Appendix D:

Selected pharmaceutical industry documents and correspondence

[Congressional Record Volume 154, Number 91 (Wednesday, June 4, 2008)]
[Senate]
[Pages S5029-S5033]
From the Congressional Record Online through the Government Publishing Office [www.gpo.gov]See URL: https://www.govinfo.gov/content/pkg/CREC-2008-06-04/html/CREC-2008-06-04-pt1-PgS5029-2.htm

PAYMENTS TO PHYSICIANS

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.

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. If you have any questions, please do not hesitate to contact Paul Thacker at (202) 224-4515.

Sincerely,

Charles E. Grassley,
Ranking Member.

SELECTED DISCLOSURES BY DR. BIEDERMAN AND
RELATED INFORMATION REPORTED BY PHARMACEUTICAL COMPANIES

Year	Company	Disclosure filed with institution	Payments revealed in March 2008	Amount company Reported
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 Squibb	No amount provided	6,266	6,266
	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
	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

Year	Company	Disclosure filed with institution	Payments revealed in March 2008	Amount company reported
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

Year	Company	Disclosure filed with institution	Payments revealed in March 2008	Amount company reported

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

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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.

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	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
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	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 Squibb	No amount provided	6,266	6,266
	Cephalon	Not reported	4,000	n/a
	Eli Lilly & Company	No amount provided	8,000	15,686
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	Medlearning	Not reported	26,000	n/a
	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

Year	Company	Disclosure filed with institution	Payments revealed in March 2008	Amount company reported
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	Not reported	46,500	n/a

	World.			
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

Year	Company	Disclosure filed with institution	Payments revealed in March 2008	Amount company reported
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.

D2 – Janssen email about MGH PBD seminar

Parish, Irene [JANUS]

From: Pandina, Gahan [JANUS]
Sent: Friday, March 22, 2002 9:38 AM
To: Cote, Christine [JANUS]; Mahmoud, Ramy [JANUS]; Deloria, Carmen [JANUS]
Subject: Feedback regarding MGH pediatric seminar

Christine, Ramy, and Carmen,

Georges and I wanted to share some information as a follow-up to the meeting with Dr. Biederman. This feedback came from an attendee of the large 3-day educational seminar (over 1000 physicians, $700 CME course) in child psychopharmacology and pediatric bipolar disorder that Dr. Biederman and his group conducted. This meeting began the day immediately after our meeting with him at Janssen last week. Dr. Biederman was very well-received by the group. The validity of the diagnosis of Pediatric Mania was completely accepted, and his diagnostic techniques deemed to be excellent. He was very balanced in his approaches to treatment, and not perceived to be aligned with any company in particular. Evidently, he made quite a point regarding the metabolic issues related to olanzapine, to the extent of stating that this drug should not be used in the treatment of children and adolescents, highlighting the issues with published data.

I think this is a clear example of the utility of partnering with a group such as MGH, who has the potential of reaching and having a significant impact upon the field of child and adolescent psychiatry with these types of professional activities in non-sponsored venues.

Regards,

Gahan

Gahan J. Pandina, Ph.D.
Assistant Director, CNS Clinical Development
Janssen Pharmaceutica Products, L.P.
1125 Trenton-Harbourton Rd • Titusville, NJ 08560
OFFICE: (609) 730 2324 • **FAX:** (609) 730 3125
EMAIL: gpandina@janus.jnj.com

D3 - Janssen email about KOL speaker payment

From: Wolfe, Michael A. (JAN)
Sent: Sunday, November 21, 1999 4:05 PM
To: Sachak, Sohel [JANUS]; Bruins, John [JANUS]
Cc: Burgos, Licette [JANUS]; Mahmoud, Ramy [JANUS]
Subject: RE: Dr. Joseph Biederman payment

John and Sohel,

I am not aware of these issues with the exception of what was discussed with Sohel over the past two weeks via aspen. Let me know if I can be of assistance. I am not sure who or where the field sales force (which ever one it was -HS, CNS or Eldercare) made this commitment. But, we need to make this right with Dr. Biederman. Johns, please advise me on how we can support you with this effort.

Regards,

Mike Wolfe

-----Original Message-----
From: Sachak, Sohel [JANUS]
Sent: Thursday, November 18, 1999 9:53 AM
To: Bruins, John [JANUS]
Cc: Burgos, Licette [JANUS]; Mahmoud, Ramy [JANUS]; Wolfe, Michael A. (JAN)
Subject: RE: Dr. Joseph Biederman payment

The check has been authorized and should be sent out in three business days.
Sohel

----Original Message----
From: Bruins, John [JANUS]
Sent: Wednesday, November 17, 1999 11:49 AM
To: Sachak, Sohel [JANUS]
Cc: Burgos, Licette [JANUS]; Mahmoud, Ramy [JANUS]; Wolfe, Michael A. (JAN)
Subject: Dr. Joseph Biederman payment

Sohel;

As I am writing this memo, I am FAXing you all the documentation which I have on this Grand Rounds Program.

As of yesterday, 11/16/99, Dr. Biederman was promised delivery via Federal Express a check for $3K. I made this promise to him since I was assured that this matter would be resolved. It has not.

Let me start from the beginning so that it is crystal clear with everyone involved:

-Dr. Biederman is not someone to jerk around. He is a very powerful national figure in child psych and has a very short fuse.

-Three or four years ago Janssen H.O. requested that he put together a study to evaluate RIS in the child and adolescent population. He submitted a thourough and lengthy proposal which amounted to approkimately $280K. We dragged our heels on this request (which we made) for over a year. He finally recieved a standard ding letter. By the time I found out about it a week later and went to see him his secretary advised me of his fury. The sales representative who called on him and I took an hour of verbal beating. I have never seen someone so angry.

-Dr. Biederman is the Head of Adolescent Psych at MGH. Since that time our business became non existant within his area of control. He now has enough projects with Lilly to keep his entire group busy for years.

-Although I occasionally call on him and invite him to our Ad Boards, he acts with scepticism about our sincerity.

-Six months ago I recieved a call from Leighton Huey (the Chairman at UConn). He informed me that Dr. Biederman was coming to give GR in September of this year. According to him, some previous discussion had taken place between the Boston rep (covering Dr. Biederman) and the Hartford rep (covering UConn). The Boston rep was doing everthing she could think of to get Dr. Biedrerman back in our graces. Anyway they had done some behind the scenes negotiating to schedule this program. Dr. Huey informed me that Dr. Biederman recieved commitment that Janssen would pay for this program. This included a promise of $2.5K honorarium and expenses. Dr. Huey and I were both surprised by the figure but we were not part of the negotiating and stayed out of it. Dr. Huey FAXed me the e-mail correspondance. I told him that I would take care of it since the sales reps were no longer working.

-I then filled out the grant request paperwork and sent it to you for approval. This was about three months ago and well before the program on September 20, 1999.

-You then returned to paperwork to me and requested me to get the sales force to pay for it.

-I discusses the issue with Mike Wolfe (new RBD for New England) and forwarded the materials to Rick Atkinson (new DM for Hartford).

-At a sales meeting in Boston which was addressing finances I committed to taking back this Grant Request since no one was willing to champion this program and pay for it.

-On or about September 20 I resubmitted the paperwork to you with a verbal explaination.

-A month later you requested further documentation.

-Over a week ago Dr. Biederman was on his way back to tirade. He was calling me and Dr. Huey's office and was starting to ruffle Dr. Huey's feathers that we had not payed him. I asked Dr. Biederman for further documentation and committed to him that we would get his check to him by yesterday in exchange for documentation from him. In two lengthy voice mails to you I explained the situation and promised the documentation to pass in the mail with the check.

-Dr. Biederman paged me yesterday and I did not know why he had not recieved his check. I told him to call you.

-Dr. Biederman has done everything we have asked of him. Again, we have jerked him around. I am truely affraid of the repercussions.

-I beg you to approve the payment of his ckeck.

Sincerely,

JBB

D4 - J&J Center at MGH, 2002 annual report executive summary

Annual Report 2002: The Johnson and Johnson Center for Pediatric Psychopathology at the Massachusetts General Hospital

Director: Joseph Biederman, MD
Co-Director: Stephen V. Faraone, PhD

Executive Summary

Overview

The mission of the Center is to create a common ground for a strategic collaboration between Johnson & Johnson (J&J) and the Pediatric Psychopharmacology Research Program an at the Massachusetts General Hospital (MGH). The Center provides an infrastructure for MGH researchers to collaborate with J&J researchers on comprehensive studies of pediatric psychopathology, including diagnostic, therapeutic, and neurobiologic studies. The formation of the Center has created a forum for multidisciplinary collaborative research in a number of key areas, with an initial focus on pediatric mood and disruptive behavior disorders.

An essential feature of the Center is its ability to conduct research satisfying three criteria: a) it will lead to findings that improve the psychiatric care of children; b) it will meet high levels of scientific quality and c) it will move forward the commercial goals of J&J. We strongly believe that the Center's systematic scientific inquiry will enhance the clinical and research foundation of child psychiatry and lead to the safer, more appropriate and more widespread use of medications in children. Considering that nearly all psychiatric medication use in children is off label, studies of safety and efficacy in children are essential for clinicians, parents and patients to feel comfortable using these medications in children. The Center is poised to test the effectiveness and safety of RISPERDAL, REDACTED and new products as the emerge from the pipeline.

Equally important to effective use of medications is the demonstration of the validity of disorders. Because parents, patients and clinicians are exposed to a media that frequently questions the validity of childhood disorders, genetic and brain imaging studies are needed to show the validity of these disorders as brain disorders that respond to medication. Epidemiologic studies are needed to show that childhood disorders are frequently chronic and severely debilitating. Without such data, many clinicians question the wisdom of aggressively treating children with medications, especially those like neuroleptics, which expose children to potentially serious adverse events. Epidemiologic studies also show the continuity of childhood and adult disorders. This provides an additional measure of validation for the childhood disorder and in some cases validates the disorder as a disorder of adulthood as we have seen for adult attention deficit hyperactivity disorder (ADHD).

Through the funding provided by J&J, we are creating a team of investigators focusing on the following issues.

Assessing the Efficacy and Safety of Medications for Child Psychopathology

We will generate and publish data on the efficacy and safety of medications for improving currently available treatment options for child psychopathology. This work is an essential precursor to the safe, appropriate and widespread use of medications given that most must be used off-label. Specific goals of this area of work include:

- Assessing the full range of symptoms treated by RISPERDAL by analyzing data from Janssen's study of RISPERDAL among conduct disordered/mentally retarded youth. This will allow us to extend Janssen's prior findings indicating efficacy for conduct disorder to mania, anxiety and other classes of psychopathology.
- Using MGH open-label studies to assess the differential effectiveness and safety of RISPERDAL and ZYPREXA in the treatment of pediatric bipolar disorder (BPD). For example, we have already shown that ZYPREXA leads to twice the weight gain as RISPERDAL.

D5 – Emails Pandina – Biederman re poster abstract AACAP 2002

From: Biederman, Joseph,M.D. [BIEDERMAN@HELIX.MGH.HARVARD.EDU]
Sent: Wednesday, June 12, 2002 1:34 PM
To: 'Pandina, Gahan [JANUS]'
Subject: RE: AACAP 2002 Draft Abstract

I will review this morning. I will be happy to sign the forms if you could kindly send them to me

> ----------
> From: Pandina, Gahan [JANUS]
> Sent: Tuesday, June 11, 2002 5:50 PM
> To: Biederman, Joseph,M.D.; Stephen V. Faraone Ph. D. (E-mail); Mick, Eric
> Cc: Gharabawi, Georges [JANUS]; Bossie, Cyndi [JANUS Non J&J]
> Subject: AACAP 2002 Draft Abstract
>
> Dear All,
>
> I am sending the most recent draft of the abstract for AACAP 2002, with some missing data (analyses were supposed to be completed this evening, but will be here in the morning instead). I was able to have our statistics department generate the summary data for each of the two symptom areas (depression and mania), but this resulted in the delay. Please take a look, and provide any comments you think appropriate. We have generated a review abstract, but I must review this longer abstract before passing this along (this is less crucial). Based upon the improvement in the placebo group, both groups may demonstrate significant improvement overall on the two domains, so, if you could, please give some thought to how to handle this issue if it occurs. I will send the results as soon as possible. Dr. Biederman, if you could be prepared to sign and fax a disclosure form as presenting author, unless you would rather have another present the data then assign a designee, as we cannot submit without a signed disclosure. I will be at an off-site meeting tomorrow, but available via cell phone at 609-954-5646, and checking my email periodically during the day as possible.
>
> Please cc: Cynthia Bossie on these communications as well, as she is helping with the coordination and technical issues. Please also forward to Stephanie for comment, as I do not appear to have her email address handy.
>
> Thank you all, and I look forward to your comments.
>
> Regards,
>
> Gahan Pandina
>
> BRIEF ABSTRACT
>
> American Academy of Child and Adolescent Psychiatry Conference - 2002
>
> Symptoms of affective instability respond to risperidone treatment in children with disruptive behavior disorders.
>
> Biederman1, J., Faraone1, S., Mick1, E, van Patten1, S., Pandina2, G., Gharabawi2, G.
>
> 1Massachusetts General Hospital, Boston, MA
>

> 2Janssen Pharmaceutica Inc., Titusville, NJ
>
> Objective: To examine the response of affective symptoms to
> risperidone treatment in children with disruptive behavior disorder (DBD).
>
> Method: Children with DBD (oppositional defiant disorder/conduct
> disorder/disruptive behavior NOS; n=118; mean, age 8.6 years, 97
> males) and subaverage IQ were randomized to placebo or risperidone in
> a 6-week, double blind study. Weekly assessments were made with the
> Nisonger Child Behavior Rating Form (NCBRF), along with other
> efficacy, safety and cognitive assessments. While the NCBRF Conduct
> Problem Subscale was the primary outcome measure, secondary analyses
> were performed on items classified as symptoms of depression or mania.
> Change in symptoms from baseline to endpoint was evaluated.
>
> Results: Analysis of covariance for symptoms of depression and mania
> showed significant improvement at endpoint in the risperidone group
> (depression: p=0.0001; mania: p=0.0001), while the placebo group did
> not (ns). Individual symptom analysis showed a greater improvement in
> children treated with risperidone than placebo. Example: the
> risperidone group improved significantly on "crying, tearful"
> (p<0.05), "irritability"
> (p<0.001) "feels worthless or inferior" (p<0.001), while the placebo group
> showed no improvement in these symptoms.
>
> Conclusions: Risperidone is effective in the treatment of manic and
> depressive symptoms frequently found in children with DBD. Implications
> for treatment are discussed.
>
>
> Gahan J. Pandina, Ph.D.
> Assistant Director, CNS Clinical Development
> Janssen Pharmaceutica Products, L.P.
> 1125 Trenton-Harbourton Rd * Titusville, NJ 08560
> OFFICE: (609) 730 2324 * FAX: (609) 730 3125
> EMAIL: gpandina@janus.jnj.com
>

>
>
>
>

From: Hagger, Simon
Sent: 8/7/2003 2:38:41 PM
To: +SEROQUEL GLOBAL BRAND TEAM; +Seroquel Global Product Team; Wilson, Ellis; Schwartz, Jack A; Tugend, Georgia L
CC: Ghavamzadeh, Lili; O'Malley, Michael; Altman, Charles; Macfadden, Wayne
Subject: IIT benchmarking report

Dear all,
please find attached the final report from an IIT benchmarking study the GIRT team commissioned earlier this year.

A series of interviews were carried out with internal AZ staff who were known to have worked for competitor companies before as well as a number of KOL investigators
from the UK, Italy, Germany and Spain.

The objective of the study was primarily to find out as much as we could about how, where and why our competitors invest in IITs. While not ascertaining any specific figures regarding levels of investment in IITs a large number of interesting
findings emerged that will help us shape our future direction with the IIT program as well as providing compelling messages to MC senior management to drive investment in local IIT activities.

Key messages emerging from the report:

• Lilly run a large and highly effective IIT program

• Significantly higher (x3 in some markets) investment than AZ
• They are perceived as open and flexible to receiving proposals but will often impose strict design changes before approval
• They impose few restrictions on the investigator once design changes are communicated and agreed
• They are fast and effective in turning studies around centrally and locally
• They offer significant financial support but want control of the data in return
• They are able to spin the same data in many different ways through an effective
publications team
• Negative data usually remains well hidden

• Janssen have a well organised IIT plan

• Significant spend in some markets but variable in others
• Well structured, protocol-driven program that turns proposals around quickly through a very small approval team
• Local investment decisions are allowed on small IIT's
• No IIT data is allowed to be published without going through Janssen for approval, and communication is controlled by Janssen
• High expectations are set on investigators who publish favorable results but they are well rewarded for their involvement
• They seem less concerned than Lilly about negative data reaching the public domain

• BMS IIT program is growing very fast in launched markets

- Quick turnaround of study proposals
- Most proposals are modified by BMS
- Strategic focus is in unlicensed indications
- All study work is run through BMS teams
- Written contracts and expectations for delivery are in place for every study

- Pfizer have limited IIT programs in place and have not made significant investments
in this area

Recommendations from the report for AstraZeneca

- Significant increases in $'s and resources required globally but especially locally if we want to compete with Lilly

- Brand advocacy is a major payback for Lilly from high investment in IITs

- Publications must be more involved in the IIT program

- Publications should also be more creative spinning the data, aka Lilly
- Publication plans should be set up with investigators at start of study
- Offer further support (e.g. stats) through the publications leader

- IITs should remain small and simple wherever possible
- Clear definition and communication of global IIT strategy is required
- Study proposals must be turned around faster
- IIT target lists should be created
- Don't impose beaurocracy on investigators but negotiate tougher contracts
- Consider IIT ad boards to review and develop strategic IIT plans
- AZ commercial physicians should spend more time visiting and supporting investigators
- Make sure the outputs and successes of the IIT program are promoted widely within the company

Clearly some of the above recommendations are already being actioned. However the report has highlighted some fundamental changes that should be considered as well as the wider need for significantly more investment if we are to maximise
the opportunity that the IIT program continues to offer the brand.

If you have any questions about the report or would like to talk further please don't hesitate to give me a call.

Regards,

Simon

Simon Hagger
Global Brand Manager, Seroquel
PS&L
AstraZeneca Pharmaceuticals, US
Tel: 302 885 1089
Fax: 302 886 8010
Mobile: REDACTED
simon.hagger@astrazeneca.com

Appendix D7

Documents relevant to the ‘High Flyer’ segment of medical practitioners, who Pharma approach and/or cultivate to become what they term ‘Key Opinion Leaders’ (‘KOLs’)

From the Eli Lilly ‘Zyprexa Documents’

Cross-Brand Segmentation: Selling Through Advanced Customer Knowledge

Answers That Matter.

ZY200083203 Neuroscience segmentation for sales

Why conduct a Neuroscience Segmentation?

Previous Success With Segmentation

[redacted]

Neuroscience Segmentation will…

Prioritize customers based on growth potential

&

Better understand customers so we can tailor our approach

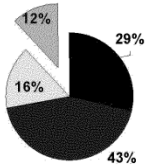
…So we can be the Neuroscience Industry Leader, know our customers better, and Sell MORE!!!!

ZY200083203 Neuroscience segmentation for sales

FAQ: ***How does segmentation work with Insights?***

ZY200083203 Neuroscience segmentation for sales

High Flyer General Profile



Who are they?

Earliest adopters of new medications & new uses of medications

Mainly general or family practice

How do they approach treating patients?

Highest comfort treating neuroscience diseases among PCPs

- Not bound by the label
- Willing to push the dose of medications they are comfortable with
- Willing to use adjunctive therapy
- Typically they are treating symptoms rather than a diagnosis

What do they like from a pharmaceutical company?

Keep them connected with the up to date information

- Prefer to learn from a psychiatrists about new information
- Interventions tailored to their interests
- Not adverse to frequent calls if new info is offered

The Importance of Neuroscience Segmentation

"I don't mind using higher doses or trying something new if it gets the job done. My patients have serious problems that require the latest medical developments so I don't have time for a sales rep who comes in with outdated information."

Dr. Cruise

- Have you met someone like Dr. Cruise?
- How would you describe him to a new representative?
- How might an early understanding of his segment type help build a stronger relationship?
- What could happen if you came unprepared for this type of doctor?

We'll talk more about Dr. Cruise later.

ZY100174816 Keyplayer Playbook Aug 2002

Key Player Playbook

Following is a summary of Zyprexa's Key Players.

Physician Segments*	Health Care Professionals	Payer Segments	Other
Rule Bound	ER Doctor (I)	Public Payer (I,R,LTC)	Thought Leaders (I,R,LTC,PCP)
High Flyer	Institutional Pharmacist (I)	Institutional Payer (I,LTC)	Advocacy (I,R,LTC,PCP)
Skeptical Experimenters	Ward Nurse (I)	Private Payer (R,PCP)	Bipolar Patient and Family (R,PCP)
Selective Majority	Psychiatric Residents (I)		
Systematic Conservatives	CMHC Treatment Team (R)		
	Retail Pharmacist (R,PCP)		

Notes

* All Psych segments practice in Institution (I), Retail (R), and LTC; All PCP segments practice in PCP office.

Tier 1: Critical to "holding on" in '03 and pretty well resourced

Tier 2: Critical in '03 meeting growth targets and under / marginally resourced

Tier 3: Important in '03 and critical beyond '03 to continue to meet growth targets and under / marginally resourced

Key Player profiles for physicians are provided below since they these doctors work across all settings. Zyprexa is focusing its marketing plan on High Flyers and Rule Bounds, who in the Psychiatric market provide the first and second highest volume of prescriptions. High Flyers will aggressively treat mental illness (off-label, high dose) and Rule Bounds are most likely to be loyal to a brand.

ZY100174816 Keyplayer Playbook

High Flyers: Priority Doctor Segment Due to Volume but Likely to Try Competitive Entrants
This key player is Zyprexa's top customer, due to the Psych's volume and early adoption. Of chief concern is this key player's tendency to try new products (notably Aripiprazole, Geodon IM, or Risperdal Depot). To prepare for new entrants in the AP / MS class, Zyprexa needs to partner with new Lilly neuroscience products to enhance our relationships with these key customers, especially through programming. High Flyers have the highest detail responsiveness and second highest DTP responsiveness.

Significant programs, and funding, will be targeted toward this key player, as well as the Rule Bounds.

	Zyprexa Strategic Opportunity
Prescriber Information	• Psych: 16% of population accounts for 31% of Zyprexa Rx (highest volume) • PCP: 12% of population accounts for 22% of Zyprexa Rx (2nd highest volume significantly behind Selective Majority)
Zyprexa Strategic Importance	• Most critical segment for Zyprexa and all NS brands due to Psych volume and adoption • High expertise / influence among peers • Push the envelope with indications and doses (note: Zyprexa only promoted per label)
Zyprexa Marketing Goal	• Turn to Lilly for new ways to treat my patients • Partner with new NS Brands or High Flyer will seek out newer competitors to Zyprexa
	Key Player Mindset and Action
Statement Defining Key Player	• I eagerly seek out new ways to treat my patients (first to adopt new medicines)
Motivation, Attitudes, Beliefs	• Actively seek new info that will allow them to treat more patients, and treat them better – Psychiatrists: Trying to get a patient to 100% and like to have treatment options; this means tailoring a medication cocktail by using the MOA of the drugs. – PCPs: Stepping out of comfort zone to treat a disease they don't often see • Seek deep understanding of *how* drugs work; make decisions based on MOA • Willing to try new medicines early because "they still have patients that are not yet 100%"
Behavior	• Not bound by rules, guidelines or system; proactively take action to get patient better • Treat based on symptoms, not formal diagnosis • Will push the envelope with off label doses and indications (based on MOA)
	Marketing Preferences
Marketing Preferences	Psychs • Detail responsiveness: Highest • DTP responsiveness: Moderate (2nd highest) • P2P responsiveness: Low to Moderate • Like pharmaceutical company sponsored programs and tools in "fun" environments. PCPs • Detail responsiveness: Highest • I-Physician Net responsiveness: Highest • P2P responsiveness: Highest
Do's	• Group interaction and patient focus • Reps as source of latest information • Key segment to learn from via CFF's and RCFF's • CME with "new" content • Patient ed / starter packs to reinforce importance of patient satisfaction • Forum / club to reinforce NS leadership in social way • Advisory Boards • Consultant web-site • Partner PCP with Psych
Don'ts	• Present well known data as if it's true or gloss over fair balance
	How We Want Them to Think and Act
Marketing Objectives	• High Flyer Psychiatrists believe that Zyprexa offers dependable control that enables a therapeutic alliance to increase patient capture and retention at the appropriate dose. • High Flyer Psychiatrists to believe that Zyprexa has the most dependable control with a known and manageable side effect profile that isn't dose dependant • Increase High Flyer Psychiatrist's perceptions of Zyprexa as a collaborative, committed leader in order to maintain current level of loyalty
Programs (promotional and non-promotional)	• Shown later

Plan based on $104.9M soft targets. Buy-ups to be discussed at BC III.

ZY100174816 Keyplayer Playbook

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ZY100174816 Keyplayer Playbook thought leaders and consultants

Thought Leaders

Cross Brand Key Players: Thought Leaders

The Zyprexa Guild and Executive level Thought Leaders are well respected and acknowledged by their peers, other experts and key audiences as leaders and influence the thinking and the treatment practices of their peers at a national, regional or local level. Guild and Executive Thought leaders are experts in the disease and the diagnosis of the disease. They are typically in the academic setting (professors/researchers) and treat a minimal number of patients, if any. The Guild and the Executive Thought Leaders usually serve on the academic advisory boards, providing feedback to the Zyprexa Product and Brand Team.

The Consultants currently have greater clinical experience and are primarily responsible for continuing to shape and to define Zyprexa as extraordinary in moving lives forward in the bipolar and the schizophrenia marketplace. The Consultant Thought Leaders are the core advocates between the Guild and those at the regional and local levels, and are on our demand realization advisory boards. These clinicians are a critical component of successful DTP interventions and stimulate the physicians at both the regional and the local level.

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