introduced the Physician Payments Sunshine Act. This bill will require companies to report payments that they make to doctors. As it stands right now, universities have to trust their faculty to report this money. And we can see that this trust is causing the universities to run afoul of NIH regulations. This is one reason why industry groups such as PhRMA and Advamed, as well as the American Association of Medical Colleges, have all endorsed my bill. Creating one national reporting system, rather than relying on a hodge-podge of state systems and some voluntary reporting systems, is the right thing to do.

Before closing, I would like to say that Harvard and Mass General have been extremely cooperative in this investigation, as have Eli

Lilly, Astra Zeneca and other companies. I ask unanimous consent that my letters to Harvard, Mass General, and the NIH be printed the Record.

There being no objection, the material was ordered to be printed in the RECORD, as follows:

U.S. SENATE,

COMMITTEE ON FINANCE,

Washington, DC, June 4, 2008.

ELIAS A. ZERHOUNI, M.D.

Director, National Institutes of Health,
Bethesda, Maryland.

DEAR DIRECTOR ZERHOUNI: As a senior member of the United States Senate and the Ranking Member of the Committee on Finance (Committee), I have a duty under the Constitution to conduct oversight into the actions of executive branch agencies, including the activities of the National Institutes of Health (NIH/Agency). In this capacity, I must ensure that NIH properly fulfills its mission to advance the public's welfare and makes responsible use of the public funding provided for medical studies. This research often forms the basis for action taken by the Medicare and Medicaid programs.

Over the past number of years, I have become increasingly concerned about the lack of oversight regarding conflicts of interest relating to the almost \$24 billion in annual extramural funds that are distributed by the NIH. In that regard, I would like to take this opportunity to notify you about five problems that have come to my attention on this matter.

First, it appears that three researchers failed to report in a timely, complete and accurate manner their outside income to Harvard University (Harvard) and Massachusetts General Hospital (MGH). By not reporting this income, it seems that they are placing Harvard and MGH in jeopardy of violating NIH regulations on conflicts of interest. I am attaching that letter for your review and consideration.

Second, I am requesting an update about a letter I sent you last October on problems with conflicts of interest and NIH extramural funding regarding Dr. Melissa DelBello at the University of Cincinnati (University). In that letter, I notified you that Dr. DelBello receives grants from the NIH, however, she was failing to report her outside income to her University.

Third, the Inspector General for the Department of Health and Human Services Office (HHS OIG) released a disturbing report last January which found that NIH provided almost no oversight of its extramural funds. But your staff seemed to show little interest in this report. In fact, Norka Ruiz Bravo, the NIH deputy director of extramural programs was quoted in The New York Times saying, ``For us to try to manage directly the conflict-of-interest of an NIH investigator would be not only inappropriate but pretty much impossible."

Fourth, I am dismayed to have read of funding provided to several researchers from the Foundation for Lung Cancer: Early Detection, Prevention & Treatment (Foundation). Dr. Claudia Henschke and Dr. David Yankelevitz are two of the Foundation's board members. As reported by The New York Times, the Foundation was funded almost entirely with monies from tobacco companies, and this funding was never fully disclosed. Monies from the Foundation were then used to support a study that appeared in The New England Journal of Medicine (NEJM) back in 2006 regarding the use of computer tomography screening to detect lung cancer. The NEJM disclosure states that the study was supported also by NIH grants held by Drs. Henschke and Yankelevitz.

Regarding the lack of transparency by Dr. Henschke and Dr. Yankelevitz, National Cancer Institute Director John Niederhuber told the Cancer Letter, ``[W]e must always be transparent regarding any and all matters, real or perceived, which might call our scientific work into question."

The NEJM later published a clarification regarding its earlier article and a correction revealing that Dr. Henschke also received royalties for methods to assess tumors with imaging technology. There is no evidence that the Foundation's tobacco money or Dr. Henschke's royalties influenced her research. But I am concerned that the

funding source and royalties may have not been disclosed when the NIH decided to fund Dr. Henschke.

Fifth, I sent you a letter on April 15, outlining my concerns about a report on the National Institute of Environmental Health Sciences (NIEHS). That report found 45 cases at the NIEHS where extramural grants had not receiving sufficient peer review scores but were still funded. This finding is yet another example that the NIH provides little oversight for its extramural program.

Dr. Zerhouni, you faced similar scandals back in 2003 when it came to light that many NIH intramural researchers enjoyed lucrative arrangements with pharmaceutical companies. It took you some time, but you eventually brought some transparency, reform and integrity back to NIH. As you told Congress during one hearing, "I have reached the conclusion that drastic changes are needed as a result of an intensive review by NIH of our ethics program, which included internal fact-finding as well as an external review by the Blue Ribbon Panel."

NIH oversight of the extramural program is lax and leaves people with nothing more than questions--\$24 billion worth of questions, to be exact. I am interested in understanding how you will address this issue. American taxpayers deserve nothing less.

In the interim, I ask you to respond to the following requests for information and documents. In responding to each request, first repeat the enumerated question followed by the appropriate response. Your responses should encompass the period of January 1, 2000 to April 1, 2008. I would appreciate receiving responses to the following questions by no later than June 18, 2008:

1. Please explain what actions the NIH has or will initiate to provide better oversight and transparency for its extramural funding program.

2. Please explain how often the NIH has investigated and/or taken action regarding a physician's failure to report a "significant financial interest," as defined by NIH regulation. For each investigation, please provide the following information:

- a. Name of the Doctor(s) involved;

- b. Date investigation began and the date ended;
- c. Specific allegations which triggered investigation;
- d. Findings of the investigation; and
- e. Actions taken by the NIH, if any.

3. Since receiving notice that the University of Cincinnati was provided incomplete information from Dr. DelBello regarding her outside income, what steps has/will NIH take to address this issue? Please be specific.

4. Please provide a list of all NIH grants received by Dr. DelBello. For each grant, please provide the following:

- a. Name of grant;
- b. Topic of grant; and
- c. Amount of funding for grant.

5. Please provide a list of any other interactions that Dr. DelBello has had with the NIH to include membership on advisory boards, peer review on grants, or the like.

6. Since reports appeared in the press regarding the undisclosed funding of the Foundation for Lung Cancer: Early Detection, Prevention & Treatment, what steps has/will NIH take to address this issue? Please provide all external and internal communications regarding this issue.

7. Please provide a list off all NIH grants received by Dr. Claudia Henschke. For each grant, please provide the following:

- a. Name of grant;
- b. Topic of grant; and
- c. Amount of funding for grant.

8. Please provide a list of any other interactions that Dr. Henschke has had with the NIH to include membership on advisory boards, peer review on grants, or the like.

9. Please provide a list off all NIH grants received by Dr. David Yankelevitz. For each grant, please provide the following:

- a. Name of grant;
- b. Topic of grant; and
- c. Amount of funding for grant.

10. Please provide a list of any other interactions that Dr. Yankelevitz has had with the NIH to include membership on advisory boards, peer review on grants, or the like.

11. Please provide a list off all NIH grants received by Dr. Joseph Biederman. For each grant, please provide the following:

- a. Name of grant;
- b. Topic of grant; and
- c. Amount of funding for grant.

12. Please provide a list of any other interactions that Dr. Biederman has had with the NIH to include membership on advisory boards, peer review on grants, or the like.

13. Please provide a list off all NIH grants received by Dr. Timothy Wilens. For each grant, please provide the following:

- a. Name of grant;
- b. Topic of grant; and
- c. Amount of funding for grant.

14. Please provide a list of any other interactions that Dr. Wilens has had with the NIH to include membership on advisory boards, peer review on grants, or the like.

I request your prompt attention to this matter and your continued cooperation. I also request that the response to this letter contain your personal signature. If you have any questions please contact my Committee staff, Paul Thacker at (202) 224-4515. Any formal correspondence should be sent electronically in PDF searchable format to brian--downey@finance-rep.senate.gov.

Sincerely,

CHARLES E. GRASSLEY,
Ranking Member.

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U.S. SENATE,

COMMITTEE ON FINANCE,

Washington, DC, June 4, 2008.
Dr. DREW GILPIN FAUST,
President, Harvard University,
Massachusetts Hall, Cambridge, MA.
Dr. PETER L. SLAVIN,
President, Massachusetts General Hospital (Partners Healthcare),
Boston, MA.

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. 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.

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.

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.

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. 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" 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. For example:

In 2000, the NIH awarded Dr. Biederman a grant to study atomoxetine in children. 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. 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 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.

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. 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. 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. 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.

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.

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.

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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 XDowney@finance-rep.senate.gov](mailto:BrianXDowney@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.