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PAID TO PRESCRIBE? EXPLORING THE RELATIONSHIP BETWEEN DOCTORS AND THE DRUG INDUSTRY

HEARING

BEFORE THE

SPECIAL COMMITTEE ON AGING UNITED STATES SENATE

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FIRST SESSION

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PAID TO PRESCRIBE? EXPLORING THE RELATIONSHIP BETWEEN DOCTORS AND THE DRUG INDUSTRY

WEDNESDAY, JUNE 27, 2007

U.S. SENATE,
SPECIAL COMMITTEE ON AGING,
Washington, DC.

The Committee met, pursuant to notice, at 10:39 a.m., in room SD–106, Dirksen Senate Office Building, Hon. Herb Kohl (chairman of the committee) presiding.

Present: Senators Kohl, Carper, and McCaskill.

OPENING STATEMENT OF SENATOR HERB KOHL, CHAIRMAN

The CHAIRMAN. Hello to one and all, and we will call this hearing to order at this time.

Today, we look forward to examining the financial relationship between the pharmaceutical industry and physicians. Interactions between doctors and drug manufacturer representatives often involve payments that can actually take the form of cash and gifts, such as meals, travel to conferences, or textbooks.

Unlike other professions, physicians are allowed to take payments from companies whose products they may choose to prescribe to their patients. Recent studies show that the more doctors interact with drug marketers, even through small gifts and modest meals, the more likely doctors are to prescribe the expensive new drugs that are being marketed to them when a more affordable generic would do just as well.

Seniors lose out with unnecessarily high drug costs while doctors and drug manufacturers benefit financially. The rising drug prices don't only harm the elderly. They hurt us all, as they undermine our private and public health systems.

Health insurance premiums continue to skyrocket, and escalating drug costs have played a large role. The Federal Government, now the largest payer of prescription drugs with the new Medicare drug benefit, feels the squeeze as well, and considerably.

Even more alarming, these gifts and payments can compromise physicians' medical judgment by putting their financial interest ahead of the welfare of their patients. Over the last several years, there have been attempts by the Federal Government, medical organizations, and drug companies to curb the excessive gifts and payments to physicians.

Unfortunately, as we will hear from some of our witnesses today, financial ties between doctors and drug companies are only deep-

ening. In fact, a study published in the *New England Journal of Medicine* earlier this year reported that 94 percent of physicians have received food and beverages, medication samples, and other gifts, as well as payments for trips, from drug companies.

The pharmaceutical industry remains one of the most profitable industries in the world, returning more than 15 percent on their investments, which is extraordinary. As a businessman myself, I fully respect an industry's right to maximize profits.

Nevertheless, I believe they are charging Americans—and it is a fact—the highest drug prices in the world, forcing some employers to drop health coverage for their employees, squeezing budgets of State and Federal Governments and, ultimately, harming our seniors by putting drug costs out of their reach.

It has been estimated that the drug industry spends $19 billion annually on marketing to physicians in the form of gifts, lunches, drug samples, and sponsorship of education programs. Companies certainly have the right to spend as much as they choose to promote their products, but as the largest payer of prescription drug costs, the Federal Government has an obligation to examine and take action when companies unfairly or illegally attempt to manipulate the market.

Today's witnesses will discuss the current state of the physician-drug industry relationship, recent attempts at the state level to increase disclosure of payments, and attempts to reduce the influence of the drug industry on physicians' prescribing behaviors. We will also hear testimony from one doctor who feels that these potential conflicts of interest have reached a disturbing level in his profession and is adversely affecting medical research.

Our second panel will include representatives of the pharmaceutical industry and the medical profession, and they will provide us insight into their voluntary guidelines addressing physician gifts and payments. We look forward to hearing from each of our witnesses in terms of their perspectives on this issue and their recommendations.

Obviously, we take this issue very seriously, and we will continue oversight of the relationship between doctors and the drug industry. While there are voluntary guidelines already in place, to us it seems clear that they are not being sufficiently followed. We intend to vigorously pursue stronger adherence to these guidelines, as well as to propose a national registry to require disclosure of payments and gifts.

I believe we need transparency at the minimum and at the outset. Many of these gifts are not illegal, but we need them disclosed. These interactions involving things of value between the pharmaceutical industry and doctors, in our judgment, need to be made public.

So we thank you all for being here today.

At this point, I will introduce our first panel.

Our very first witness today will be Dr. Jerome Kassirer, who is a distinguished professor of medicine at Tufts University. Dr. Kassirer has published numerous original research and clinical studies regarding quality health care, and he served as the editor-in-chief of the *New England Journal of Medicine* from 1991 to 1999.

After that, we will hear from Dr. Greg Rosenthal, the chief of ophthalmology at Toledo Hospital and Toledo Children's Hospital and the director of retina care at Vision Associates in Toledo. He has extensive training in all diseases and surgery of the retina, and he serves on several national committees with respect to eye health.

Our third witness today will be Dr. Peter Lurie, who is the deputy director of Public Citizen's Health Research Group, a consumer advocacy group here in Washington, DC. Dr. Lurie has worked on a myriad of issues related to pharmaceutical policy, including the cost and safety of prescription drugs.

Our fourth witness on the first panel will be State Representative Sharon Treat. She is a member of the Maine legislature, where she has served for nearly 15 years, including two as Senate majority leader. Representative Treat is also executive director of the National Legislative Association on Prescription Drug Prices.

So we welcome all of you here today, and we look forward to your testimony.

Dr. Kassirer, we will start with you.

STATEMENT OF JEROME KASSIRER, M.D., DISTINGUISHED PROFESSOR, TUFTS UNIVERSITY SCHOOL OF MEDICINE, BOSTON, MA

Dr. KASSIRER. Thank you, Mr. Chairman.

As you heard, I am Jerome P. Kassirer. I am a distinguished professor at Tufts University School of Medicine in Boston and visiting professor at Stanford University. I am a former editor-in-chief of the *New England Journal of Medicine* and author of the Oxford University Press book, "On the Take: How Medicine's Complicity with Big Business Can Endanger Your Health." I represent no institution and no medical professional organization.

I have been asked to provide a brief overview—actually, you did it pretty well already—of the complex intertwining of the medical profession and the pharmaceutical, biotechnology, and device industries and the consequences of these relationships.

I will assert that the medical profession has become excessively dependent on the largest of industry, that these financial connections have a negative influence on the quality and cost of patient care and the trust of the public, and that the profession's response to these threats has been inadequate.

American doctors train for many years, and many accumulate substantial debt to become physicians. They then work long hours, struggling in a complex health care delivery system to reduce the burden of illness.

There is no other country where I would prefer to get care for my family or myself. Our physicians, hospitals, medical centers, and medical professional organizations are respected around the world.

In the same vein, the pharmaceutical, biotech, and device industries have revolutionized clinical practice by developing, often with the help of academic physicians, new diagnostic tools, prostheses that improve day-to-day living, and life-saving medications.

The companies are also a vigorous engine that accounts, in part, for our country's phenomenal economic growth. But these compa-

nies require big profits, and, to do so, they mount massive marketing campaigns, much of it directed at doctors. Doctors are human and, like the rest of us, they respond to financial incentives.

I need not remind any of you what a struggle it has been to eliminate physician self-referral of patients to their personally owned health care facilities. But the extent of self-referral pales compared with the enormous financial incentives generated by these industries.

The magnitude of drug promotion astonishes, as 100,000 drug reps visit doctors, residents, nurses, and medical students every day and ply them with free gifts, meals, and gadgets. Medical meetings are mini-circuses, replete with enormous glittering displays and hovering attractive personnel. Although couched as education, these marketing efforts are thinly disguised bribes.

Just as surprising is the magnitude of physician involvement with industry. As you pointed out a few minutes ago, among a random sample of doctors reported just weeks ago in the *New England Journal of Medicine,* more than three-quarters had taken free samples, free food, and free tickets to sporting events from industry; more than one-third accepted free continuing medical education; and another third had received payments for speaking or consulting for the companies or enrolling patients in clinical trials.

Some have estimated the industry's total advertising bill at $70 billion. There is nothing fundamentally wrong with advertising products, but when financial incentives yield inappropriate or dangerous care, when they inordinately raise the cost of care, when they risk patients' lives in clinical trials, and when they damage the profession, they have gone too far.

We need not look back very far. Only 2 weeks ago, the New York Times reported that drugs were being selected for cancer patients depending on the profit they would achieve for a medical practice. The same week, we read a study that showed that sponsorship of controlled trials of statins was closely correlated with positive results of such trials.

Three weeks ago, we learned that payments for enrolling patients in clinical trials were leading to shabby research practices by unqualified researchers. This spring, we learned that physicians with financial ties to the company that makes Epogen were inappropriately represented on a National Kidney Foundation committee that recommended potentially dangerous doses of the drug.

These recent revelations are just a continuation of reports over the past 10 years or so. Dozens more are detailed in my book.

Financial payments have swayed professional medical organizations to make inappropriate clinical recommendations. They have influenced industry-paid speakers to recommend risky drugs. They have biased FDA panels and yielded inappropriate behavior by NIH scientists.

Free drug samples encourage doctors to use the newest and most expensive drugs, and the samples themselves often get into the wrong hands. Drugs such as Natrecor, approved for acute heart failure only in the hospital, found widespread use in doctors' offices, costing taxpayers hundreds of millions of dollars.

What have leaders in the profession done to counter a trend in which the profession has become increasingly beholden to industry? Not much.

The American Medical Association and many other physician organizations permit their members to receive gifts and meals and to serve on pharmaceutical companies' speakers bureaus. Most of them have no proscription against members' involvement as consultants to industry for marketing or for the development of educational materials. In fact, most medical society rules are no more stringent than those of PhRMA.

Last year, my colleagues and I recommended conflict-of-interest policies for academic medical centers. We proposed that industry-paid gifts and meals be eliminated; that faculty should not join industry speakers bureaus; that all faculty consulting with industry be strictly overseen by contract; that drug formulary committees be free of conflicted physicians; and that free drug samples be regulated by a voucher system.

Since then, a number of medical centers, including Stanford, Penn, Yale, and U.C.-Davis, have revised their policies along these lines, but most of them have picked off the low-hanging fruit, proscribing visits by drug reps and eliminating industry-supported meals. None of them has eliminated faculty involvement on speakers bureaus or consultations on marketing issues.

Doctors are at risk of corruption from the perverse incentives from industry. I prefer that the profession police itself, but in the 3 years since publication of my book, progress in extricating medicine from industry influence has been minimal.

Newspaper reports and State reporting requirements have not been sufficient. I would like to see a Federal registry for reporting analogous to those of some States. I would also like to see a congressional mandate to the Institute of Medicine of the National Academy of Sciences for studies that mirror those that called attention to medical errors.

We must put more pressure on both the profession and the industry. In my opinion, both have reneged on their ethical responsibilities for the care of the sick.

Thank you, Mr. Chairman.

[The prepared statement of Dr. Kassirer follows:]

TESTIMONY OF JEROME P. KASSIRER, M.D.

TO
SENATE SELECT COMMITTEE ON AGING

HERB KOHL, CHAIR
GORDON H. SMITH, RANKING MEMBER

JUNE 27, 2007
WASHINGTON DC

I am Jerome P. Kassirer, M.D., Distinguished Professor at Tufts University School of Medicine in Boston and Visiting Professor at Stanford University. I am a former Editor-in-Chief of the *New England Journal of Medicine*, and author of the Oxford University Press book, "On The Take: How Medicine's Complicity With Big Business Can Endanger Your Health." I represent no institution and no medical professional organization. I have been asked to provide a brief overview of the complex intertwining of the medical profession and the pharmaceutical, biotechnology and device industries and the consequences of these relationships. I will assert that the medical profession has become excessively dependent on the largesse of industry, that these financial connections have a negative influence on the quality and cost of patient care and the trust of the public, and that the profession's response to these threats has been inadequate. (1)

American doctors train for many years, and many accumulate substantial debt to become physicians. They then work long hours, struggling in a complex health care delivery system to reduce the burden of illness. There is no other country where I would prefer to get care for my family or myself. Our physicians, hospitals, medical centers and medical professional organizations are respected around the world.

In the same vein, the pharmaceutical, biotech, and device industries have revolutionized clinical practice by developing, often with the help of academic physicians, new diagnostic tools, prostheses that improve day to day living, and life saving medications. The companies are also a vigorous engine that accounts, in part, for our country's phenomenal economic growth.

But these companies require big profits and to do so they mount massive marketing campaigns, much of it directed at doctors. And doctors are human, and like the rest of us they respond to financial incentives. (2) I need not remind any of you what a struggle it has been to eliminate physician self-referral of patients to their personally owned health care facilities. But the extent of self-referral pales compared with the enormous financial incentives generated by these industries.

The magnitude of drug promotion astonishes. 100,000 drug reps visit doctors, residents, nurses, and medical students every day and ply them with free gifts, meals, and gadgets; (3, 4) medical meetings are mini-circuses, replete with enormous glittering displays and hovering attractive personnel. (5, 6) (Although couched as education, these marketing efforts are thinly disguised bribes. Just as surprising is the magnitude of physician involvement with industry. Among a random sample of doctors reported just weeks ago, more than 3/4 had taken free samples, free food, and free tickets to sporting events from industry, more than 1/3 accepted free continuing medical education, and another 1/3 had received payments for speaking or consulting for the companies or enrolling patients in clinical trials. (7) Some estimate the industry's total advertising bill at 70 billion dollars. (8)

There is nothing fundamentally wrong with advertising products, but when financial incentives yield inappropriate or dangerous care, when they inordinately raise the cost of

care, when they risk patients' lives in clinical trials, and when they damage the profession, they have gone too far.

We need not look far back. Only two weeks ago the NY Times reported that drugs were being selected for cancer patients depending on the profit they would achieve for a medical practice. (9) The same week we read a study that showed that sponsorship of controlled trials of statins was closely correlated with positive results of such trials. (10) Three weeks ago we learned that payments for enrolling patients in clinical trials were leading to shabby research practices by unqualified researchers. (11) This spring we learned that physicians with financial ties to the company that makes Epogen were inappropriately represented on a National Kidney Foundation committee that recommended potentially dangerous doses of the drug. (12-15) These recent revelations are just a continuation of reports over the past 10 or so years; (11, 16-24) dozens more are detailed in my book, "On The Take." (1)

Financial payments have swayed professional medical organizations to make inappropriate clinical recommendations, (25, 26) influenced industry-paid speakers to recommend risky drugs, biased FDA panels, and yielded inappropriate behavior by NIH scientists. Free drug samples encourage doctors to use the newest and most expensive drugs, and the samples themselves often get into the wrong hands. (27) Drugs such as Natrecor, approved for acute heart failure only in the hospital, found widespread use in doctors' offices, costing taxpayers hundreds of millions of dollars. (28)

And what have leaders of the profession done to counter a trend in which the profession has become increasingly beholden to industry, at times to the detriment of the public? Not much. The American Medical Association and many other physician organizations permit their members to receive gifts and meals and to serve on pharmaceutical companies' speaker's bureaus. (25) Most have no proscription against members' involvement as consultants to industry for marketing or for the development of educational materials. In fact, most medical society rules are no more stringent than those of PhRMA! (1)

Last year my colleagues and I recommended conflict-of-interest policies for academic medical centers. We proposed that industry-paid gifts and meals be eliminated; that faculty should not join industry speaker's bureaus, that all faculty consulting with industry be strictly overseen by contract, that drug formulary committees be free of conflicted physicians, and that free drug samples be regulated by a voucher system. (29) Incidentally, the recommendations in my book are even stricter. Since then a number of medical centers, including Stanford, Penn, Yale, and UC Davis have revised their policies along these lines, (4) but most have "picked off the low-hanging fruit," proscribing visits by drug reps and eliminating industry-supported meals. None has eliminated faculty involvement on speaker's bureaus or consultations on marketing issues.

Doctors are at risk of corruption from the perverse incentives from industry. I prefer that the profession police itself, but in the three years since publication of my book, progress in extricating medicine from industry influence has been minimal. Newspaper reports and

state reporting requirements have not been sufficient. I'd like to see a congressional mandate to the Institute of Medicine for studies that mirror those that called attention to medical errors. We must put more pressure on both the profession and the industry. In my opinion, both have reneged on their ethical responsibilities for the care of the sick.

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The CHAIRMAN. Thank you so much for your testimony.

Mr. Rosenthal.

STATEMENT OF GREG ROSENTHAL, M.D., RETINAL SPECIALIST, TOLEDO, OH

Dr. ROSENTHAL. Thank you very much. I am Dr. Greg Rosenthal [off-mike]—I am having microphone problems.

Is that better?

The CHAIRMAN. That is good.

Dr. ROSENTHAL. OK. I have a number of leadership positions, and I am also a co-founder of Physicians for Clinical Responsibility, or PCR.

We are living in an age of pharmaceutical influence, where companies sponsor physicians, medical research, and clinical decisionmaking. Pricing of retinal pharmaceuticals is such that one agent could cost CMS as much as the entire eye care budget, so the motivation to control this market is strong.

Such influence is inappropriate when it serves company interests at the expense of patient and societal interests. In the retinal field, this is a particular threat to seniors due to the prevalence of macular degeneration and diabetic retinopathy common in this group.

There is a schism in the retina community between the majority who want to do legitimate research and patient care and a strategically cultivated group of doctors willing to help corporate interests in exchange for valuable consideration.

Drug companies exert control by controlling drug trials and linking them to marketing efforts; nurturing key opinion leaders, or KOLs, to influence medical decisionmaking; providing money, travel, and publicity for community doctors when they agree to promote certain products; funding professorships and other academic needs of those who support company interests; using unrestricted grants to influence journals, societies, meetings, and Web sites; controlling speakers and presentation of CME courses and materials; and creating bogus expert panels to promote products and treatments.

Physician opposition to this complicity is growing and summarized in a recent quote from Dr. Jerry Sebag, a leader in our community. He writes, "It is becoming increasingly obvious to me that many speakers on the AMD circuit, the so-called experts, are puppets serving their needs and the companies that pay them. While many of us may not be 'key opinion leaders,' we are 'key care leaders,' and as such, it is up to us to promote the interests of our patients and society at large."

The influence of Big Pharm, as we call it, is pervasive. Research used to be independently funded and designed, but with the decrease in public funding, drug companies have moved in aggressively. The independent trials have been replaced by corporate-sponsored RCTs, or randomized control trials.

Although bias in such trials has been well-documented, companies have, largely through their KOLs, promoted the idea that only sponsored data is valid, and there is growing pressure to ignore any non-CSRCT data. Either through financial inducement or fear tactics, many physicians are persuaded to comply. There have also

been efforts to block studies and ignore data that might conflict with CSRCTs.

In redefining the RCT, pharmaceutical companies are exerting control over what to study, which questions to ask or not ask, IRB independence—that is, Institutional Review Board independence—what to report or not report, and the presentation of the data. Drug companies also tightly coordinate their studies with their marketing plans.

Researchers are recruited, some with conflicts of interest ranging from excessive cash to stock options and lab and professorship funding. Some of these same doctors are then cultivated as key opinion leaders and are further compensated to promote the company's message. I recently spoke with an M.D. employed by a major drug company whose actual title was "Thought Leader Liaison" and whose job was to recruit and tend to the KOLs.

Even good research is tainted by the possibility of bias, and it is very difficult to know what and what not to believe. We recently declined participating in a study of a promising drug simply because the study was so laden with perks for doctors that participation would have begged unavoidable questions about the credibility of our work.

Drug companies also work at the community level. Doctors whose only qualification is that they use a product are recruited and paid to do studies or sit on "expert panels" and travel to exotic destinations to discuss, that is, promote products. Invitations to nominal scientific advisory boards are made on a similar basis.

Retina doctors often complain that society meetings have lost credibility since almost every speaker is compromised by financial relationships. These same meetings serve as little more than preliminaries for after-hours seminars, usually in luxurious hotels where doctors can receive CME credits, meals, and often gifts for listening to the sponsor's spin on standard care.

Societies and medical journals have become dependent on unrestricted grants from numerous pharmaceutical companies. In this context, "unrestricted" means, "Use this for whatever you want, but if you ever want another one, don't displease us."

As an example, last year, I wrote an op-ed criticizing conflicts of interest, and although it was hailed by several retina leaders as "right on the mark, very important, and the right thing to do," it was proved unpublishable. Several journal editors praised the article but indicated that they could not publish it, due in part to concern about advertisers and the reviewer's relationships with the pharmaceutical companies.

None of these concerns was put in print. One editor even suggested that I "shouldn't take this on." Another time, I was to speak on this topic, but 5 minutes before the talk, I was asked to change topics because the society had just received a large sponsorship check from a drug company.

Physicians face a difficult choice. One path is to go along. With drug company money, you can increase your income, prestige, build your practice, or fund a department, research, or professorships. The middle ground is to simply look away.

The hard choice is to fight back. The road back to credibility is long. Opposing forces are well-funded and well-motivated. Still,

there are many, many retinal specialists who are disturbed by the slide of our profession. The formation of PCR is a first step.

Current dynamics will continue to permit uncontrolled compromise of the public welfare for personal or corporate gain. The system needs to be changed in response to this extreme opportunism. Dr. Kassirer, Dr. Marsha Angell, and others have outlined steps that can be taken to restore the independent practice of medicine.

The majority of physicians desire to practice honest medicine in their patients' and in society's best interests, and these doctors would welcome any changes that would mitigate financial conflicts and restore credibility to our research, our education, and our practice of medicine.

Thank you very much.

[The prepared statement of Dr. Rosenthal follows:]

I am Dr. J Gregory Rosenthal, MD., a fellowship-trained retinal surgeon in Toledo, Ohio. My medical degree is from Washington University in St. Louis. I was a resident and Chief Resident at St. Louis, University, and did my retinal fellowship at the Irwin Retina Institute and Rush Medical College. I am now the Director of the Retinal Service of Vision Associates in Toledo, Ohio and Chief of Ophthalmology at The Toledo Hospital and Toledo Children's Hospital. I have no financial interest in any pharmaceutical company except undetermined and incidental interests as may apply to mutual funds.

I would like to expound on several comments offered by Dr. Kassirer as they apply to the field of retinal surgery. In the last several years, we have seen the rapid evolution of the "age of pharmaceutical influence" in our field. This has created a growing rift in the retinal community. Physicians for Clinical Responsibility (PCR) is a grass roots organization opposing what one of our patriarchs described as "the pathetic slide of our profession into the hands of the drug companies".

We are living in an era of massive corporate sponsorship of sports and entertainment, which manifests itself as appropriate support of those activities. Similar sponsorship of medical activities by pharmaceutical companies becomes inappropriate when such activity influences research and care according to pharmaceutical company interests. Such activity has been growing and has created a clear threat to public welfare. In the retinal field, this is a particular threat to seniors due to the prevalence of macular degeneration and diabetes, common in this group.

We are literally trading independent medical integrity for corporate profits. In the retinal world, this is manifesting as

- Companies taking over the administration of randomized controlled trials which are inappropriately linked to marketing efforts
- Companies recruiting and compensating "Key Opinion Leaders" (KOLs) to influence decision making in the retinal cimmunity
- Companies proving money, travel, and false research prestige for community docs
- Corporate-funding of chaired professorships and other academic funding
- Influence through "Unrestricted Grants" for journals, societies, meetings, and websites
- Control of speakers, agendas, and presentation of CME courses and materials
- Companies creating bogus expert panels to promote products and treatments

This inappropriate influence of physicians by drug companies has created a schism in the retinal community between the majority of retina docs who want to take optimal and cost effective care of their patients and the growing minority of strategically cultivated doctors willing to help corporate interests in exchange for valuable consideration of various sorts.

To quote one well-respected and non-conflicted retinal physician:

It is becoming increasingly obvious to me that many speakers on the AMD circuit, the so called experts, are puppets serving their needs and the companies that pay them... While many of us may not be Key Opinion Leaders, we are Key Care Leaders, and as such, it is up to us to promote the interests of our patients and society at large.

J. Sebag , MD , FACS, FRCOphth
Professor of Clinical Ophthalmology
University of Southern California

This opinion is not unique. Many others have spoken up in the last year. Following is a brief synopsis of many e-mails received by PCR:

- *I have also been disappointed by my friends and colleagues who at least in appearance, seem shills for the Pharmaceutical companies. My disappointment in no way implies that I am not appreciative of the R&D of the pharmaceutical companies, which has helped make American medicine the best in the world. I also appreciate the research efforts of our colleagues in full-time academia.--it's the suspicion of loss of objectivity that is bothersome.*
- *My opinion of pharma has changed steadily over my 7 years in practice, and (the situation with) Lucentis was the last nail in the coffin.*
- *Those who pretend that the speaker's fees and such don't affect their judgment are just "full of it."*

The influence of "Big Pharm" on retinal medicine is pervasive. The layers of control include clinical research and patient care. Research used to be independently funded and designed, but with decreased independent funding in recent years, and with the emergence of pharmaceutical-based retinal treatments, the drug companies have moved in aggressively. The Independent Randomized Controlled Trial (IRCT) has been replaced by the corporate sponsored RCT (CSRCT), which differs from the former in critical ways. Although bias in CSRCTs has been well documented, companies have promoted the idea that only CSRCT data (i.e. their sponsored data) is valid and is in fact the only data that should be considered in patient care. In recent years there has been growing pressure to ignore any data that is not in the CSRCT. There have also been efforts to block, suppress, or ignore data that might conflict with CSRCTs.

In redefining the RCT, pharmaceutical companies are exerting increasing control over

- What to study
- Study design
- Which questions to ask or not ask (according to corporate interests)
- The IRB process
- Data analysis; what to report; what not to report
- Presentation of the data
- Tightly coordinating the study with post-study marketing

Research and the post-research marketing have been melded by recruiting doctors to do research with conflicts of interest ranging from cash to stock options to lab and professorship funding. Doctors are then cultivated as "Key Opinion Leaders" who are compensated for giving talks at meetings and other venues to support the corporation's interpretation of their studies and to promote the company's, and therefore their own interests. I recently spoke with an MD employed by a major drug company whose actual title was "Thought Leader Liaison" and whose job was to recruit and tend to the KOLs. By co-opting those identified as our specialty's "leaders", there is a significant pressure to influence the behavior of doctors "on the front lines" of patient care.

Even good research is tainted, and it is virtually impossible to know what and what not to believe. I have recently had to decline participating in a study of a promising drug simply because the study design was so "juiced" that participation would have violated my ethical requirement to avoid financial conflicts.

The drug companies also work at the community level. Doctors whose only qualification is that they use a product are recruited to be on "expert" panels and travel to exotic destinations to discuss (i.e. promote) products. Invitation to nominal "Scientific Advisory Boards" are made on a similar basis. They are brought in to "consult" at exotic destinations, where meetings can be little more than a venue to "wine and dine" the "consultants", who provide no more input than could be obtained from a phone call.

Rank and file retina doctors have repeatedly complained that society meetings have lost their credibility since almost every speaker is compromised by financial relationships. We have reached the point where it would be more convenient for speakers to simply wear NASCAR style jackets emblazoned with their sponsors' logos. These same meetings serve as little more than preliminaries for the company-sponsored focus seminars, usually in luxurious hotels, where doctors can receive more CME credits for listening to further promotional presentation.

Societies themselves and our medical journals have become dependent upon the infamous "unrestricted grant" from numerous pharmaceutical companies. In this context, "unrestricted" means, 'use this for whatever you want, but if you ever want

another, don't displease us.' I have had two recent experiences that punctuate this problem in a small way. Last year, I wrote an op-ed criticizing conflicts of interest, and although it was hailed by several retinal leaders as "great", very important", and "the right thing to do", it proved unpublishable. Several journal editors praised the article but indicated that they could not publish it in large part due to their concern about their advertisers' opinions or their reviewers' relationships with the pharmaceutical companies. All were careful not to put this in print. I was to speak on this topic at a recent meeting, but literally five minutes before the talk I was asked to change topics because the society had just received a large sponsorship check from a drug company.

Physicians face a difficult choice. One path is to go along. With corporate money you can, for example, increase your income, increase your (perceived) prestige, build your practice, fund a department, and fund research and professorships. The middle ground is to look the other way.

The hard choice is to fight back. The road back to credibility is long. Opposing forces are well funded and well motivated, but there are a growing number of retinal specialists who are disturbed by the slide of our profession. The formation of Physicians for Clinical Responsibility is a first step. Current dynamics as outlined by Dr. Kassirer, Dr. Marcia Angell and others will continue to permit uncontrolled compromise of the public trust for personal and corporate gain. Dr. Kassirer and others have also outlined steps that can be taken to restore the independent, evidence based practice of medicine. The majority of physicians desire to practice honest medicine in their patients' best interest, and these doctors would welcome guidelines and/or regulatory changes that would mitigate financial conflicts and restore credibility to our research, educational system, and practice of medicine.

The CHAIRMAN. Thank you, Dr. Rosenthal.

Dr. Lurie.

STATEMENT OF PETER LURIE, M.D., MPH, DEPUTY DIRECTOR OF PUBLIC CITIZEN'S HEALTH RESEARCH GROUP, WASHINGTON, DC

Dr. LURIE. Good morning, Senator. Thank you for inviting me to speak.

I have brought along the people who helped me prepare this testimony, who are able to take any more detailed questions you might have.

I am here to talk about the State laws that require disclosure of gifts from drug companies to doctors, and let me start with my conclusion.

What we really need is a national law. We have a minority of States that have laws, and as I will show, those laws are riddled with holes and poor enforcement. So I think your idea and that of Senator Grassley to move forward with a national reporting law is spot-on.

The laws are on the ascendancy. The Minnesota statute dates from 1993, but nobody took any further action on this until 2001. But since then, we have seen three States and D.C. that have enacted similar laws. Eleven States thought about imposing them in 2006, but none of them, to our knowledge, became law.

The drug industry estimates that it spent $25.3 billion in 2003 on marketing. The doctors think that they are exempt from this. They think they are unaffected by such interactions. But it seems unlikely that pharmaceutical companies would be catering to the culinary and travel preferences of doctors if they didn't think that they were getting some bang for the buck.

The evidence, as reviewed by Dr. Kassirer in his written testimony, strongly suggests that the drug companies are right. There are multiple studies showing an impact upon changes in prescribing of doctors, upon their early adoption of new medications which themselves might be hazardous, and changes in formularies, all of them the result of interactions with drug representatives, with all-expenses-paid travel to various exotic locations and the like.

The companies, therefore, have a clear conflict of interest, and yet we have surrendered the marketplace to them by allowing them to influence physicians. The result can be prescribing that is based on marketing instead of on science. Patients are the victims of all this.

The physician disclosure laws are just one of many ways that we might go about trying to limit the damage of this marketing, and we have already seen the benefits of these laws. We published our article in the JAMA back in March, and in Minnesota, there have been already at least four positive results: firstly, an undertaking by the executive director of the Minnesota Board of Pharmacy to actually put the data up on the Internet. Although, when I last looked, it actually wasn't there.

Several clinics contacted us, alarmed that physicians in their employ were taking money in such large amounts from drug companies and they had been unaware of it.

There were two important articles in the New York Times, the first of which identified physicians who had been used by pharmaceutical companies to run clinical trials, even though they had long records of discipline from the Minnesota Board of Medical Practice, and another which documented particularly large payments to the thought leaders to which Dr. Rosenthal just referred.

My testimony has two parts, and the first is a review of existing State physician payment disclosure laws. We, for this testimony, conducted a detailed analysis of five State laws which are currently in place, and they are summarized in a table on page 3 of my testimony and in more detail in an appendix.

What we learned was that none of the statutes requires device or biologic manufacturers to report payments, and I think that will be the first error to correct. Two of the five States do not require separate reporting of each payment, permitting various forms of data aggregation and the loss of important detail. In West Virginia, you don't even have to report the name of the physician, so that is a particularly weak statute.

Exclusions from reporting are common. The threshold for reporting ranges from $25 to $100. Four States exempt certain payments related to medical conferences and research studies from the reporting requirement, and all exempt free samples for patients, even though most studies show that the samples are, in fact, the largest expenditure for the pharmaceutical companies when it comes to marketing.

We don't think that these exclusions are justified, as long as each payment is clearly identified as having a particular purpose. We think that researchers, patients, and congressmen are able to look at these particular payments and make decisions for themselves as to whether or not they think they are appropriate. Only the Minnesota statute makes all of the disclosed information part of the public record without exception, although the four remaining States do require annual summary reports to the legislature.

Now I want to turn to the second part of my testimony, to the paper that we published in the JAMA relating only to Vermont and Minnesota, which are the only two that are actually in place right now. In both States, payment disclosures can be obtained, but you really have to run through the hoops in order to get them.

In Vermont, we had to enter into extensive negotiations with the attorney general's office and submit simultaneously an Open Records Act request. It took 12 months before we got any of this information, and even then, 30 of the 68 companies in the most recent year designated at least some of their payments as trade secret, and, as a result, all of those records were withheld.

Subsequently, we initiated a lawsuit against the attorney general, and most of the companies have now settled with us, providing some form, often of redacted data, but some data at least, but setting no precedent for release to others.

In Minnesota, the data are easier to find but harder to use. You have to make a trip to Minneapolis to the office of the Minnesota Board of Pharmacy, and there you will find a bunch of boxes gathering dust because no one has bothered to open them for the last several years, let alone enter them into a database.

So they are there for you. You pay to photocopy them. We did that and then entered them into a database for our study. But that hardly qualifies as adequate access for the public.

Now, as far as the quality of the payment data in these two States is concerned, again, many of the entries aggregated the data, describing payments made to multiple physicians. Others describe payments made to individuals, so it is very hard to interpret.

In Minnesota, some of the disclosures were handwritten, and I can speak for myself in saying that the handwriting of a doctor is not to be trusted, and, certainly, we encountered that kind of difficulty in Minnesota. The data quality was also poor, with many entries providing no information on the payment purpose.

Now, as to the value of these disclosures, which we think is a dramatic understatement of the amount of payments that actually take place due to the various exemptions and because of the threshold for reporting and underreporting by the companies—because it is clear that many of them don't report each time. We focused on those payments that are valued at over $100, because that is what the AMA and the PhRMA codes say is the limit that one ought to respect.

In dollar terms, in Vermont, 61 percent of all of the State payments were withheld on trade secret grounds, which I alluded to earlier, and of the publicly disclosed ones, which were a minority, there were 2,416 to physicians for $100 or more, totaling $1 million over a 2-year period. The median payment was $177, and the largest payment was $20,000.

Sixty-eight percent of these payments were in the form of food, which clearly provides no patient benefit and, therefore, in our view, is likely to violate the AMA and the PhRMA guidelines.

In Minnesota, over a 3-year period, there were 6,238 payments to physicians for $100 or more, totaling $22.4 million; median, $1,000; highest gift, $922,000. Again, because of deficiencies in the laws and their enforcement, we think these are substantial underestimates of the extent of actual gift giving.

Payment disclosure laws are a first step toward addressing the overall problem of drug company marketing, but they are not the only method, and they are not necessarily even the most effective one. No physician is obligated to accept the gifts. It does take two to tango, and there is an organization which has identified at least about 500 physicians who have taken a pledge not to take any gifts whatsoever from drug companies.

Certain prominent medical schools, as laid out by Dr. Kassirer, have severed their ties in various respects with the drug industry. The industry and the AMA have their own guidelines, but as we pointed out, those are voluntary and rather weak. We also need stronger enforcement of existing restrictions on marketing at the levels of the Justice Department, the Federal Trade Commission, the FDA, and State Governments.

So let me conclude with my recommendations.

The first overriding point is that any national law should include device and biologic companies as well.

But, really, my most important point is where I started. What we really need here is a national law. The overall quality of the statutes in the different States has been poor. Their implementation

has been worse. Because the physician payment issue is a national one, not a State one, the most rational approach to this issue is a national reporting requirement.

Thank you.

[The prepared statement of Dr. Lurie follows:]

Testimony of

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Deputy Director, Public Citizen's Health Research Group
Joseph S. Ross, MD, MHS
Instructor, Mount Sinai School of Medicine
Adina H. Rosenbaum
Staff Attorney, Public Citizen Litigation Group
Jason Krigel
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on State Laws Requiring Disclosure of Pharmaceutical Company Payments to Physicians
Before the Senate Special Committee on Aging
June 27, 2007

Thank you for the opportunity to address the Committee on Aging on the issue of state laws requiring the disclosure of pharmaceutical company payments to physicians. These laws are on the ascendancy; the Minnesota statute dates from 1993, but since 2001 three states and the District of Columbia have enacted similar laws. Eleven states proposed disclosure laws in 2006.[1] To our knowledge, none became law.

Payment disclosure laws offer an important mechanism to monitor pharmaceutical industry marketing, a practice valued at $25.3 billion in 2003.[2] Pharmaceutical marketing to physicians includes free samples, promotional detailing, and continuing medical education activities, and has been shown to alter physician behavior. Physicians typically claim that they are unaffected by such interactions (although they are willing to acknowledge that their colleagues might be influenced).[3] But pharmaceutical companies would not be catering to the culinary and travel preferences of physicians if they thought their efforts were for nought. The evidence strongly suggests that the companies are right. For instance, contact with pharmaceutical company representatives is associated with changes in the prescribing practices of residents and physicians[4] and more rapid adoption of new drugs by prescribers.[5] Sponsorship of continuing medical education programs by a pharmaceutical company[6] and all-expenses-paid travel to

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[1] National Conference of State Legislatures. 2006 Prescription drug state legislation, November 6, 2006. Available at: http://www.ncsl.org/programs/health/drugbill06.htm.
[2] Pharmaceutical Marketing & Promotion. Pharmaceutical Research and Manufacturers of America, Fall 2004. Available at: http://www.phrma.org/files/Tough_Questions.pdf.
[3] Steinman MA, Shlipak MG, McPhee SJ. Of principles and pens: attitudes and practices of medicine housestaff toward pharmaceutical industry promotions. *American Journal of Medicine* 2001;110:551-7.
[4] Lurie N, Rich EC, Simpson DE, et al.Pharmaceutical representatives in academic medical centers: interaction with faculty and housestaff. *Journal of General Internal Medicine* 1990;5:240-3.
[5] Peay MY, Peay ER. The role of commercial sources in the adoption of a new drug. *Social Science and Medicine* 1988;26:1183-89.
[6] Bowman MA, Pearle DL. Changes in drug prescribing patterns related to commercial company funding of continuing medical education. *Journal of Continuing Education in the Health Professions* 1988;8:13-20.

conferences[7] are associated with increases in the prescribing rate of the sponsors' drugs. Finally, interactions with a pharmaceutical company representative are associated with an increased likelihood of requesting that the representative's company's drug be added to the hospital formulary.[8] Thus, as companies with a clear conflict of interest in promoting a specific product continue to influence physicians, the result can be prescribing based on marketing, rather than science. Moreover, if this effort results in the prescribing of unnecessary drugs or newer, more expensive drugs with little marginal benefit, it will needlessly add to health-care spending. These newer medications are more likely to have undiscovered dangers.[9]

Equally important, these interactions are eroding the public's trust in the medical profession. These conflicts bear a strong resemblance to the recently reported scandals in the student loan business; the difference is that in medicine they are formally condoned by the profession.

In 2002, the American College of Physicians, the nation's largest association of internists, issued a policy statement regarding pharmaceutical company payments to physicians.[10] It offered three criteria for determining the appropriateness of a payment, the first of which is: "What would my patients think about this arrangement? What would the public think? How would I feel if the relationship was disclosed through the media?" Payment disclosure laws in effect put these theoretical questions to the test.

Already, despite the limitations described below, these physician disclosure laws have yielded beneficial results. In Minnesota, the publication of our article in the *Journal of the American Medical Association* (*JAMA*; see Appendix 1)[11] in March 2007 and our provision of the underlying data to local newspapers have led to significant media interest and an undertaking by the Executive Director of the Minnesota Board of Pharmacy (to whom we also provided the data electronically) to post the data his office has collected on the internet. (We do not see such data posted at the present time.) After reading the press reports, which named specific doctors, several clinics contacted us, unaware that their physicians had been accepting such large payments from pharmaceutical companies. An article in the *New York Times*, using similar data, identified physicians being used by pharmaceutical companies to run clinical trials despite long histories of discipline for substandard medical care by the Minnesota Board of Medical Practice.[12] Another in the same series documented large payments to medical "thought leaders"[13] – those with a role in developing guidelines that might affect the prescribing of the company's drugs.

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[7] Orlowski JP, Wateska L. The effects of pharmaceutical firm enticements on physician prescribing patterns. *Chest* 1992;102:270-3.
[8] Chren MM, Landefeld CS. Physicians' behavior and their interactions with drug companies. *Journal of the American Medical Association* 1994;271:684-9.
[9] Lasser KE, Allen PD, Woolhandler SJ, Himmelstein DU, Wolfe SM, Bor DH. Timing of new black box warnings and withdrawals for prescription medications. *Journal of the American Medical Association* 2002;287:2215-20.
[10] Coyle SL. Physician-industry relations. Part 1: individual physicians. *Annals of Internal Medicine* 2002;136:396-402.
[11] Ross JS, Lackner JE, Lurie P, Gross CP, Wolfe S, Krumholz HM. Pharmaceutical company payments to physicians: early experiences with disclosure laws in Vermont and Minnesota. *Journal of the American Medical Association* 2007;297:1216-23.
[12] Harris G, Roberts J. After sanctions, doctors get drug company pay. *New York Times*, June 3, 2007, p. A1.
[13] Harris G, Roberts J. Doctors' ties to drug makers are put on close view. *New York Times*, March 21, 2007, p. A1.

Our comments today will address two principal areas: (1) a legal analysis of the strengths and weaknesses of all enacted state payment laws; and (2) a summary of our research examining the effectiveness of physician payment disclosure laws in Vermont and Minnesota.

A. Review of Existing State Physician Payment Disclosure Laws

In preparation for this testimony, we conducted a detailed analysis of the five state laws on doctor payment disclosure currently in place. A summary of the most important elements appears in the table below; the details are attached as Appendix 2 to this testimony.

		DC	ME	MN	VT	WV
Company Disclosures to Agency	Itemized report of each payment	Yes	Yes	No	Yes	No
	No payment categories exempt from disclosure	No	No	No	No	No
	Submission via internet	No	Yes	No	Yes	No
	Enforcement mechanism	Yes	Yes	Yes	Yes	No
Public Access to Disclosed Info	Disclosures explicitly made public record	No	No	Yes	No	No
Agency Reports to Legislature	Required annual report of aggregate data	Yes	Yes	No	Yes	Yes
	Easily accessible on the internet	Reporting not yet begun	Reporting not yet begun	N/A	Yes	Reporting not yet begun

Although these statutes are undoubtedly intended to increase the transparency of the physician-pharmaceutical company relationship, it is clear that all fall well short of their aspirations.

None of the statutes requires device or biologic manufacturers to report payments, although there is no basis for such a distinction. Two of the five states (Minnesota and West Virginia) do not require separate reporting of each payment, permitting various forms of aggregation either across payment type or by physician. In West Virginia, no physician names need be reported; each company is required only to report (in dollar ranges) the total value of payments in that year and

the number of physicians who received payments of that value. This is by far the weakest of the disclosure statutes so far enacted.

Although food, travel, and honoraria/consulting fees must typically be reported, exclusions from reporting are common. The threshold for any reporting ranges from $25 (District of Columbia, Maine, and Vermont) to $100 (Minnesota and West Virginia). Four states (all except Minnesota) exempt certain payments related to medical conferences and research studies from the reporting requirement, and all exempt free samples for patients. Such exclusions are not justified as long as each payment is clearly identified as being for a particular purpose. Researchers and patients can decide for themselves if they consider highly remunerative research relationships with manufacturers, for example, to be problematic.

Only two states (Maine and Vermont) permit electronic filing of reports and one state (West Virginia) has no enforcement mechanism available under the statute. Only the Minnesota statute makes all the disclosed information part of the public record, without exception, although the remaining four states require annual summary reports to the legislature. A model statute would require both.

In sum, all existing statutes are deficient in at least one significant respect. Only one (Minnesota) requires physician-specific data to be made public and all are subject to major exemptions from disclosure.

B. Pharmaceutical Company Payments to Physicians: Early Experiences with Disclosure Laws in Vermont and Minnesota

In our *JAMA* paper, we examined the effectiveness of the physician payment laws in Vermont and Minnesota, enacted in 2001 and 1993, respectively. We had three research objectives: (1) to determine the accessibility of the data available in Vermont and Minnesota; (2) to assess the quality of the public data; and (3) to describe the prevalence and magnitude of disclosed payments to physicians of $100 or more. The $100 cutoff was selected to facilitate comparisons between two states with different disclosure thresholds and because the guidelines of both the American Medical Association (AMA)[14] and the Pharmaceutical Research and Manufacturers of America (PhRMA)[15] suggest that gifts be under $100 in value and should benefit patients.

Accessibility of Payment Data

In both states, payment disclosures can be obtained, although obtaining the records required much effort. In Vermont, payment data were released by the Attorney General's office as Internet-accessible annual summary reports to the legislature. These reports do not provide physician-specific payments; rather, they provide aggregated data, broken down by company, recipient type, form of payment, and purpose.

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[14] American Medical Association. Opinion E-8.061, gifts to physicians from industry. Available at: http://www.ama-assn.org/ama/pub/category/4001.html.

[15] Pharmaceutical Research and Manufacturers of America. PhRMA code on interactions with health-care professionals, revised January 2004. Available at: http://www.phrma.org/files/PhRMA%20Code.pdf.

In order to obtain physician-specific data, we entered into extensive negotiations with the Attorney General's office, while simultaneously submitting a Freedom of Information Act request. After nearly 12 months, the state did release physician-specific payment data, but withheld all data designated by the companies as trade secret. In the most recent year, 30 of 68 companies (44%) designated at least some of their payments as trade secret.[16] We subsequently initiated a lawsuit against the Attorney General of Vermont to obtain those payments designated as trade secret; numerous pharmaceutical companies were eventually joined in the litigation. Most of these companies have settled, providing some form of redacted data but setting no precedent for release to others. It is unrealistic to expect individual patients to engage in this sort of litigation to obtain their doctor's payment information.

In Minnesota, payment data have never been made available as a public report. Indeed, the disclosure forms submitted have literally sat in boxes for up to a decade, gathering dust and never being analyzed. In order to obtain the records, we were required to travel to the Minnesota Board of Pharmacy office in Minneapolis and to photocopy each form at a fee of $0.25 per page. Again, this hardly qualifies as adequate public disclosure.

Quality of Payment Data

Vermont provided us with data that had been entered into an Excel spreadsheet. However, despite a statute requiring separate reports for each payment, some entries described payments made to multiple physicians/healthcare professionals, whereas others described payments made to individuals. Moreover, many companies designated their records trade secret, and the AG refused to disclose such records. In our study, during the first year, 13 companies designated their payments as trade secret and nine additional companies did so in the second year, despite having released information during the first year.

In Minnesota, some disclosures were typed while others were hand-written (with varying degrees of legibility). As in Vermont, some entries described payments made to multiple physicians/healthcare professionals, whereas others described all payments made to individuals. Data quality was poor, with many entries providing no information on payment purpose or else generically quoting the Minnesota payment disclosure law (e.g., "reasonable honoraria or payment of the reasonable expenses of a practitioner ..."). Overall, 60 companies disclosed payments, but only 15 companies did so in each of the three years we studied.

Disclosed Payments

According to the summary reports released by the Vermont Attorney General's office, 58 pharmaceutical companies disclosed to the state $5.58 million in payments between July 1, 2002, and June 30, 2004. Of these, 12,227 payments totaling $2.18 million were publicly disclosed. Thus, in dollar terms, 61% of all payments reported to the state were withheld on trade secret grounds. Of the publicly disclosed payments, 2,416 (20%) were to physicians for $100 or more, totaling $1.01 million; the median payment was $177 (range: $100-$20,000). Sixty-eight percent of these payments were in the form of food, clearly providing no patient benefit and therefore

[16] Sorrell WH. Marketing disclosures. Vermont Attorney General, June 15, 2006. Available at: http://www.atg.state.vt.us/upload/1150802902_2006_Pharmaceutical_Marketing_Disclosures_Report.pdf.

potentially violating the AMA and PhRMA guidelines. By number, 28% of these payments were for educational activities, 26% were for detailing, and 16% were for unspecified purposes. In dollar terms, 35% of payments were for speaking activities, 20% were for unspecified purposes, and 17% were for educational activities.

In Minnesota, between January 1, 2002, and December 31, 2004, pharmaceutical companies disclosed 7290 payments. Of these, 6,238 (86%) were to physicians for $100 or more, totaling $22.39 million; the median such payment was $1,000 (range: $100-$922,239). By number, 46% of such payments were for unspecified purposes, 27% were for educational activities, and 13% were for speaker activities. In dollar terms, 42% of these payments were for unspecified purposes, 20% were for educational activities, and 16% were for research activities. Because the name of the recipient was fairly consistently provided and because, unlike in Vermont, all disclosed payments must be publicly available, we were able to identify particular physicians who had received multiple payments. We identified 2388 distinct physician recipients, approximately 14% of the 17,445 physicians holding an active license and who had a home address within the state. For these individual physicians, the median number of payments of $100 or more was 1 (range: 1-88) and the median total amount received was $1000 (range: $100-$1,178,203).

In summary, we identified large numbers of payments to physicians but, due to deficiencies in the laws and their enforcement, these estimates are likely substantial underestimates of the actual value of payments from pharmaceutical companies to physicians and the number of physicians involved.

C. Conclusions

The extraordinary measures taken by pharmaceutical companies to influence prescribers bear little resemblance to actual public health needs. Payment disclosure laws are a first step toward addressing the problem, but they are not the only method or even necessarily the most effective one. No-one requires physicians to accept the gifts offered. Certain prominent medical schools have recently decided to exclude pharmaceutical company representatives from their clinics and hundreds of physicians have personally undertaken to refuse all gifts (Goodman R, personal communication, June 24, 2007).[17] The guidelines of the major medical associations must be tightened but, due to their voluntary nature, these guidelines are likely to be more effective at staving off legislation than reducing marketing excesses. Enforcement of existing restrictions on marketing must be more strenuously enforced at the levels of the Justice Department, Federal Trade Commission, Food and Drug Administration and state governments.

We would like to conclude with some recommendations based on our research. An overarching point is that the disclosure laws should include device and biologic companies. But the most important recommendation is this: Due to the overall poor quality of the statutes and their implementation to date, and because the physician payment issue is a national one, not a state one, the most rational approach to this issue is a national reporting requirement. Our more specific recommendations would apply equally to state and national disclosure statutes and are detailed below.

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[17] www.nofreelunch.org

D. Recommendations

Company Reports to Agency

1) Itemize each payment to each prescriber.
2) Allow for electronic submission.
3) Permit no payment categories to be exempt from disclosure.
4) Standardize entries to minimize missing information, such as by using drop-down menus and by linking payments to a unique National Provider Identifier. This would facilitate aggregation of data on specific providers within and between companies.
5) Create enforcement mechanisms that will maximize compliance. Substantial fines and/or penalties for non-reporting are needed. Penalties could include:
    a. suspending interactions between physicians and pharmaceutical companies for periods of time; or
    b. excluding products for which there is a satisfactory therapeutic alternative from Medicaid or state and county hospital formularies.

Public Access to Disclosed Information

1) Make all individual disclosures available free and online.
2) Develop web tools to permit patients to search and aggregate payments by physician and payment type.

Agency Reports to Legislature

1) Require the implementing agency to annually report aggregate data.
2) Make annual reports easily accessible online.

The CHAIRMAN. Thank you very much, Dr. Lurie.

Now we will hear from Representative Treat.

STATEMENT OF HON. SHARON TREAT, STATE REPRESENTATIVE, EXECUTIVE DIRECTOR, NATIONAL LEGISLATIVE ASSOCIATION ON PRESCRIPTION DRUG PRICES, HALLOWEL, ME

Hon. TREAT. Thank you very much, Chairman Kohl. I am very pleased to be here today to testify on behalf of State legislators on what is a very important issue.

I am Sharon Treat, a member of the Maine House of Representatives, as well as executive director of the National Legislative Association on Prescription Drug Prices, which is a network of State legislators around the country, stretching from Alaska to Maine, working on prescription drug issues, trying to increase access to lower-priced drugs.

Since at least 1993, as you have heard, when Minnesota passed the first State law banning certain gifts and requiring the disclosure of drug industry marketing payments, States have been at the forefront of efforts to ensure that the pharmaceutical industry does not unduly influence the practice of medicine and adversely affect patient health and safety.

As of this month, at least 30 States have enacted laws or introduced legislation on one or more of the following topics: disclosing spending, as we have just heard; beefing up State authority to enforce misleading advertising and marketing rules; protecting privacy by restricting the marketing use of prescription data; regulating instant messaging and advertising in electronic prescribing software; regulating drug industry sales representatives' activities; establishing independent, evidence-based, detailing programs; and requiring disclosure and posting of clinical trials information.

The States' actions find their legal and policy support in the traditional State role of licensing doctors, pharmacists, and other healthcare professionals; protecting consumers from misleading advertising and unsafe products; protecting the public health; ensuring that private information is protected from unwarranted invasions of privacy; and partnering with the Federal Government in funding and administering Medicaid and now Medicare Part D.

Without the data collected through the Minnesota disclosure law, we would not have had the week-long series of front-page articles in the New York Times detailing payments to doctors and the questionable or unsafe prescribing patterns attributed to some of those doctors.

Without the public online clinical trials databases required by the Paxil settlement, a case brought by State attorneys general, spearheaded by New York, the data would not have been available which formed the basis of a study linking a popular diabetes drug to increased risk of heart attack. We have heard about that already this morning.

Maine law requires the results of all clinical trials to be published online, and other States are following suit. State attorneys general have been in the forefront, initiating consumer protection and Medicaid fraud prosecutions for kickbacks and misleading marketing tactics, including off-label promotions and failure to ac-

curately and completely disclose adverse effects. The multi-State Neurontin litigation and Oxycontin cases are examples.

States are concerned that marketing activities affect patient safety and provider prescribing patterns. Vermont, West Virginia, California, the District of Columbia, and Maine have joined Minnesota in requiring disclosure of marketing and advertising spending, as you have heard, with some concern about how effectively they have done it. However, they have gone ahead to try to get the information.

Maine and Vermont also grant clear authority to enforce misleading marketing standards in the courts. These States have acted, in part, in response to a significant reduction in recent years in the overall number of Federal enforcement actions for misleading marketing as well as FDA delay in acting to curb abuses.

Vermont now requires in a recent law enacted just this last month that pharmaceutical sales representatives disclose to the prescriber evidence-based information, including alternatives to the drugs that they are marketing, as well as the cost of treatment.

Pennsylvania has a comprehensive evidence-based academic detailing program to provide objective information and "unadvertisements" to physicians to counteract biased or at least one-sided information that is provided by sales representatives. Several other States have followed suit.

With Medicaid costs always a significant factor in State budgets, States are looking at issues of doctor and drug company conflicts of interest, payments for prescribing and for specialty drugs, and the targeting techniques for marketing, such as data mining. Data mining also raises issues of privacy that resonate with State legislators and their constituents familiar with these issues in other policy areas.

Many States have passed medical records confidentiality laws that predated HIPAA by many years. Some of these laws were significantly more protective of patient privacy than the Federal law that followed.

Over the past decade, States have also dealt with privacy issues related to credit cards and credit ratings, debating between opt-in and opt-out approaches that mirror the debate right now over prescription data. A landmark 2006 New Hampshire law prohibits the use of doctor specific prescription information for drug marketing purposes. The data can still be used for health purposes, such as tracking patient safety. At least 13 States have similar proposals with two more signed into law this month, Vermont and Maine.

There certainly is a strong role for the Federal Government to take action in many of these areas. To begin with, just to shine a light on marketing practices, as this Committee is doing, is of great value.

There is also a need to have much stronger standards governing conflicts of interest, to take action to curb misleading marketing, and to require disclosure of payments and gifts, as well as of clinical trials data and other safety data.

It would also, I need to stress, be a major step forward if the Federal Government would start by vigorously enforcing the laws already on the books which bar misleading advertising and off-label

promotion, and if labeling standards and enforcement were not subject to negotiation with the industry.

That said, we do have concerns about laws which might preempt State authority to act, particularly in those cases where States are acting within their traditional regulatory and enforcement functions and have actually stronger State laws. States have a traditional and effective role in enforcing consumer protection and misleading advertising laws, protecting public health, regulating medical professionals, implementing Medicaid, and safeguarding the privacy of their citizenry. It would be a bad bargain to trade strong State laws, even if they are in place only on a patchwork basis, for weak Federal laws that limit or prohibit State action.

States are passing laws because there is a regulatory and enforcement void. But public health issues need to be addressed, nonetheless, and they are taking action to do that. Congress should act, but it should partner with the States rather than preempt them.

I do have a whole lot of information about the specifics of what every State is doing appended to my testimony, which I can go over in more detail later on if you are interested.

Thank you very much.

[The prepared statement of Ms. Treat follows:]

Testimony of Rep. Sharon Anglin Treat
Executive Director,
National Legislative Association on Prescription Drug Prices

"State Perspectives on the Relationship Between Doctors and the Drug Industry: The Role of States and the Federal Government"
Senate Special Committee on Aging
June 27, 2007

Chairman Kohl, Senator Smith, and members of the Committee. It is an honor to be here today to testify on this important issue on behalf of state legislators. I am Sharon Treat, a member of the Maine House of Representatives, and Executive Director of the National Legislative Association on Prescription Drug Prices, a nonprofit, nonpartisan organization of state legislators who network across state lines to find ways to reduce prescription drug costs and expand access to medicines.[1]

Since at least 1993, when Minnesota passed the first state law banning certain gifts and requiring disclosure of drug industry marketing activities and payments targeted to doctors and other health practitioners, states have been at the forefront of efforts to insure that the pharmaceutical industry does not unduly influence the practice of medicine and adversely affect patient health and safety.

As of June 2007 at least 30 states had enacted laws, or had legislation pending, on one or more of the following topics:

- Disclosing marketing spending and practices, including gifts and payments to doctors; banning gifts to health practitioners
- Beefing up state authority to enforce misleading advertising and marketing rules
- Protecting patient and doctor privacy by restricting the commercial use of prescriber-identifiable prescription data
- Restricting advertising in electronic prescribing software
- Regulating drug industry sale representatives or detailers
- Establishing independent academic or counter detailing programs
- Requiring disclosure and posting of clinical trials information
- Establishing conflict of interest rules, especially with regard to pharmacy benefit managers

[1] The National Legislative Association on Prescription Drug Prices is a nonpartisan, nonprofit organization of state legislators from across the country who advocate for lowering prescription drug costs and increasing access to affordable medicines. Legislators from the District of Columbia and all of the New England states plus New York, West Virginia, Oklahoma, Texas, Alaska, Arizona, Colorado and Hawaii are members.

Although the federal government has a major role regulating drug safety, advertising and marketing, states have continued to exercise their traditional authority to protect public health and safety, and fill the gaps where the federal government has failed to regulate or vigorously enforce that laws.

Without the data collected through the **Minnesota** gift disclosure law, we would not have the week-long series of front-page articles in the New York Times detailing payments to doctors and questionable or unsafe prescribing patterns linked to those doctors.

Without the public, online clinical trials databases required in the Paxil settlement - a case brought by state attorneys general, spearheaded by **New York** – the data would not have been available which formed the basis of a study linking a popular diabetes drug to increased risk of heart attacks. **Maine** law requires the results of *all* clinical trials to be published online, and other states are following suit.

State attorneys general have been in the forefront initiating consumer protection and Medicaid fraud prosecutions against pharmaceutical companies and doctors for kickbacks and misleading marketing tactics including off-label promotions and failure to accurately and completely disclose adverse effects. Examples are the multistate Neurontin litigation and Oxycontin cases, which were in part a response to criminal activity spawned by drug abuse facilitated by off-label marketing and lax or fraudulent prescribing practices.

States are concerned that marketing activities affect patient safety and provider prescribing patterns, and have enacted legislation to rein in harmful marketing practices and to promote evidence-based prescribing. **Vermont, West Virginia, California,** the **District of Columbia** and **Maine** have joined **Minnesota** in requiring disclosure of marketing and advertising spending; Maine and Vermont also grant clear authority to enforce misleading marketing standards in the courts. These states have acted in part in response to a significant reduction in the overall number of federal enforcement actions for misleading marketing, as well as FDA delay in acting to curb abuses.[2]

Vermont's law not only regulates misleading advertising, but also marketing to health care practitioners, including at educational conferences, and requires pharmaceutical sales

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[2] Federal enforcement of marketing rules is lax. A 2005 report issued by Congressman Henry Waxman of the House Committee on Government Reform found that "there has been a marked decline in enforcement actions taken against drug manufacturers for illegally promoting their products" since December 2001. From 1999 to 2001, The FDA issued 250 "Notice of Violation" or "Warning" letters to drug companies, but from 2002 through 2004, the FDA sent only 70 letters. This is a reduction of more than two-thirds, despite a sharp increase in the number of drug ads and the money spent on them. The FDA does not have the resources to adequately police drug advertising. For example, in 2003, the FDA had only 18 staff assigned to review the roughly 37,000 ads and promotional pieces submitted by drug companies that year. See "*FDA Struggles to Police Print Ads for Prescription Drugs*," by Tony Pugh, January 29, 2004, Knight-Ridder.

representatives to "disclose to the prescriber evidence-based information as provided for by rule describing the specific health benefits or risks of using other pharmaceutical drugs, including drugs available over the counter; which patients would gain from the health benefits or be susceptible to the risks described; the range of prescription drug treatment options; and the cost of the treatment options."[3] **Pennsylvania** has a comprehensive academic detailing program to provide objective, evidence-based information and "unadvertisements" to physicians to counteract biased – or at least one-sided - information provided by sales representatives. Several other states have followed suit.

To the extent that marketing activities increase spending on prescription drugs, and encourage prescribing drugs that are not on a state's preferred drug list, they are also a concern for state Medicaid programs. With Medicaid costs always a significant factor in state budgets, state legislators are looking at issues of doctor and drug company conflicts of interest caused by payments for prescribing and specialty drugs which are administered in physician's offices.[4]

Data mining and targeted marketing techniques raise issues of privacy that resonate with state legislators and their constituents familiar with these issues in other policy areas. Many states passed medical records confidentiality laws predating HIPAA by many years, and some of these laws were significantly more protective of patient privacy than the federal law that followed. Over the past decade states have also dealt with privacy issues related to credit cards and credit ratings, debating between "opt in" and "opt out" approaches that mirror the debate right now over prescription data and the American Medical Association's opt out policy.

The privacy issue has taken on new currency with the recent ability of large data mining companies to purchase computerized prescription records from insurers and pharmacies, and to match that data with AMA-collected physician records and then sell that information to pharmaceutical companies to track every prescription a doctor writes. Coincident with the rise of physician identity data mining, the pharmaceutical industry has increased its spending on

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[3] According to NCSL data, as of January 2007, eight states and District of Columbia (2003), California (2004, 2005, 2006), Florida (2006) Maine (2003, 2005), New Hampshire (2006), South Carolina (2006), Vermont (2002), West Virginia (2001) and Minnesota (1993) have laws or resolutions on the books affecting pharmaceutical marketing. Maine, Vermont and New Hampshire have since amended their laws to expand oversight of marketing activities. The NCSL report is here: http://www.ncsl.org/programs/health/rxads.htm.

[4] A survey last year of 33 state Medicaid programs anticipated Medicaid prescription drug spending increases of 14.3% for 2005-06 FY, consistent with the prior year's growth of 12.9%. (Crowley & Ashner, "State Medicaid Outpatient Prescription Drug Policies: Findings of a National Survey, 2005 Update," (October 2005). Since 1990, U.S. consumer spending for prescription drugs has increased over five-fold to $251.8 billion (2005). (Kaiser Family Foundation, *Prescription Drug Trends,* 1 (June 2006); U.S. PIRG Education Fund, *Paying the Price: The High Cost of Prescription Drugs for Uninsured Americans* 6 (July 2006); Centers for Medicare and Medicaid Services, *Table 2, National Health Expenditures Aggregate Amounts and Average Annual Percent Change, by Type of Expenditure: Selected Calendar Years 1980-2004*, http://www.cms.hhs.gov/NationalHealthExpendData/downloads/tables.pdf.

direct marketing to doctors by over 275 percent[5] and doubled its sales force to over 90,000 drug reps.[6] There is now a pharmaceutical sales representative for every five office-based physicians in the U.S.[7] In 2004, the industry spent $27 billion on drug marketing (more than any other sector in the U.S. on its sales force or media advertising),[8] over 85 percent of which was targeted at doctors.[9]

It is no coincidence that states that have been vocal about privacy in other contexts (such as Real ID) have also been leading the way protecting both patient and prescriber privacy. A landmark 2006 **New Hampshire** law prohibits the use of doctor-specific prescription information for drug marketing purposes; the data can still be used for public health purposes such as tracking patient safety. At least 13 states have similar proposals, with two more signed into law so far this year. Vermont's new law creates an "opt in" system for prescribers to waive confidentiality of their data for marketing purposes; the Maine law creates a state-run system through medical licensing boards for prescribers to "opt out" of marketing use of their data.

The states' actions find legal and policy support in the traditional state role licensing doctors, pharmacists and other health care practitioners; protecting consumers from misleading advertising and unsafe products; protecting the public health; insuring that private information is protected from unwarranted invasions of privacy; and partnering with the federal government in funding and administering Medicaid and now Medicare Part D. Many of the laws enacted by the states are in fact amending the consumer protection laws or the physician or pharmacy licensing provisions.

While many of these laws have been implemented without legal challenge, others have been the subject of industry litigation, on a variety of constitutional and statutory grounds, including Commerce Clause preemption, ERISA conflicts, and First Amendment violations. While initially overturned on ERISA grounds, the Maine and D.C. pharmacy benefit manager conflict of interest and fiduciary duty laws have now been upheld.[10] The New Hampshire prescriber privacy law was recently overturned by the federal District Court on First Amendment grounds,

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[5] Kaiser, *Trends and Indicators*, exhibit 1.20.

[6] Manchanda & Hokna, *Pharmaceutical Innovation and Cost*, 5 Yale J. of Health Pol'y L. & Ethics at 788.

[7] Center for Policy Alternatives, *Prescription Drug Marketing*, www.stateaction.org/issues.cfm/issue/prescriptiondrugmarketing.xml

[8] Puneet Manchanda & Elisabeth Hokna, *Pharmaceutical Innovation and Cost: The Effects and Role of Direct-to-Physician Marketing in the Pharmaceutical Industry: An Integrative Review*, 5 Yale J. of Health Pol'y L. & Ethics 785, 785 (2005).

[9] Kaiser Family Foundation, *Trends and Indicators in the Changing Health Care Marketplace*, http://www.kff.org/insurance/7031/print-sec1.cfm, exhibit 1.20 (2005).

[10] *Pharmaceutical Care Management Association v. Rowe*, 429 F.3d 294 (1st Cir. 2005), *cert. denied*, 126 S. Ct. 2360 (2006)

and that case is being appealed.[11] States taking action to address pharmaceutical marketing do so under constant threat of litigation, whether justified or not.

There certainly is an important role for the federal government to shine a light on these marketing practices, as this Committee is today. There is also a need to have much stronger standards governing conflicts of interest, to take action to curb misleading marketing, and to require disclosure of clinical trials and other safety data. It would also be a major step forward if the federal government would start by vigorously enforcing the laws already on the books barring misleading marketing and off-label promotion, and if labeling standards and enforcement were not subject to negotiation.

That said, we have real concerns about any law which may preempt state authority to act, at least in those areas where the states act on the basis of their traditional state regulatory or enforcement function. As I have discussed, states have a traditional and effective role enforcing consumer protection and misleading advertising laws, protecting public health and regulating medical professionals, implementing Medicaid, and safeguarding the privacy of the citizenry. It would be a bad bargain to trade strong state laws - even if in place on a patchwork basis only – for weak federal laws that limit or prohibit state action.

States are passing laws because there is a regulatory and enforcement void, and major public health issues that need to be addressed. Congress should act, but it should partner with the states rather than preempt them.

SUMMARY OF STATE LAWS OF INTEREST:

- ***Regulating gifts and perks distributed to the medical community by the drug industry.*** The Minnesota law dates back to 1993 (151.461) and is an outright ban on certain gifts; it prohibits any manufacturer or wholesale drug distributor, or any agent thereof, to offer or give any gift of value to a practitioner over $50. Some exceptions apply, including payments to the sponsor of a bona fide educational purposes, honoraria for a practitioner who serves on the faculty at a professional or educational conference or meeting; compensation for consulting services of a practitioner in connection with a genuine research project; publications and educational materials; or salaries or other benefits paid to employees. Similar legislation (without some of the loopholes in the Minnesota law) is pending in several states, including **Massachusetts**.

- ***Disclosure of advertising & marketing spending:*** **Vermont, Maine, Minnesota, West Virginia, California** and the **District of Columbia** require reports disclosing spending on advertising and marketing activities. These laws have not been challenged in the courts,

[11] *IMS Health v. Ayotte*, NH District Court, No.CV-06-280-PB (April 30, 2007).

and the West Virginia Attorney General has issued a legal opinion that the state has broad powers in the area of disclosure of marketing activity.

- ***Restricting electronic marketing activities:*** In 2006 **Florida** enacted Chapter 2006-271 restricting advertising as part of electronic prescribing software including "instant messaging, and pop-up ads, to influence or attempt to influence, through economic incentives or otherwise, the prescribing decision of a prescribing practitioner at the point of care." Similar legislation was just passed this year in **Vermont** (S.115), **Maine** (LD 1440), and **New Hampshire** (HB 134) and is pending in **South Carolina** (S.528).

- ***Cracking down on misleading advertising and marketing***: In 2005, **Maine** passed a law adopting federal misleading advertising standards and giving its Attorney General explicit authority to go after violators. The law also requires posting data on clinical trials and a consumer education initiative by the state, funded with a fee paid by manufacturers. 2007 **Vermont** law (S.115) not only regulates misleading advertising, but also marketing to health care practitioners, including at educational conferences, and requires pharmaceutical sales representatives to "disclose to the prescriber evidence-based information as provided for by rule describing the specific health benefits or risks of using other pharmaceutical drugs, including drugs available over the counter; which patients would gain from the health benefits or be susceptible to the risks described; the range of prescription drug treatment options; and the cost of the treatment options."

  This provision addresses concerns that have prompted several states to propose bills to require drug detailer registration or qualifications. In past years, such legislation has been introduced and defeated in **New York, West Virginia** and **Maine.** Legislation filed this year in **Oklahoma**, HB 1938, would require the registration of pharmaceutical sales representatives with a commission, certain reporting and for termination procedures.

- ***Posting clinical trials results***: **Maine** law requires internet posting of all clinical trials and results, including adverse results. The law went into effect in 2005. The rules implementing this law require data to be posted through the NIH website www.clinicaltrials.gov . Unlike the NIH site, the Maine law requires results as well as registration of ongoing trials. The state also plans a public and medical provider education effort and easy-to-access web portal to communicate this information to the public. Similar legislation is pending in several states including **Minnesota** and **New York**.

- ***Prescription data confidentiality:*** A first-in-Nation 2006 **New Hampshire** law (HB 1346) prohibits the use of patient or prescriber-identified data for marketing purposes. There are exceptions for aggregated data and uses defined as non-commercial purposes such as tracking patient safety. This law is being challenged

in court *(IMS Health v. Ayotte)* on first amendment and commerce clause grounds, and the Federal District Court recently ruled in favor of the datamining company which is challenging the law. The State is appealing. **Vermont** (s.115) and **Maine** (LD 4) enacted laws in 2007 to create mechanisms for prescribers to act to either waive privacy protections or opt in to a state-run system to preserve privacy. At least 13 states have proposed similar legislation, which is still pending in **Massachusetts** and **New York**.[12]

- ***State-sponsored "academic detailing" to counter the effectiveness of targeted sales tactics.*** Some states are betting that academic detailing will save money in state pharmacy programs and lead to better health outcomes. A survey of state Medicaid programs in 2005 found that 22 states have programs to educate providers or provide "counter detailing" to promote the use of generics instead of more expensive brand name drugs.[13] The **Pennsylvania** Independent Drug Information Service (www.rxfacts.org) is the most comprehensive of the state programs. The program makes use of sophisticated "marketing" materials ("unadvertisements"), clinical information, drug information consultants, and patient education materials to help facilitate prescribing change. The academic detailers have clinical background (nursing, pharmacy). ***Vermont*** and ***Maine*** have each enacted comprehensive academic detailing legislation in 2007 ("evidence-based research education program") and ***West Virginia*** has a program through its pharmacy school.

- ***Financial disincentives***: Unsuccessful 2006 New York legislation, A 1027 would have prohibited pharmaceutical manufacturers and distributors from deducting the costs of advertising drugs to consumers from their personal or corporate income taxes. ***West Virginia's*** disclosure regulation has a link to drug pricing; the rules are intended to assist the state in negotiating drug prices that do not reflect the cost of marketing.[14]

- **Conflict of interest and fiduciary duty legislation:** A number of states now require oversight or regulation of pharmacy benefit managers, including a fiduciary relationship and conflict of interest restrictions or disclosure. **Maine's** law enacted

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[12] Legislation similar to the New Hampshire law was defeated in 2006 Arizona, Hawaii, West Virginia and in California, where the California Medical Association is promoting an opt-out option for doctors, and in Washington and Nevada in 2007. See NCSL data; "Doctors Object as Drug Makers Learn Who's Prescribing What," by Stephanie Saul, New York Times, May 4, 2006, pg. A.1; "State Pharma: Regulations are Becoming Increasingly Complicated as More Watchdogs Step In," by Jonathan Vatner, Meetings & Conventions, July 2006.

[13] Crowley & Ashner, "State Medicaid Outpatient Prescription Drug Policies: Findings of a National Survey, 2005 Update," (October 2005).at 10.

[14] See also 2006 legislation **New York** S 2258 (Sen. Krueger) which would require a cost benefit analysis of pharmaceutical advertising and promotional activities associated with the provision of prescription drugs to citizens in the state, and **Pennsylvania** HR 114 Concurrent Resolution (Rep. Walko), which would direct the state Health Care Cost Containment Council to conduct a study on the impact of prescription drug advertising and promotion on drug prices in Pennsylvania.

in 2003 remains the most comprehensive; the **D.C**. law is very similar. Both the Maine and D.C. statutes have withstood legal challenge. **South Dakota** and **North Dakota** also have PBM transparency laws though without the fiduciary requirements (South Dakota requires "fair dealing") and several other states have more limited laws governing registration and/or payment provisions. 24 PBM bills were pending in at least 17 states this year, with comprehensive legislation enacted in **Iowa and Vermont**.

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The CHAIRMAN. Thank you very much, Representative Treat.

To the entire panel, I would like to devote the time of my questioning to this issue of a registry that would require virtually all payments of any sort that are made from the industry to physicians to be made public and to be made available to people wherever and whenever they wish.

Do you think that this is something that we should be doing, that it is necessary, that it would have an impact, a positive impact, would be a great step to take? Do you see problems in doing it? Do you think we ought to get after it as quickly as we can?

What is your opinion, your experienced opinion, on this question of full disclosure of payments of any sort that are made between the industry and physicians?

Dr. Kassirer.

Dr. KASSIRER. Thank you, Mr. Chairman. I was extremely impressed with the reporting of Gardner Harris on the information that he was able to obtain as a consequence of the State laws.

What surprised me about it was that there were insights that I hadn't even thought about that came out, including the notion that there were physicians who had lost their licenses and were not practicing anymore, who were still allowed to do research for industry. That information would never have been otherwise available. These were physicians who were incapable of doing adequate clinical research.

I would certainly support the notion that a Federal registry of some kind would be of value in identifying at least the extent of the involvement of physicians and industry. I think that more needs to be done besides that, and I made the point about shining more light on the problem by commissioning the National Academy of Sciences to study the issue.

I spent time with the president of the Institute of Medicine about a year ago. He indicated that he would be interested in doing such a study, but didn't have the funding to do it. The study that the Institute of Medicine did on medical errors shined a light on a series of extremely important issues that were, before that, hidden. I think the same could be true of a study by the IOM of this particular issue.

But in terms of a Federal registry of some kind, I am all for it.

The CHAIRMAN. Dr. Rosenthal.

Dr. ROSENTHAL. Thank you, Mr. Chairman. I agree with [off-mike]—I am still having microphone problems, but I think it is OK. I agree that the concepts of light and disclosure are very useful in this area, and there are a number of areas that need light shed upon them, and this is one.

The data as to which doctors are receiving which kinds of valuable consideration, whether they be payments or stock options or whatever, is available. It exists, and I think that that data needs to be disclosed. It needs to be completely transparent, and we should demand it. I think that would be a great and fairly easy way to generate a database of that information for public use.

There are several other areas that need illumination, and I assume we can talk about that later.

The CHAIRMAN. Thank you.

Dr. Lurie.

Dr. LURIE. I think my testimony makes clear that I do think it is a good idea, but let me make three points—well, four.

The first is that there is a tendency to think of disclosure as a panacea in a lot of areas, not just this one. So, as welcome as a registry would be, I think we need to think beyond that, and some of those are laid out in my testimony.

The second point is just to refer to what Representative Treat had to say. I certainly agree that the last thing we need is a national registry that is weak and has the effect of preempting the, at least, good attempts that have been made at the State level, so preemption should not be of stronger State laws. Of course, a good cure for that is just to have a good Federal one.

My next point is when it comes to shining light on this, I mean, part of what has allowed all of this to take place to date is, in fact, that it occurs, in effect, in darkness. I think it is worth thinking about the 2002 American College of Physicians' policy statement regarding pharmaceutical companies.

They offer three criteria for determining the appropriateness of a payment, and the first one is, "What would my patients think about this arrangement? What would the public think? What would I feel if the relationship was disclosed through the media?"

What these disclosure laws do, in effect, is to put these theoretical questions that the ACP says are so important to the test and allows patients to make up their minds for themselves.

My final point is this. When we set about writing our JAMA paper—and my co-authors who are here will attest to this—I was somebody who was rather skeptical about the naming of physicians. I thought that what we wanted to do was provide aggregate information and be able to describe the extent of things in a kind of public health way, not in an individual way.

But in the course of doing the study, a lot of private information—not private, but personal information did come out. I have become a strong convert to the idea that, in fact, there is a lot to be gained from putting out the actual names of the doctors. There is a lot of creative work, some of it done in the New York Times, in which you can link particular people to other information, be it doctor disciplinary records, whether or not they are key opinion leaders, et cetera, et cetera, whether they sit on FDA advisory committees.

All of those kinds of things can only be done when you have the doctors' names. If the doctors are not ashamed of this, they shouldn't be objecting to this.

The CHAIRMAN. All right. Thank you so much.

Representative Treat.

Hon. TREAT. Yes, thank you. I would concur that if we can do it right, a national registry would be great.

I was interested in Dr. Lurie's testimony, because those are a lot of the issues that we, as an organization, are advising States, about what is the best way to write these State laws when they go about it.

We are trying to make sure that they don't look at a law that has been passed somewhere else and say, "Well, that passed. This is the way to go," because many of those, of course, include compromises that went into effect and were the only reason the law

passed. Those compromises really are the loopholes that Dr. Lurie has identified.

Certainly, having prescriber identity is important. I know that that is something that the Vermont legislature has been trying to focus on and make sure that its laws, which initially had that only in the aggregate, now provide in more specificity.

I think we need to remember that some of the State laws were initially passed without really understanding the relationships between these payments and actual prescriber behavior. A lot of the States were actually looking initially to shine a light on how much money was being spent on marketing and advertising activities.

So many of the laws are really focused on just collecting information on how much money was spent as opposed to really making the link between prescriber behavior and payments to those prescribers. I think States have become more and more aware of that, particularly as the data in Minnesota is now being analyzed, and I give a lot of credit to the New York Times and the reporters there for actually spending, as I understand, well over a year going through those boxes.

Just in Minnesota's defense, I think that the Web and Web-based information was a lot less common in 1993 than it is in 2007. That brings me to my point that having Web access, and having it in a format that is, in fact, accessible would be very important.

I agree with Dr. Lurie that the trade secret exemption is an exemption that can be a loophole that swallows the whole rule. This comes up in many, many contexts. It is very important to get that right and to make sure that just anything can't be claimed to be a trade secret and thus be protected from disclosure.

I agree on the medical devices, making sure that those are in. I think, again, that is something that when State legislators were passing these laws, they were focused on prescription drugs and not so much on medical devices. But that is an issue that has come to light.

Another area where there are loopholes in the Minnesota and other laws is the definition of educational activities and continuing medical education activities and making sure that those are included as well.

I just say that transparency alone may not be enough, and I think many States think that it isn't enough. Certainly, an analysis of the data from Minnesota shows that the voluntary guidelines that are in place are not being honored. So it may be that since no one knew what was in those documents, since they were all in big boxes, it is not a fair test of transparency, and a registry that had information posted on the Web somewhere where everyone could go see might be much more effective.

But that said, there are a lot of other issues. Some of them have been alluded to by other members of the panel, and some of them are addressed in the State legislation that I mentioned, including the kinds of practices that go on in doctors' offices, the data mining issues, and some of the other things around actually banning gifts that might be appropriate for this Committee and Congress itself to consider doing.

The CHAIRMAN. Dr. Kassirer.

Dr. KASSIRER. Thank you, Mr. Chairman. Dr. Lurie's comments reminded me of a point that we really must make, and that is that we have spent a lot of time talking about disclosure. In fact, if you look at the reports in the newspapers, it has been largely about the lack of disclosure.

So people have made a lot about the fact that physicians have done various things and made various comments but have not disclosed their ties with industry, which could have influenced their opinions.

The fact is that we must pay attention to a much more fundamental issue, and that is that disclosure is perhaps necessary in terms of identifying those who have conflicts of interest, but it is not sufficient, because disclosure doesn't solve the problem. The problem is the conflict, and disclosure doesn't solve the conflict.

The CHAIRMAN. Very important point.

Well, we have with us today a distinguished senator from the State of Delaware, Mr. Tom Carper.

We would love to hear your comments and questions, Senator Carper.

Senator CARPER. Thank you, Mr. Chairman.

I am happy to be here, and I think this is a busy time—we have three separate hearings going on at once. We are being briefed by the director of national intelligence, we are doing immigration reform on the floor, and we have got a bunch of people here from Delaware. But I wanted to be here at least for part of this, because this is a good and important hearing.

I have missed your statements, and what I am going to ask you to do—and I do this sometimes when I am sort of in and out of a hearing. But could each of you take maybe a minute or so and give me a couple of major takeaways, from your opening statements please.

Representative Treat, that is a great name. That would be a great name to have as a politician. If I had a name like that, I could go somewhere. [Laughter.]

Hon. TREAT. Especially when you are going door to door right before the election, which would be around Halloween.

Senator CARPER. You probably have a lot of fun with that.

Hon. TREAT. Yes. Well, thank you very much for an opportunity to reiterate everything I said already, which I won't do. [Laughter.]

Senator CARPER. Not everything, not everything.

Hon. TREAT. No, I won't do that. But my takeaway would be that, you know, States have really been in the forefront on this issue, not only on disclosure, but in a lot of other areas.

Let me just give you an example. I think as sort of an early warning system, one of the bills—actually, it is a bill I sponsored, and it was initially passed into law in Florida, and Vermont just did it, and it looks like New Hampshire is just about to. It focuses on a whole new area of electronic prescribing, where there is this huge push, a lot of it going on here in Congress, to get doctors to put everything onto electronic recordkeeping, you know. Well, what that means—and actually have electronic prescribing, where you just write into your PDA and it goes straight to the pharmacist.

That enables tremendous new tools in terms of mining that data, questions about privacy. Questions in this legislation—the legisla-

tion I had and others had, which are actual messages that pop up from a pharmaceutical company. Let's see. You are just about to write a prescription for a particular drug, and it says, "Hold on there. I will show you one that is prescribed as—Drug Y has much better effects," and all this clinical information, and that could be a lot better.

Well, you could see that being done in a way that is very objective and presenting information on all sides. But you could also see it—as has been the experience in Australia, which is much farther along this road of electronic, you know, records and prescribing—as really interfering with doctors' behaviors and actions. This is an issue that the States are focused on, and the Federal Government is very far behind.

So, I guess, you know, my message is that States may not be doing it perfectly, but they are kind of an early warning system, and they are tackling issues that aren't likely to be addressed anytime soon by the Federal Government. We need to make sure that as Congress moves ahead in doing things like a registry, which I think is a great idea, that we are not preempting State laws that might actually be stronger.

Maine has a clinical trials database law that is far more comprehensive than the Federal law on the books. If there were preemption of State laws, you would end up not actually getting the data from Maine. So that would just be my proviso on it, and there are a lot more issues than just transparency for you to focus on.

Senator CARPER. Thank you, Representative Treat.

Dr. Lurie.

Dr. LURIE. As long as you are making observations on Representative Treat's name, I will point out that she is the right person to be speaking at a meeting about conflict of interest. It really seems just the right name for that.

The points that I made in my testimony were, one, that physicians typically believe they are unaffected by interactions from drug companies though they believe that their colleagues are likely to be affected, which is, you know, kind of a logical contradiction.

Senator CARPER. What we hear around here sometimes, you know, we work on ethics legislation, you know.

Dr. LURIE. Right. It is, "I am immune, but nobody else is." I went on to talk about some of the successes of the State payment disclosure laws. Then I went on to talk about the five that have so far been enacted, and I pointed out that there were a number of gaping holes in those, and I pointed out that sometimes the exemptions swallow up the law itself.

But there are ways to make them better, to be sure, and we lay out a series of recommendations at the end of our testimony, which run the gamut from literally how to enter things on the Internet to what the exemptions should be and so forth—how often reporting should be made to the legislature and so on.

Anyway, the point is that there are holes in all of the existing State pieces of legislation so far. Then we went on to look in more detail at Minnesota and Vermont, which are the two that actually have reporting requirements that are in place.

We showed that the accessibility of payment data is very poor, that either through the legal loopholes or through, really, neg-

ligence on the part of the Board of Pharmacy in just not analyzing the data that kept coming in, there is de facto little access to information, that the quality of the payment data in data terms is often poor, allowing aggregation of data where individual data would be much more helpful, both for the public and for researchers, that——

Senator CARPER. Doctor, I am going to ask you to go ahead and sum it up, because I need to hear——

Dr. LURIE. Absolutely.

Senator CARPER [continuing]. From the other witnesses, and——

Dr. LURIE. That is fine.

Senator CARPER [continuing]. Senator Kohl has infinite—well, almost infinite patience, but he won't let me go on forever, so just wrap it up, please.

Dr. LURIE. I am sorry.

So the disclosed payments are large in our study in the JAMA, although they are probably underestimates. Finally, as a result of this, we conclude that a national State reporting law is what is required, although we agree with the comments of Representative Treat about preemption.

Senator CARPER. Good. Thank you. Thanks so much.

Dr. Rosenthal, just a minute or 2 of a takeaway, please.

Dr. ROSENTHAL. Thank you, Senator.

I would encourage you to read the written statements and, also, some of the media coverage of this is covered on our Web site, the Physicians for Clinical Responsibility Web site, which is clinicalresponsibility.org.

In a nutshell, my testimony was the view from the trenches, particularly in retinal surgery. It is a before-and-after story.

Until seven years ago, research was independently funded. It was credible. It was trustable. People would get up at meetings and give talks that you knew were fact based and unbiased.

About seven years ago, with the advent of a treatment called photodynamic therapy, this brought in the era of corporate sponsored clinical trials. Since then, it has been one example after another, and with each succeeding iteration, the drug companies have gotten better at marketing to doctors, crossing the line to paying poorly qualified clinical doctors to do paint-by-numbers research according to their dictates, and we are supposed to just trust their altruism that it is all unbiased. Studies don't support that unbiased character.

We have seen the sort of perfection of the recruitment of doctors to be key opinion leaders and to either fail to disclose or, more commonly, euphemistically disclose their relationship with companies to the point where we have very little credibility at society meetings, in many of the—not all, but many of the journal articles and this sort of thing.

This has created a significant pressure on doctors to follow drug company party lines on clinical decisionmaking. The monetary impact of this is phenomenal. There is a single drug——

Senator CARPER. I am going to ask you, if you will, to wrap up because my time is limited. Thank you.

Dr. ROSENTHAL. This is my last thing.

There is a single drug that we are currently expected to use, that if all patients were treated with this drug, according to the study protocol, out of Part B, it would cost about $5 billion per year. That is just a little bit more than the entire eye care CMS budget.

So, as you can see, the stakes are very high.

Senator CARPER. Yes, thank you.

Dr. is it Kassirer?

Dr. KASSIRER. Yes.

Senator CARPER. Has your name been mispronounced?

Dr. KASSIRER. No, it is pronounced correctly. Thank you. It is usually not.

A couple of words. I have asserted that the medical profession has become excessively dependent on the largest of industry, that these financial connections have had a negative influence on the quality and the cost of patient care and the trust of the public, and that the profession's response to these threats have been inadequate. I made the point that the leaders of the profession have done little to counter a trend.

It always amazes me that there is a paradox in their policies. On the one hand, they admit that physicians can be influenced by gifts and trips and things like that, and yet they allow it, anyway, and that seems to me to be something that is counter productive in terms of the cost of care and the quality of care.

Thank you, sir.

Senator CARPER. Thanks very much for both of those points.

Mr. Chairman, I have a couple of questions I want to submit for the record to this panel, if I may.

But thank you for your testimony and for summarizing for me. Much obliged.

The CHAIRMAN. Thank you, Senator Carper. We thank you very much for your questions.

Senator McCaskill.

Senator MCCASKILL. Thank you very much.

I apologize for not being here to hear all of your testimony, although I heard it. You know, it is so funny, because we have senators give speeches on the floor, and afterwards, someone says, "Well, I heard your debate." You realize that most people watching things around here are watching on television while they are trying to multitask. So, I was listening to your testimony as I was multitasking upstairs in my office.

I wanted to focus a little bit on this panel—and anyone can address this question that would like. I am concerned about the research component of this.

I am very concerned about the conflicts—if I look through JAMA and I look through the *New England Journal*, first of all, I am concerned about all the ads, and then I am concerned that we are going to get to the point that the conflict paragraph at the end of these articles is longer than the article.

Now, the good news is that there is disclosure, and that these doctors are disclosing that they are receiving money from these various pharmaceutical companies and these various prescription drug companies, and that is good. But what I am worried about is the research that is going on that is not getting published because

maybe the results aren't what the people who paid for the research wanted.

I am particularly worried about PhRMA research that is ongoing and that maybe, because the results of that PhRMA research are not what they hoped it would be, it never sees the light of day. I would welcome your comments on that potential problem that we have under the current scenario.

Dr. KASSIRER. Well, as a former medical editor, I feel somewhat compelled to speak out. You are absolutely right about the disclosures at the end of these articles. They are monumental, it seems to me.

When I was the editor of the *New England Journal*, we had a simple policy, and that is that if someone had a financial conflict of interest, we would not allow them to write an editorial or a review article. We also had a policy in which none of our editors had a financial conflict of interest. I got a report every single year from all of the editors, and anyone who developed a financial arrangement was no longer an editor.

With respect to scientific studies, the kinds of studies you were referring to, first of all, it is possible that one could eliminate those studies in which people had a conflict of interest. The problem would be that you would have no studies left, because most of the studies that are published in major journals are supported in some part by industry, and many of the investigators have financial arrangements with industry. That is the reason for all these disclosures that you have now begun to see in medical journals.

What I am always surprised about is how many of these investigators have how many conflicts of interest—some of them, 15 or 20 or 30 conflicts of interest with companies that they work with. You have to ask yourself, "What are they doing at home if they have conflicts of interest with all these different companies?" Whether or not these conflicts influence the science is a critical question. I can tell you that two British editors, Richard Smith, the former editor of the British Medical Journal, and the editor of the Lancet, Richard Horton, have recently spoken up, saying that they don't trust the studies that even they themselves have published in their journals.

With respect to the advertising in the journals, well, it is a complex problem. I can tell you that the *New England Journal*—when I was there, the *New England Journal* could have survived financially with just the job ads and the subscription cost of the journal, and you could have eliminated all pharmaceutical ads.

But the Massachusetts Medical Society that owned the journal would never have heard of that. I mean, they made a lot of profit on the journal, and they built an incredible organization as a consequence of all those profits.

I can tell you one thing about—at least, I can tell you about the *New England Journal*, and I am sure it is certainly true today—and that is that the ads in the journal have never had any kind of effect on the content of the journal, the editorial content of the journal. I am sure that is also true for JAMA. I can't tell you for sure if it is true for all medical journals.

It certainly is possible that, in some way, medical journal editors are influenced by their advertising. In fact, you heard already—

Greg mentioned an example where a medical journal editor refused to publish one of his conflict of interest pieces because he was afraid an advertiser would go away. So I think there may be examples in which editors craft their content, their editorial content, based on their advertising.

With respect to negative studies, it is a mixed bag, I think, in the sense that journal editors are not excited about publishing negative studies, anyway. They are not very exciting studies. So some of the reason for these studies not getting published might be the fact that journal editors just turn them away. They are not interesting.

On the other hand, the current crop of medical journal editors have set out a series of guidelines requiring the registration of clinical trials, and that registration would at least alert you to the fact that there is a study that hasn't been published. It is not complete. It needs a big fix before it can function effectively.

So is it possible that there are studies with negative results that are not being published? Yes, it still is possible.

Senator MCCASKILL. Well, I think figuring out a way that everyone knows when clinical trials are going on would be really, really important, because then there would be an opportunity for research—even if they were not published.

Now, with our technological capability in terms of the Internet, there is absolutely no reason that non-published stories could not be available to people who are interested, and that information that clinical trials are ongoing, I think, would be key.

Just briefly, one follow-up question, Mr. Chairman, if you don't mind.

If, in fact, the large hand of the pharmaceutical industry is essential to these research projects going forward, then would it be the opinion of the panel that independent research at—and here is what I am referring to now.

At higher education institutions, where these companies are coming in and saying, "We will give you money at your school if your academicians in the medical field will do these studies," and then you have academicians now kind of being harnessed by virtue of the flow of money—and what worries me is where are we going to end up 10 or 20 years from now in terms of truly independent academic studies.

Are these academicians that may want to go and research something that would be a terrible outcome for the flow of money—and I think this may be, frankly, a corollary of the fact that we have sadly, sadly, in this country, short-changed higher education in terms of research money and the kind of money that we need to be investing in terms of keeping the prominence of our country in terms of the field of higher education.

Now, that is my own political bias about funding higher education. But if any of you would comment on that? Yes?

Dr. LURIE. Well, I certainly agree with all of this.

I think when we talk about the conflict-of-interest statements, first of all, I mean, I think they have become so long that we literally risk turning them into a laugh line at some point, where it becomes a joke the way the surgeon general's warning on tobacco became a joke after a while, and you wind up on "Saturday Night

Live" joking about the extent of the disclosures. I once read the transcript of an FDA advisory committee meeting, where they are busy disclosing all of this, and somebody gets up to say, "I just want to say you didn't mention my conflicts. I don't have any, but I sure wish I did," you know.

So it becomes a bit of a joke, and that is one of the limitations of disclosure, as important as it is.

I think when it comes to the research, as important as all of the data suppression examples—which there are, be they the class study with regard to Celebrex, where the company published half the data, because it knew that the full data set that it had in its possession didn't show the benefit that half the data set showed; or be it withholding of the studies on SSRIs, many of which turned out to be negative, as far as the company was concerned.

By the way, the FDA knew all of this, and because of its own secrecy laws wasn't able to expose the way that the companies were withholding the information. So the levels of secrecy at the FDA are also a part of the problem here.

But with regard to the funding of research, as important as the data withholding is, probably more important is the fact that as industry is a larger and larger funder of research in this country, they are setting the agenda. They are asking the questions. They decide which questions get asked and which ones, in effect, do not, because the academicians have only so much time to do their work.

You know, physicians could say no to that—the researchers could say no to that money, but they don't. So what we have are questions that are of interest to drug companies that may be of absolutely trivial interest to the public health: whether the 24th non-steroidal anti-inflammatory drug has some minor advantage over the 25th non-steroidal anti-inflammatory drug. I am just not that interested in that question.

I am interested in questions about diet and exercise and truly breakthrough drugs. But those studies are harder to get funded, and the industry is not nearly as interested in them.

I will point out that back in the 1970's, there were proposals that the pharmaceutical industry would pay into a large pot from which studies would be done, selected in terms of their public health importance by impartial people and then conducted by people who would be responsible for both doing them and analyzing them. That is really the way out of this problem. I mean, it is——

Senator MCCASKILL. What happened to that suggestion in the 1970's?

Dr. LURIE. You know, it went the way of many proposals, I am afraid. We hear about it periodically as if it is, you know, something completely impossible. Actually, the New Yorker has a little article about it just this week in which that idea is revived as if it were something new. But it is something that periodically percolates up as——

Senator MCCASKILL. I think that would be a spectacular idea.

Dr. LURIE. I would agree.

Senator MCCASKILL. It would solve the problem.

Dr. LURIE. Yes, it would. Unfortunately, certain of the monied interest wouldn't be terribly happy with it, and that is probably where it went. But I agree with you.

If you think about it, as Dr. Kassirer was saying, when you think of conflict, I mean, the best solutions to conflicts are not merely disclosure. They are structural approaches that remove conflict, and this would be an example of the same.

Senator MCCASKILL. Right.

Mr. Rosenthal.

Dr. ROSENTHAL. If I could quickly comment on a couple of things, first, I would like to point out that, in my field of retinal medicine, there are many very, very good researchers who are trying to do good work and trying to do non-conflicted work. I believe that they find it annoying that there is so much pharmaceutical influence, because it does make it hard for the reader to know what is biased and what isn't, and I think that casts good work in a more tentative light as well.

I also wanted to agree that there are many areas where it is the way you ask a question, it is what you decide to look at, that sort of thing. There is one study of a commonly used treatment where they redefined visual success to include three lines of visual failure. If they hadn't done that, the data wouldn't have looked so good.

Senator MCCASKILL. Right.

Dr. ROSENTHAL. That same study elected not to look at toxicity effects for 3 months after the treatment. We now know that that particular treatment is highly toxic to the macula.

There is another example where a company had two versions of the same drug. One had already been priced for another treatment and could be available in doses we needed for eye care at around $50 a dose. The other version of the same molecule is $2,000 a dose, and you have to give it more often. So which would you choose to study in a randomized trial and get approved? It is not hard to see.

Senator MCCASKILL. Thank you, Mr. Chairman, very much.

The CHAIRMAN. Thank you, Senator McCaskill.

We thank this panel exceedingly for being here today. You have provided great testimony, great observations, and, hopefully, we will be able to make some progress as a result of your testimony. Thank you for being here.

Our second panel consists of two witnesses.

The first will be Dr. Robert Sade. Dr. Sade is chair of the American Medical Association's Council on Ethical and Judicial Affairs, and he is a professor of cardiovascular and thoracic surgery at the Medical University of South Carolina.

Our second witness will be Marjorie Powell. Ms. Powell is the senior assistant general counsel at the Pharmaceutical Research and Manufacturers of America. Her current work focuses on the legal implications of State legislation regarding prescription drugs as well as oversight of PhRMA's legal matters.

We thank you both for being here.

Dr. Sade, we will take your testimony.

STATEMENT OF ROBERT SADE, CHAIR, COUNCIL ON ETHICAL AND JUDICIAL AFFAIRS, AMERICAN MEDICAL ASSOCIATION, WASHINGTON, DC

Mr. SADE. Thank you, Chairman Kohl and members of the Committee, for convening this hearing to examine financial relationships between physicians and the pharmaceutical industry.

The topic is very timely, and the AMA sees today's hearing as an opportunity to communicate the ethical standards that guide all physicians in the practice of medicine and in their interactions with the pharmaceutical industry.

My name is Robert Sade. I am chairman of the Council on Ethical and Judicial Affairs of the AMA, and I am also professor of surgery and director of the Institute of Human Values and Healthcare and the Medical University of South Carolina in Charleston.

Physician prescribing decisions depend heavily on a quality of available scientific information. The pharmaceutical industry and Federal regulators are important information sources. There is a clear need for interactions between physicians and the pharmaceutical industry to ensure the free flow of valid scientific information.

When the information is accurate and complete, physicians have the necessary tools to make the right prescribing decisions for their patients. If information is not properly provided by industry, or if physicians never receive such information, quality medical care can be jeopardized.

The AMA was created in 1847 for the specific purpose of establishing ethical standards for all physicians. The AMA code of ethics has been continually revised for 160 years, guided by the Council on Ethical and Judicial Affairs, and serves as the primary compendium of medical professional ethical statements in the United States.

The code has clear ethical guidelines that govern physician interaction with the pharmaceutical industry. For example, physicians must not place their own financial interests above the welfare of their patients.

A physician's medical recommendations must not be inappropriately influenced by financial considerations. Accordingly, it is unethical for a physician to accept any kind of compensation from a pharmaceutical company as a quid pro quo for prescribing its products.

The AMA code acknowledges that the giving of gifts reflects a customary social practice. However, it warns that gifts to physicians from commercial businesses may not be consistent with the AMA code. The code requires that gifts accepted by physicians must mainly benefit patients and should be of only modest value.

Also, the AMA code explicitly provides that no gifts should be accepted if conditions are attached, such as prescribing certain drugs. All gifts, however, are not inappropriate. Indeed, many of them will benefit patients. An example is when physicians provide drug samples to patients who have a medically indicated need for treatment but cannot afford to buy the necessary drugs.

The AMA works with State medical associations and specialty societies to disseminate ethical standards. To ensure compliance with

these standards, the AMA relies not only on the Council on Ethical and Judicial Affairs, but also on medical licensing boards.

About six years ago, the AMA undertook a major campaign to educate physicians and industry representatives about the AMA's ethical guidelines regarding promotional gifts to physicians from industry. More than 30 other physician and healthcare organizations came together to form the working group on the communication of ethical guidelines for gifts to physicians from industry. As a result of this collaboration, the AMA created an awareness program to educate physicians and other stakeholders on ethical guidelines and developed an educational program.

The AMA is currently developing a series of educational programs for medical students and physicians designed to promote the importance of sound prescribing, focusing on how to minimize and eliminate undue influence by industry marketing practices. Special attention is given to medical students in resident positions in addressing this important issue, since interactions with industry often start very early in a physician's professional career.

The interactions between industry and the medical profession must be defined by the exchange of sound scientific information which benefits patients. All practices that surround those encounters, from the visits of pharmaceutical representatives to large educational gatherings, must be framed in terms of such an exchange and must not constitute an attempt to inappropriately influence the medical treatment that physicians provide to patients. The health and welfare of patients depend on this.

The AMA looks forward to working with the Committee to achieve our shared goals. Thank you for the opportunity to be here today.

[The prepared statement of Mr. Sade follows:]

Statement

of the

American Medical Association

to the

Special Committee on Aging
United States Senate

RE: Paid to Prescribe?: Exploring the Relationship Between Doctors and the Drug Industry

Presented by: Robert M. Sade, MD

June 27, 2007

(202) 789-7426
Division of Legislative Counsel

Statement

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RE: Paid to Prescribe?: Exploring the Relationship Between Doctors and the Drug Industry

Presented by: Robert M. Sade, MD

June 27, 2007

The American Medical Association (AMA) appreciates the opportunity to provide its views regarding the ethics that govern the interactions between physicians and the pharmaceutical industry. We commend Chairman Kohl, Ranking Member Smith, and members of the Committee for convening this hearing to examine financial relationships between physicians and the pharmaceutical industry that, if inconsistent with accepted medical ethics, could affect physician prescribing behaviors. I am Robert M. Sade, MD, Chairman of the AMA's Council on Ethical and Judicial Affairs (CEJA). I am also Professor of Surgery and Director of the Institute of Human Values in Health Care at the Medical University of South Carolina in Charleston.

The AMA has clear ethical guidelines that govern physician interaction with the pharmaceutical industry. In brief, based on the AMA Principles of Medical Ethics (Principles) and the AMA Code of Medical Ethics (AMA Code), physicians' responsibility to their patients is paramount. This means that physicians must not place their own financial interests above the welfare of their patients and their medical recommendations must not be inappropriately influenced by financial considerations. Accordingly, it is unethical for a physician to unnecessarily prescribe a drug for financial benefit; rather prescriptions must be based on the best medical interests of patients. This requires that physicians' prescribing be consistent with the latest scientific information and consistent with the physician's best medical judgment.

In support of these standards, approximately six years ago the AMA undertook a major campaign to educate physicians and representatives of the pharmaceutical, device, and medical equipment industries about the AMA's ethical guidelines regarding promotional gifts to physicians from the industry. In launching this educational initiative, the AMA

was joined by more than 30 other physician and health care organizations and corporations, which came together to form the Working Group on the Communication of Ethical Guidelines for Gifts to Physicians from Industry. As a result of this collaboration, the AMA designed an awareness program to sensitize the various stakeholders concerning ethical guidelines and developed an educational program that includes four modules that address issues typically arising in this area.

Physician prescribing decisions are heavily dependent on the quality of the scientific information available, provided to them, in part, by industry and federal regulators. There is a clear need for interactions between physicians and the pharmaceutical industry to ensure the free flow of valid scientific information. When the information is accurate and complete, physicians have the necessary tools to make the right prescribing decisions. If information is not properly provided by industry, or if physicians never receive such information, necessary and appropriate medical care can be jeopardized.

Within this context, the AMA has developed ethical standards to guide physicians in their interactions with industry, particularly in relation to the direct interaction of pharmaceutical representatives with physicians.

AMA Principles of Medical Ethics & Code of Medical Ethics
The AMA was founded with the purpose of establishing ethical standards for all physicians. First developed in 1847, the AMA Code undergoes continual revision, as guided by CEJA. The opinions contained in the AMA Code address relevant issues in medical practice that establish core standards of conduct for the medical profession. The AMA Code constitutes the most comprehensive source of ethical guidance for physicians and serves as the primary compendium of medical professional ethical statements in the United States.

Jurisdiction and Scope of CEJA
CEJA is composed of seven practicing physicians, a resident or fellow, and a medical student. The members are nominated by the AMA's President and elected by the AMA's House of Delegates. CEJA prepares reports that analyze timely ethical issues confronting the medical profession and makes recommendations to guide physician behavior. When these reports are adopted, its recommendations become the opinions that constitute the AMA Code.

In addition to its responsibility to maintain and update the AMA Code, CEJA has judicial responsibilities, which include jurisdiction over membership in the AMA to ensure compliance with the AMA Code. CEJA does not have explicit authority to investigate non-member physicians. However, many state medical licensing boards use the AMA Code to establish standards of physician conduct and courts look to the AMA Code for guidance in resolving disputes involving physicians. Thus, the reach of the AMA Code extends throughout the medical profession. The AMA Code, therefore, is a key element in the medical profession's commitment to ethical conduct, and its reach goes well beyond its direct influence on AMA members. However, professional self-regulation cannot be fully accomplished by a single institution; it requires the collaboration of other

bodies. While the AMA establishes ethical standards, it works in concert with state medical associations and specialty societies to disseminate the information. To ensure compliance with these standards, the AMA relies not only on CIA, but also on medical licensing boards.

CEJA & AMA Code

There opinions in the AMA Code are relevant to governing the interactions between physicians and the pharmaceutical industry. They establish an ethical framework that guides physicians in matters of conflicts of interest, gifts from industry, and appropriate factors to consider when prescribing drugs. In addition, physicians have an ongoing professional obligation to remain informed and knowledgeable about drug treatment options for patients, so the AMA Code has ethical guidance concerning continuing medical education (CME), as well.

Conflicts of Interests

The broadest provision governing conflicts of interest clearly states that physicians must subordinate reward or financial gain to their paramount responsibility to their patients.. If a conflict develops between the physician's financial interest and the physician's responsibilities to the patient, the AMA Code unambiguously requires that the conflict must be resolved in a manner that benefits the patient.

Gifts from Industry

The AMA Code acknowledges that the giving of gifts reflects a customary social practice; however, it warns that gifts to professionals, such as physicians, from commercial businesses, such as pharmaceutical companies, may not be consistent with the AMA Code. To avoid accepting inappropriate gifts, physicians must comply with a number of guidelines. Among the salient guidelines, gifts accepted by physicians should primarily entail a benefit to patients or be related to the physician's work and should not be of substantial value. Also, the AMA Code explicitly provides that no gifts should be accepted if there are conditions attached. For example, physicians should not accept gifts that depend on the physician's prescribing practices or that establish expectations that may influence the patient-physician relationship. All gifts are not inappropriate. Indeed, many of them will inure primarily to the benefit of patients. An example is the practice of physicians providing drug samples to patients who would not otherwise have access to necessary drugs. This provides a clear and direct benefit to patients who have a medically indicated need for treatment, but lack the resources to obtain the necessary care. Physicians are on the front lines and know first hand the importance of gifts from pharmaceutical representatives in the form of free samples.

Prescribing Drugs

The AMA Code contains a specific requirement that concerns the obligations that physicians have when prescribing drugs. It provides that physicians should prescribe drugs based solely upon medical considerations, patient need and reasonable expectations of the effectiveness of the drug for the particular patient. This standard reemphasizes that physicians may not accept any kind of payment or compensation from a pharmaceutical company as a *quid pro quo* for prescribing its products.

Continuing Medical Education
Like physician prescribing, the AMA also has guidelines designed to help frame how industry may support educational activities certified for Continuing Medical Education (CME) credit for physicians. The AMA Code provides that physicians should strive to further their medical education throughout their careers because only through participation in CME can physicians continue to serve patients to the best of their abilities and maintain professional standards of excellence. CME consists of educational activities that serve to maintain, develop, or increase the knowledge, skills, and professional performance and relationships that a physician uses to provide services for patients or the profession. CME is based on a body of knowledge or skills generally accepted by the profession as within the basic medical sciences and clinical medicine, as well as the provision of health care to the public. Most state medical licensing boards, acting under the state's medical practice act, require physicians to complete a certain amount of CME every year. Additionally, several national specialty societies require CME credits to maintain membership. Generally CME credit indicates that the educational event is a meritorious learning activity sponsored by an accredited organization.

Guidance pertaining to CME activities is derived from one of the nine AMA Principles of Medical Ethics: a physician has an affirmative obligation to "continue to study, apply, and advance scientific knowledge, [and to] maintain a commitment to medical education...." Subsidies to underwrite the costs of CME can contribute to the improvement of patient care and therefore are permissible. However, industry subsidies to underwrite the costs of certified educational activities must not undermine the foregoing ethical commitment. As a result, subsidies should not be granted in a manner that compromises the medical profession's control over the selection of content, faculty, educational methods, and materials. Because a company's representative giving a subsidy directly to a physician may create a relationship that could inappropriately influence the use of the company's products, any subsidy should be accepted by the CME provider instead. In turn the accredited CME provider may use the funds to reduce the accredited educational activity cost for all participants. Payments from a company should not be accepted directly by physicians attending a CME activity.

Physicians serving as presenters, moderators, or other faculty at a CME conference should ensure that research findings and therapeutic recommendations are based on scientifically accurate, up-to-date information and are presented in a balanced, objective manner. Faculty must ensure that the content of their presentation is not modified or influenced by industry or other financial contributors. All conflicts of interest, such as a financial connection to a particular commercial firm or product, should be disclosed by faculty members to the CME provider and to the audience. Faculty may accept reasonable honoraria and reimbursement for expenses.

Physicians involved in organizing CME activities should ensure that the program is balanced, with faculty members presenting a broad range of scientifically supportable viewpoints related to the topic at hand. Any non-CME activity that is primarily

promotional must be identified as such to faculty and participants, both in its advertising and at the conference itself.

The AMA has worked with health care stakeholders—including the Food and Drug Administration (FDA) and the U.S. Department of Health & Humans Services' Office of the Inspector General (OIG)—on concepts of content independence for certified educational activities through the National Task Fore on CME Provider-Industry Collaboration. Currently, the AMA chairs the Task force which meets annually. Over the years, the faculty has included representatives of the FDA, the OIG, the Accreditation Council for Continuing Medical Education (ACCME), the American Academy of Family Physicians (AFFP), and CEJA, among others, to address issues related to physician and CME provider interactions with industry. The materials from the Task Force annual meetings are often made available at another key meeting, the Alliance for Continuing Medical Education annual meeting, as well.

AMA Educational Initiatives

Continuing education is critical to ensure that physicians identify and resolve possible conflicts of interest that may interfere with the integrity and independence of a certified CME activity. In addition to the AMA's participation with the Working Group on the Communication of Ethical Guidelines for Gifts to Physicians, the AMA has provided substantial ongoing support for the work of the National Task Force on CME Provider and Industry Collaboration. Equally important to the foregong initiatives, five years ago, the AMA communicated to all medical schools and residency programs the importance of including education on ethical guidelines regarding gifts to physicians from industry within their curricula. The AMA also recommended to all medical school deans and residency program directors that appropriate policies be developed for medical students, residents, and faculty regarding the issue of gifts to physicians from industry. Four years ago, *Virtual Mentor*, the online AMA Journal of Ethics visited by tens of thousands of medical students and medical educators every month, devoted an entire issue to interactions with the drug industry. These articles are continuously available online to anyone seeking information related to this topic.

The AMA is currently developing a series of educational programs for medical students and physicians to promote the importance of sound prescribing. Partly funded by the state Attorneys General of the United States. These programs build on previous AMA efforts to educate physicians about their ethical responsibilities in making cost-effective prescribing decisions and how they can minimize and eliminate undue influence by industry marketing and promotional practices. Special attention is given to the next generation of physicians—medical students and resident physicians—in addressing this important issue, especially because interactions with industry often start very early in a physician's professional career. The AMA is committed to educating physicians about sound prescribing from their first days in medical schools to their last day in clinical practice. The health and welfare of patients depend on it.

In sum, interactions between industry and the medical profession must be defined by the exchange of sound scientific information, which benefits patients. All practices that

surround those encounters, from the visits of pharmaceutical representatives to a physician's office to large educational gatherings, must be framed in terms of such an exchange and must not constitute an attempt to inappropriately influence the medical treatment that physicians provide to patients.

The AMA, along with other stakeholders in the medical profession, continues to take appropriate measures to reduce the actual or perceived conflicts-of-interest that might arise from gifts from industry to physicians, in order to safeguard the delivery of quality health care based on the best available science, thus earning and maintaining the trust of patients.

The AMA appreciates the opportunity to provide our views to the Special Committee On Aging on the relevant ethical principles and AMA Codes that govern physician interactions with the pharmaceutical industry.

The CHAIRMAN. Thank you, Dr. Sade.

Ms. Powell, we would like to hear from you.

STATEMENT OF MARJORIE POWELL, ESQ., SENIOR ASSISTANT GENERAL COUNSEL, PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA, WASHINGTON, DC

Ms. POWELL. Thank you, Mr. Chairman, Senator McCaskill. My name is Marjorie Powell. I am the senior assistant general counsel at PhRMA, which is the trade association representing those companies that are researching and developing new medicines.

One of the important responsibilities of a pharmaceutical company when FDA has approved a new medicine is to make sure that physicians know that the medicine is available and know how and when to use that medicine and how and when not to use that medicine. That is the purpose of what is called pharmaceutical marketing or promotion. It is to make sure that physicians know when to use and when not to use medicines.

In 2002, PhRMA adopted a significantly revised marketing code, which focused exactly on that, identifying that the role of a physician's prescribing is to meet the patient's medical needs using the physician's medical knowledge and clinical experience. But some of that medical knowledge comes from using prescription drugs once they have been on the market and experience with those drugs. It also comes from learning about new medicines, and that is the role of the pharmaceutical industry which has developed those new medicines.

In our code, we have clearly identified that if a pharmaceutical sales representative is providing a gift to a physician, it should be to benefit the patient. It should be of insubstantial value, not of any substantial value. It should not be frequent. It should also not be in exchange for prescribing any particular drug.

We also talked about a number of other things in our code, including the ways that pharmaceutical companies might enter into consulting arrangements with physicians and other members of the healthcare profession, because those healthcare professionals have important information to convey to pharmaceutical companies, partly running clinical trials, but also helping a company to identify, for example, why it is that a patient may not be compliant with a drug regimen and what kinds of possible changes in a medicine would improve compliance.

Our pharmaceutical code has been a leader in the industry, although I must admit that we have clearly followed the AMA in many of our issues and worked closely with the AMA in trying to make sure that physicians are aware of the provisions of the code.

A number of other groups also regulate pharmaceutical promotion and marketing. The FDA clearly has a major role in that, as you know, particularly, because you have just considered the new prescription drug user fee bill that has moved through the Senate and now moved through the House Energy and Commerce Committee. In addition, the Inspector General of HHS has said that compliance with the PhRMA code, while it is not a guarantee that you will be compliant with Federal law, goes a long way to indicating that a company is making a major effort to comply with all the Federal regulations.

Let me turn now to the other side of my testimony, which is the importance of pharmaceutical marketing. Physicians recognize that they get valuable information from pharmaceutical representatives. They also recognize that some of that information is promotional and that they need to ask a variety of questions. Physicians are, in fact, trained professionals who know how to ask questions and how to evaluate both their own experience and all of the information that they receive.

Pharmaceutical marketing is an important counter to many of the other influences on physicians' choices of treatment. For example, one study found that physicians don't even talk to patients about treatments that their healthcare insurers will not pay for. That is a way of screening physician actions that has nothing to do with pharmaceutical marketing, and, in fact, one study found that 54 percent of physicians said that formularies had a major impact on their prescribing.

Another thing that formularies and managed care have done is to increase the percentage of scripts that are actually generic prescriptions. In the United States, this past year, 63 percent of all scripts written were for generics. That is a much higher percentage than in other countries, particularly Europe, where there is much less pharmaceutical promotion.

Let me wind up by saying—and if Senator Carper were still here, I would give him my summary by saying—that there are a number of chronic conditions that are the drivers of healthcare expenditures. A number of people have identified that approximately 75 percent of healthcare spending is on chronic diseases, many of which are undiagnosed or underdiagnosed and clearly are undertreated.

Prescription medicines are prescription medicines, not over-the-counter medicines, because they have both benefits and risks, and they can only be used, in the opinion of the FDA, when they are prescribed by somebody with medical education and professional clinical experience. That is why it is important that the companies who have developed those medicines communicate information about both the benefits and the risks of those products to the people who will be prescribing them.

[The prepared statement of Ms. Powell follows:]

Marjorie E. Powell
Senior Assistant General Counsel
Pharmaceutical Research and Manufacturers of America

Before the
U.S. Senate Special Committee on Aging
"Paid to Prescribe? Exploring the Relationship Between Doctors and the Drug Industry"
June 27, 2007

Mr. Chairman, Senator Smith, and Members of the Committee:

Thank you for the invitation to participate in today's hearing on pharmaceutical company relationships with physicians. My name is Marjorie Powell and I am the Senior Assistant General Counsel at the Pharmaceutical Research and Manufacturers of America (PhRMA). PhRMA is the nation's leading trade association representing research-based pharmaceutical and biotechnology companies that are devoted to inventing new, life-saving medicines that help patients achieve longer, healthier, more productive lives.

Pharmaceutical education of health care providers, often referred to as "marketing and promotion" is a short-hand expression for interaction between pharmaceutical representatives and healthcare professionals regarding pharmaceutical treatments for patients. The role of pharmaceutical promotion is to educate health care professionals on the latest, most accurate information available regarding prescription medicines, which play an ever increasing role in healthcare.

Ethical relationships between healthcare professionals and prescription drug manufacturers are critical to the pharmaceutical industry's mission of developing and marketing medicines that allow patients to live longer, healthier, and more productive lives. Direct communication with healthcare professionals allows pharmaceutical

manufacturers to inform healthcare professionals about the benefits and risks of their products, provide scientific and educational information, support medical research and education, and obtain information and advice about their products through consultation with medical experts.

PhRMA Code on Interactions with Healthcare Professionals

PhRMA's member companies are committed to following the highest ethical standards as well as all legal requirements in their interactions with healthcare professionals. An expanded version of the "PhRMA Code on Interactions with Healthcare Professionals" ("the Code" or "the PhRMA Code") was adopted in 2002 to demonstrate our intention of interacting with healthcare professionals for the benefit of patients and to enhance the practice of medicine. The Code starts with the fundamental principle that a healthcare professional's care of patients should be based, and should be perceived as being based, solely on each patient's medical needs and the healthcare professional's medical knowledge and experience.

The PhRMA Code sets out concrete rules that apply in particular situations. The Code, for example, states clearly that it is inappropriate for companies to provide to a healthcare professional entertainment or recreational activities, such as golf or theater tickets. Companies may provide modest meals in connection with presentations by pharmaceuticals representatives or other speakers, if meal is conducive to the exchange of information. Similarly, companies may offer healthcare professionals educational gifts that are primarily for the benefit of patients and are not of substantial value. The Code

does not condone offering items that are of only personal benefit to healthcare professionals.

The Code allows a company to engage healthcare professionals for bona fide consulting services, provided that the company has a legitimate need for the services and compensation is based on the fair market value of those services. In certain circumstances, a company may also provide financial support for conferences and professional meetings and for scholarships that permit medical students, residents, and others in training to attend these conferences. The Code provides that a grant, consulting arrangement, contract, gift, or other benefit may never be offered to a healthcare professional in exchange for agreeing to prescribe a product.

PhRMA Code Endorsed by Office of the Inspector General of the Department of Health and Human Services

Although adherence to the PhRMA Code is voluntary, the Office of the Inspector General (OIG) of the Department of Health and Human Services (HHS) has endorsed the Code as a measure for compliance with the legal requirements that govern pharmaceutical marketing practices.[1] The OIG is the agency within HHS that is responsible for protecting the integrity of government programs and for enforcing federal fraud and abuse laws that apply to the provision of goods and services to the government. In its Compliance Program Guidance for Pharmaceutical Manufacturers, the OIG provided its views on fundamental elements of pharmaceutical manufacturer compliance programs and principles that pharmaceutical manufacturers should consider when

[1] *See* OIG Compliance Program Guidance for Pharmaceutical Manufacturers, 68 Fed. Reg. 23731 (May 5, 2003).

developing and implementing an effective compliance program. The OIG stated that compliance with the PhRMA Code is not an absolute safe harbor, but noted that compliance would "substantially reduce the risk of fraud and abuse and help demonstrate a good faith effort to comply with the applicable federal health care program requirements."[2]

Lewis Morris, OIG's General Counsel, has explained that adherence to the PhRMA Code serves as an indicator of a company's commitment to compliance.[3] According to Morris, conduct inconsistent with the Code "indicates something about how that manufacturer is approaching its relationship to our programs and consumers."[4]

In addition to endorsement by the OIG, the PhRMA Code has received praise from individual federal prosecutors responsible for enforcing the fraud and abuse laws. James Sheehan, an Assistant U.S. Attorney in Philadelphia, stated at the time the current version of the Code was issued: "If people comply with this code as it is currently drafted, we are going to see, in my view, a major difference in how this industry operates, and I think a major difference in how it is perceived by consumers and physicians."[5] In particular he cited the limitations on entertainment, meals, and gifts to healthcare professionals as particularly significant.[6]

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[2] Id.
[3] "IG Rx Compliance Guide Sets PhRMA Marketing Code as Minimum Threshold," *The Pink Sheet*, Oct. 7, 2003.
[4] Id.
[5] "PhRMA Marketing Code Should Cover Preceptorships, Surveys," *The Pink Sheet*, June 10, 2002.
[6] Id.

PhRMA Code Similar to Codes of Other Health Care Associations

The PhRMA Code is similar in many ways to the American Medical Association's ethical opinion on "Gifts to Physicians From Industry," which was revised just before publication of the Code—except that it is stricter than the AMA guidelines on the topic of meals and entertainment.

Subsequent to the issuance of the PhRMA Code, a number of other industry associations released similar documents. AdvaMed, whose member companies develop medical devices, diagnostic products, and health information systems, issued its "Code of Ethics for Interaction with Health Care Professionals"[7] in September of 2003. The AdvaMed Code incorporates many of the same principles and limitations as the PhRMA Code. A year later, the Accreditation Council for Continuing Medical Education adopted the "Updated Standards for Commercial Support,"[8] which provides guidelines for providers of continuing medical education in the same spirit as the PhRMA Code.

The PhRMA Code has therefore become a de facto benchmark for industry practices among both member and non-member companies. A 2003 survey found that 96 percent of industry promotional meetings and events were compliant with the Code.[9] Today it is common practice for pharmaceutical companies to incorporate the provisions of the PhRMA Code into their compliance programs and standard operating procedures, and often explicitly refer to the Code in these materials. Lawyers rely on the Code when

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[7] Available at: http://www.advamed.org/NR/rdonlyres/FA437A5F-4C75-43B2-A900-C9470BA8DFA7/0/coe_with_faqs_41505.pdf.
[8] Available at: http://www.accme.org/dir_docs/doc_upload/68b2902a-fb73-44d1-8725-80a1504e520c_uploaddocument.pdf
[9] Herman R. and Schonbachler D., *PhRMA Code: New Rules, Same Game,* Med. Educ. Meetings. Aug. 2004, at 8, 10.

advising their clients on compliance matters. In addition, the OIG requires pharmaceutical companies to have a compliance officer who reports directly to the president or CEO of the company. These compliance officers look to the PhRMA Code as a baseline in overseeing their companies' compliance efforts.

Value of Pharmaceutical Education of Health Care Providers

Published research has looked at whether physicians see value in pharmaceutical promotional and marketing efforts. One survey found that over 90 percent of physicians surveyed said that the education provided by pharmaceutical representatives about specific drug therapies was either "somewhat valuable" (53 percent) or "very valuable" (38 percent).[10] Another survey found that the "sources of greatest importance (to physicians) were those involving the transfer of information through the medium of personal contact."[11] This kind of contact comes mostly in the form of pharmaceutical representatives and industry-sponsored educational events.

The fact that pharmaceutical representatives interact with physicians, does not mean that doctors uncritically accept everything they are told. One study of physicians examined the relationship between doctors and pharmaceutical representatives and separated the discussions into "unsolicited" and "solicited." "Solicited" discussions involve requests from the doctor for information – for example, new study results, information on potential side effects of a medication, etc. "Unsolicited" discussions are those initiated by the pharmaceutical representative. The study found that physicians find

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[10] 2002 BCG Proprietary Physician Survey (400 respondents), 2002, as reported in "Pharmaceutical Marketing and Promotion, Creating Access to Innovation," Economic Realities in Health Care Policy, Pfizer, 2003: 3(1):11.

[11] McGettingan P. et al., "Prescribers Prefer People: The Sources of Information Used by Doctors for Prescribing Suggest that the Medium is More Important than the Message," *British Journal of Clinical Pharmacology*, 51:184-189.

pharmaceutical representatives to be a highly credible source of information. Doctors did, however, exhibit some skepticism when they were approached with new information that they had not requested. One reason for this may be that information is often presented to doctors in a short meeting. The doctor then often returns to the pharmaceutical representative with questions once he/she has reviewed the information. Rather than unduly influencing doctors, as some critics suggest, pharmaceutical representatives appear to play a valuable role in providing important and timely information. The study suggests that while doctors are not easily persuaded by unsolicited information, those same physicians depend on industry representatives for credible data on the frequent occasions when they find the information useful or valuable.[12] Whether the information is solicited or unsolicited, it is derived from evidence approved by the Food and Drug Administration (FDA).

While some critics have questioned the reliability of information provided by pharmaceutical companies in their marketing to healthcare providers, the reality is that there are state and federal government regulations that govern the marketing of products and serious consequences exist for non-compliance. Only a product's scientifically proven capabilities, verified by the FDA, can be used in its marketing. Furthermore, pharmaceutical representatives depend on good, long-term relationships with physicians, relationships that are built on trust. If a medical representative provides information that a physician believes to be or later learns to be false, significant damage is done to that relationship, and the physician is less likely to rely on information from that

[12] Slotnick, H.B. et al., "How Physicians 'Learn' from Pharmaceutical Representatives: An Exploration," *The Journal of Continuing Education in the Health Profession*, Spring 1999: 19(2):84-96.

representative or company again. Finally, there is competition among sellers of medical products, so it is unlikely that incorrect information will go unchallenged for very long.

Helping Translate New Technologies and Therapies into Practice

An Institute of Medicine report issued in 2001 noted that medical science and technology have advanced at an unprecedented rate during the past half-century. In tandem, the complexity of healthcare has grown.[13] Faced with these rapid changes, our healthcare delivery system has fallen short in its ability to translate knowledge into practice and to apply new technology safely and appropriately. In fact, the report noted that it now takes an average of 17 years for new knowledge to be incorporated into practice, and even then the application is highly uneven. Pharmaceutical marketing and promotion plays a valuable role in the healthcare system by delivering the newest information regarding pharmaceutical therapies to physicians and helping to bridge this gap and translate new technologies into practice. Research suggests that without the information provided by pharmaceutical representatives, utilization of valuable medical innovation would decrease significantly.

In fact, according to an article in *Health Affairs*, variations in prescribing patterns from location to location are not nearly as severe as variations in diagnostics and surgical procedures. The authors suggest one explanation may have to do with the valuable role pharmaceutical representatives play in informing doctors. "Drug firms' marketing efforts may truly educate consumers and providers and lead to greater uniformity of practice."[14]

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[13] "Crossing the Quality Chasm: A New Health System for the 21st Century," Institute of Medicine, March 2001.

[14] Dubois R. W., Batchlor E. and Wade S., "Geographic Variation in the Use of Medications: Is Uniformity Good News or Bad?" *Health Affairs*, January/February 2002: 21(1): 240-250.

Similarly, pharmaceutical marketing and promotion has played a valuable role in raising physician awareness of the most recent clinical practice guidelines, and thus improving health outcomes. According to an article in the *Journal of the American Medical Association* (*JAMA*)[15], "physician adherence to practice guidelines is critical in translating recommendations into improved outcomes. [The guidelines] successful implementation should improve quality of care by decreasing inappropriate variation and expediting the application of effective advances to everyday practice." However, "a variety of barriers undermine this process," such as physicians' lack of awareness and/or lack of familiarity with a guideline. In the case of high cholesterol, for example, in May of 2001, the National Institutes of Health updated their National Cholesterol Education Program [NCEP] guidelines. These guidelines called for greater numbers of individuals to be treated for high cholesterol. According to October 2002 article in the *American Journal of Managed Care*, "[c]oncurrent public and private efforts aimed at physicians and consumers were related to increased diagnosis and treatment. Physician-directed initiatives have included pharmaceutical industry marketing, continuing medical education programs, and promotion of NCEP guidelines. Consumer-directed initiatives have included direct-to-consumer advertisements sponsored by various pharmaceutical companies and patient education programs...."[16]

According to Francine Kaufman, M.D., then-President of the American Diabetes Association (ADA) and current head of the endocrinology division at Children's Hospital in Los Angeles, much progress has been made in diabetes care since 1995. While

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[15] Cabana M., MD, MPH et al., "Why Don't Physicians Follow Clinical Practice Guidelines? A Framework for Improvement," *JAMA*, October 22, 1999: 282(15).
[16] Dubois R. W. et al., "Growth in Use of Lipid-Lowering Therapies: Are we Targeting the Right Patients," *The American Journal of Managed Care*, October 2002: 8(10).

acknowledging that the management of diabetes is getting more complicated, with numerous new agents available, she stated, "I think the gap between the standard of care and what's going on out there is getting narrower." Kaufman credited associations like ADA and other groups with helping to narrow the gap, along with the role of the pharmaceutical industry educating physicians.[17]

Pharmaceutical marketing and promotion has also been credited with helping to improve treatment of mental illness. According to a study by David Cutler and Mark McClellan, through promotional activities, "manufacturers of SSRIs [medications used to treat depression] encouraged doctors to watch for depression and the reduced stigma afforded by the new medications induced patients to seek help." As a result, diagnosis and treatment doubled over the 1990s.[18]

Helping Patients Find the Right Medicine

Another important role that pharmaceutical promotion plays is providing free samples to physicians. Doctors may distribute samples to patients for several reasons – for instance, to get patients started on therapy right away, to help patients who might not be able to afford medicines on their own or to optimize dosing or choice of drug before committing to a particular course of treatment. These samples can allow the patient and physician to work together to determine what medicine is best for the patient. According to a *Wall Street Journal* article, "If you're open to switching prescriptions, ask your doctor for samples...Not only will you stave off having to pay, but doctors advise trying various medicines because they differ. Samples are 'an important way of trying to find

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[17] Hitchens K., "Diabetes Care Closing the Gap Between Standards and Practice," Special Supplement to *Drug Topics*, October 2002: p. 2-27.
[18] Cutler D. and McClellan M., "Is Technological Change in Medicine Worth It?" *Health Affairs* September/October 2001: (20)5:11-29.

out which ones work' for patients, says Anthony Montanaro, chairman of the Asthma and Allergy Foundation's Medical-Scientific Council."[19] A poll of physicians reported that over 90 percent found product samples "valuable" or "extremely valuable" in their practices.[20]

While some industry critics have suggested that free samples may do more harm than good by encouraging people to take medications they may not need or take a newer medicine when an older medicine may be more appropriate, the available data on patients who receives samples and how doctors view the value of samples suggest that patients benefit from sample medicines and that samples are an important part of the healthcare safety net for low-income and uninsured patients. Researchers have examined physicians' decisions to distribute free samples to their patients: one study, funded by the U.S. Agency for Health Care Policy and Research, examined the use of samples in primary care practices. According to the study, samples were used in about 20 percent of all patient interactions across a wide range of diseases and conditions. The study concluded that with regard to the impact of pharmaceutical company representatives, patients "...profited in a spectrum of ways. While samples represented tangible cost savings, immediate relief and convenience to the individual patient....patient education materials facilitated further understanding of their diagnosis, potentially leading to a higher degree of satisfaction with their health care."[21]

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[19] Saranow J. and Marcus A.D., "The Higher Cost of Sneezing – As Nonprescription Claritin Hits Shelves, Insurers Jack up Prices of Other Allergy Drugs," *The Wall Street Journal*, December 10, 2002.
[20] Boston Consulting Group, Physician Poll, 2002, as reported in "Pharmaceutical Marketing and Promotion, Creating Access to Innovation," Economic Realities in Health Care Policy, Pfizer, 2003: 3(1).
[21] Backer E. et al., "The Value of Pharmaceutical Representative Visits and Medication Samples in Community-Based Family Practices," *Journal of Family Practice*, September 2000: 49(9): 811-816.

Other research looked at the reasons doctors provided samples to some patients more than others. For example, in one study of the use of samples for 71 hypertension patients, nearly half of patients who received samples had no insurance.[22] A different survey of physicians looked at the key factors influencing physicians' decisions to distribute free samples. The authors found that the "patient's financial situation" was a considerable or strong influence 86 percent of the time and a patient's insurance status was of influence 63 percent of the time.[23]

Pharmaceutical Marketing as a Counterbalance to Other Aspects of the Healthcare System

Pharmaceutical marketing also plays a role as a counterbalance to other aspects of our health care system. Debate about pharmaceutical marketing and promotion virtually always seems to assume that it is the sole influence on prescribing, rather than one factor among the wide array of powerful influences in the health care system.

For example, according to research published in *Health Affairs*, one-third of physicians do not discuss treatment options when those options would not be covered by the patient's insurer.[24] A survey of physicians conducted by the Boston Consulting Group found that payors have much greater influence over prescribing decisions than patient requests or pharmaceutical representatives. The survey asked how much formularies, peers, practice guidelines, patient requests, pharmaceutical representatives, and information found on the Internet) had on their prescribing decisions. Fifty-four

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[22] Zweifler J. et al., "Are Sample Medicines Hurting the Uninsured?" *Journal of the American Board of Family Practice*, September–October 2002: 15(5): 361-366.
[23] Spiller L. and Wymer W., "Physicians' Perceptions and Uses of Commercial Drug Information Sources: An examination of Pharmaceutical Marketing to Physicians," *Health Marketing Quarterly*, 2001: 19(1): 91-106.
[24] Wynia M. et al., "Do Physicians Not Offer Useful Services Because of Coverage Restrictions," *Health Affairs*, July/August 2003: 22(4).

percent of physicians responded that formularies had a major impact on prescribing decisions, as opposed to 36 percent who said they had a minor impact. Peers (50 percent) and clinical guidelines (47 percent) also had a major impact in terms of physician prescribing decisions. In contrast, pharmaceutical representatives (14%), the Internet (9%), and patient requests (24%), had much smaller impacts on physician prescribing behavior.[25]

Moreover, debate about marketing and promotion rarely, if ever, begins with an acknowledgment that generic medicines now represent 63 percent of all prescriptions filled today, according to IMS Health.[26] In fact, this percentage has grown rapidly—just 8 years ago, it was 47 percent. In contrast, in most European countries, where pharmaceutical marketing and promotion is curtailed by legal restrictions, the percentage of prescriptions that are generic is significantly lower. This clearly demonstrates the power of several influences other than pharmaceutical marketing and promotion to determine which medicines patients receive.

The range of influences on prescribing extend beyond those identified in the Boston Consulting Group survey of physicians discussed above. For example, a study in *Health Affairs* noted that physician counterdetailing by insurance companies and pharmacy benefit managers to encourage the use of generics is "finally gaining momentum." For example, Blue-Cross/BlueShield of Florida sends letters to doctors that are low prescribers of generics. According to the study, other health plans are planning to distribute generic drug samples to contracted physicians. In the public sector, some Medicaid programs have recently hired physicians and pharmacists to visit doctors'

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[25] 2002 BCG Proprietary Physician Survey, n=399
[26] http://www.gphaonline.org/Content/NavigationMenu/AboutGenerics/Statistics/default.htm

offices and encourage them to prescribe generics.[27] Some states have adopted counterdetailing programs aimed to provide information about alternative treatments to physicians participating in the state-funded health care programs. For example, Vermont and Pennsylvania have implemented counterdetailing programs, and Oregon has an extensive program to inform physicians about medicines that the state has determined are, on average, more cost-effective. It is worth noting that counterdetailing and other efforts by payors and their agents to influence prescribing decisions are not subject to FDA regulation, while detailing by pharmaceutical companies is FDA regulated.

Economic Value of Pharmaceutical Marketing and Promotion

As the U.S. population grows and ages, its health care needs continue to expand. Diseases that affect the elderly, such as Alzheimer's, and chronic conditions, such as diabetes, are becoming increasingly prevalent. In fact, according to the Centers for Disease Control and Prevention, chronic conditions account for 75 percent of total health care spending today.[28] Public health officials have shown growing concern over the increasing incidence of diabetes, obesity, depression, asthma, hypertension and many other conditions. Today, many patients with these conditions are not treated at all or are not treated according to recommended guidelines. In fact, there is wide-scale underdiagnosis and undertreatment of many common, chronic diseases. In a landmark study RAND researcher Elizabeth McGlynn and colleagues reported that underuse was the principal quality of care problem associated with use of medicines in seven of nine

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[27] Malkin J. et al., "The Changing Face of Pharmacy Benefit Design," *Health Affairs*, 2004: 23(1): 194-199.
[28] Centers for Disease Control and Prevention, Chronic Disease Overview, http://www.cdc.gov/nccdphp/overview.htm

diseases studied and 83 of 103 individual quality measures.[29] Likewise, a study in California – using claims data from 3 of the 10 largest health plans to determine the appropriateness of prescription medication use based upon widely accepted treatment guidelines – found that "effective medication appears to be underused."[30] Of the four therapeutic areas examined in the study – asthma, congestive heart failure (CHF), depression, and common cold or upper respiratory tract infections – asthma, CHF and depression were undertreated. A study by Medco researchers found that increased compliance or adherence to prescription drug treatment regimens can result in reduction of medical costs.[31] For diabetes, the average incremental drug cost for a 20 percent increase in drug utilization was $177 and the associated disease related medical cost reduction was $1251, for a net savings of $1074 per patient (an average ROI of 7.1:1). For cardiovascular conditions, the average ROI for a 20 percent increase in drug utilization was 4.0:1 (hypertension) and 5.1:1 (hypercholesterolemia). Recent press reports explain that leading-edge employers are taking steps, such as reducing copays for both brand and generic drugs, to increase use of medicines by employees with conditions such as diabetes, in an effort to achieve better health outcomes and lower overall costs.[32]

Undertreament exacts a cost – for example, one study found that untreated depression costs employers over $30 billion per year.[33] Another study found that if all

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[29] McGlynn E.A., "The Quality of Health Care Delivered to Adults in the United States," *New England Journal of Medicine*, June 26, 2003: 348(26): 2635-2645.
[30] Gilberg K. et al., "Analysis of Medication Use Patterns: Apparent Overuse of Antibiotics and Underuse of Prescription Drugs for Asthma, Depression and CHF," *Journal of Managed Care Pharmacy*, 2003: 9(3): 232-237.
[31] Sokol M. et al., "Impact of Medication Adherence on Hospitalization Risk and Healthcare Cost," *Medical Care*, 2005: 43(6): 521-530.
[32] Freudenheim M., "To Save Later, Some Employers are Offering Free Drugs," *New York Times*, February 21, 2007; Freudenheim M., "New Urgency in Debating Health Care," *New York Times*, April 6, 2007; and Aetna, "New Preventive and Chronic Medications Option," August 2005.
[33] Finkelstein J.B., "Mental Health Parity Extended Another Year," *Am News*, December 2, 2002.

patients with high blood pressure were treated with medicines according to recognized guidelines, 89,000 lives could be saved and 420,000 hospitalizations avoided annually—on top of the 86,000 lives saved and 833,000 hospitalizations avoided by those using antihypertensive medicines.[34] As discussed above, pharmaceutical marketing and promotion plays a role in increasing treatment rates, improving the quality of life for patients and lowering overall costs.

New medicines help avert surgeries and trips to the ER, prevent disability, and improve quality of life for patients everywhere. The benefits ripple beyond individual patients to society in general. For example, findings by a Columbia University researcher indicate that new medicines generated 40 percent of the two-year gain in life expectancy achieved in 52 countries between 1986 and 2000.[35] Some new medicines and vaccines help prevent disease; others cure or alleviate previously fatal or debilitating conditions. Innovative new medicines also make it possible to prevent or slow the progress of many diseases and avoid costly hospitalization and invasive surgery. For example, between 1980 and 2000, the number of days Americans spent in the hospital fell by 56 percent. As a result, Americans avoided 206 million days of hospital care in 2000 alone.[36] New medicines clearly played an important role in this improvement.

Increased spending on pharmaceuticals often leads to lower spending on other forms of more costly health care. New drugs are the most heavily promoted drugs, a point critics often emphasize. However, the use of newer drugs tends to lower all types

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[34] Cutler D. et al., "The Value of Antihypertensive Drugs: A Perspective on Medical Innovation," *Health Affairs*, January/February 2007: 26(1): 97-110.
[35] Lichtenberg F.R., "The Impact of New Drug Launches on Longevity: Evidence from Longitudinal, Disease-Level Data from 52 Countries, 1982-2001," National Bureau of Economic Research, Working Paper No. 9754 (Cambridge, MA: NBER, June 2003).
[36] MEDTAP International Inc., "The Value of Investment in Health Care: Better Care, Better Lives," (Bethesda, MD: MEDTAP, 2003).

of non-drug medical spending, resulting in a net reduction in the total cost of treating a condition. For example, on average replacing an older drug with a drug 15 years newer increases spending on drugs by $18, but reduces overall costs by $111.[37]

Innovative medicines not only extend life and lower spending on other forms of health care but can also make life itself better for patients. New medicines can improve quality of life for patients suffering from long-term illnesses or help patients remain independent by preventing disability. Patients' lives are often improved by medicines because the medicines can avert complications or limit the severity of a sickness. For example, one study found that inner-city children who had asthma, but were enrolled in a comprehensive disease management program that included appropriate medications, experienced significant quality of life improvements. As their symptoms decreased and their capacity for activity rose, they reported greater emotional well-being.[38]

Continued discovery of new medicines helps strengthen the U.S. economy by making it possible for workers to go back to their jobs sooner and to be more productive when they are at work. One study showed that 50 percent of workers receiving a drug injection for a migraine attack returned to work within two hours, compared to only 9 percent of workers who received a placebo.[39]

Pharmaceutical R&D v. Marketing and Promotion

In debates about pharmaceutical marketing and promotion, it is often claimed that pharmaceutical companies spend more on marketing and advertising than on research and

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[37] Lichtenberg F.R., "Benefits and Costs of Newer Drugs: An Update," National Bureau of Economic Research Working Paper, No. W8996 (Cambridge, MA: NBER, June 2002).
[38] Munzenberger P.J. and Vinuya R. Z., "Impact of an Asthma Program on the Quality of Life of Children in an Urban Setting," *Pharmacotherapy*, 2002: 22(8): 1055-1062.
[39] Cady R.C. et al., "Sumatriptan Injection Reduces Productivity Loss During a Migraine Attack: Results of a Double-Blind, Placebo-Controlled Trial," *Archives of Internal Medicine*, May 11, 1998: 158:1013-1018.

development (R&D) of new drugs. The facts do not support this claim. In 2005, pharmaceutical manufacturers spent an estimated $7.2 billion[40] on pharmaceutical professional promotion (which includes costs associated with sales activities of pharmaceutical representatives that are directed to office-based physicians, hospital-based physicians and directors of pharmacies, and advertising for prescription products appearing in medical journals) and $4.2 billion on direct-to-consumer (DTC) advertising, according to IMS Health.[41] This $11.4 billion compares to $51.3 billion in total R&D spending by the biopharmaceutical industry, according to Burrill & Company. PhRMA members alone spent $39.9 billion on R&D in 2005.[42]

Uwe Reinhardt of Princeton University has explained how marketing and promotion costs often are inaccurately characterized in policy debates. According to Reinhardt, "...the [selling, general and administration or SGA] category represents many expenses other than selling expenses and should not be seen as an estimate purely of outlays on marketing, as the industry's critics occasionally do."[43] Harvard economist Joe Newhouse notes, "One sometimes hears it said that the industry would have more money for R&D if it would cut down its marketing costs. This comment reflects misunderstanding of the economics of the industry. If a firm did so, it would be less profitable and have would attract less capital for R&D or would have fewer internally generated funds to invest."[44] And the Federal Trade Commission has stated that DTC advertising does not significantly affect prescription drug prices: "[DTC advertising] can

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[40] IMS Health, Integrated Promotional Services™ and CMR, 5/2006.
[41] Id.
[42] Pharmaceutical Research and Manufacturers of America, *Pharmaceutical Industry Profile 2006* (Washington, D.C.: PhRMA, March 2006).
[43] Reinhardt U.E., "Perspectives on the Pharmaceutical Industry," *Health Affairs*, September/October 2001: 20(5): 136-149.
[44] Newhouse J.P., "How Much Should Medicare Pay for Drugs?" *Health Affairs*, January/February 2004: 23(1): 89-102.

empower consumers to manage their own health care by providing information that will help them, with the assistance of their doctors, to make better informed decisions about treatment options...Consumers receive these benefits from DTC advertising with little, if any, evidence that such advertising increases prescription drug prices. DTC accounts for a relatively small proportion of the total cost of drugs, which reinforces the view that such advertising would have a limited, if any, effect on price."[45]

Thus, as the Congressional Budget Office recently reported, "The pharmaceutical industry is one of the most research-intensive industries in the United States. Pharmaceutical firms invest as much as five times more in research and development, relative to their sales, than the average U.S. manufacturing firm."[46] At the same time, marketing and promotion play an important role in informing physicians and patients about the fruits of this investment—new medicines that improve and save lives.

Conclusion

Pharmaceutical marketing and promotion provides value to physicians by allowing pharmaceutical research companies to inform healthcare providers about the benefits and risks of new medicines in accordance with FDA regulation, provide educational and scientific information, support medical research and education, and obtain information and insight about our products through consultation with medical experts. Published research has reinforced the value physicians see in promotional and marketing efforts and the PhRMA Code confirms our commitment to interact with

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[45] Federal Trade Commission, Comments before the Department of Health and Human Services Food and Drug Administration in the Matter of Request for Comments on Consumer-Directed Promotion (Docket No. 2003 N-0344), December 1, 2003.

[46] Congressional Budget Office, "Research and Development in the Pharmaceutical Industry," October 2006.

healthcare professionals for the benefit of the patient and to enhance the practice of medicine.

The CHAIRMAN. Thank you very much, Ms. Powell.

Dr. Sade, the guidelines that the AMA has out there, would you support making these guidelines mandatory, and would you support enforcing your guidelines?

Mr. SADE. Thank you, Senator Kohl.

The guidelines of the American Medical Association already are being enforced. The Council on Ethical and Judicial Affairs, of course, has jurisdiction only over its own members.

But the council screens between 250 and 300 alleged physician violations of the ethical code every year, and of those, 30 to 40 actually come to a due process hearing. Sanctions are levied against some members of the AMA in the form of having their membership revoked or having their membership suspended or being put on probation, et cetera.

But the reach of the disciplinary value of the AMA code goes far beyond that. Most medical boards in the United States use the AMA's code of medical ethics as their standard for ethical behavior of physicians, and they sanction physicians based on violations of the AMA code. That is a very powerful influence of the code on medical practitioners.

The courts also refer to the code in deciding, actually, many cases, and that is another way in which the code is very useful in the American judicial system. So I don't think it is quite accurate to say that the code of ethics of the American Medical Association isn't being enforced. In fact, it is.

The CHAIRMAN. So you would support full disclosure in a national registry?

Mr. SADE. I don't know the answer to that question, because the AMA has not yet considered it or deliberated over it.

The CHAIRMAN. Well, do you consider it to be a good idea?

Mr. SADE. I don't know that, because we only have a limited experience with the States, which I think are very valuable experiments in determining the benefits of such a program, as well as the potential risks of such a program. Both the benefits and the risks were pointed out by the previous panel.

The CHAIRMAN. How do you feel about Minnesota's law?

Mr. SADE. Well, I will say the same thing, that the analysis of the data is too incomplete at this time to make a decision. But the fact of the matter is that AMA has not developed any policy on this, but it is monitoring the situation closely and will be creating policy in the near future.

The CHAIRMAN. Ms. Powell, how do you feel about full disclosure in a national registry?

Ms. POWELL. We have been working with a number of States as they have first considered legislation and then developed regulations. It is very clear that the State legislators, as they have been putting together legislation and making amendments, have not fully understood the complexities of what it was that they were dealing with or the potential interaction with FDA regulations, which, of course, are national and are the ones that pharmaceutical companies have to abide by.

As they have moved to the regulation stage, they have had even more difficulty in defining what it is they think should be included in a registry. So we would caution that that indicates that perhaps

there is a need for much consideration about what would be included. Take, for example, the question of pharmaceutical samples, which some States have defined as gifts, but which we think are essential practice tools for physicians and patients to learn about whether a new medicine will be helpful for them, particularly when a patient may not have insurance.

There has been one study that found that a large number of the patients to whom physicians have given samples were patients without insurance. If you define those as gifts, that implies that the physician is receiving a benefit, when, in fact, the samples are, under FDA law, required to be given free of charge to patients who need them. So there are those kinds of complexities that would make the effort toward developing a national registry very difficult.

The CHAIRMAN. OK.

Senator McCaskill.

Senator MCCASKILL. I know, Mr. Chairman, they have called a roll-call vote, and so we don't have much time.

You know, we are trying to go through the process of lobbying reform in Congress right now, and I think anyone would have to be honest and acknowledge that a lot of what is going on with the pharmaceutical industry, as it relates to their contact with doctors, is lobbying. It is lobbying, pure and simple.

My brother ran a restaurant in Springfield, and he said the most lucrative part of their business was the private room that was reserved by pharmaceutical companies four nights a week. The wine consumed was unbelievably expensive. The dinners were unbelievably expensive. Now, I have got to tell you, I don't think most Americans think that is about patients first. That is about lobbying.

What I would ask of PhRMA is if we are going to limit the lunches that can be bought for Members of Congress in the context of lobbying, shouldn't we have the same kind of disclosures with doctors, because there is a financial relationship there. If, in fact, it is about the patient, then PhRMA should have no problem with disclosing how much money they are spending on doctors in terms of recreational time.

I am not talking about a member of the pharmaceutical industry visiting an office and dropping off some sample packs. I am talking about golf. I am talking about trips. I am talking about dinners. I am talking about expensive wine. Why in the world would we allow that to go on without the public and the patients knowing that is going on?

Ms. POWELL. Senator McCaskill, under the PhRMA code, as it was issued in 2002, expensive dinners, wine, golfing trips, sporting events are inconsistent with the PhRMA code. They are inconsistent with the inspector general's description of the guidance for the pharmaceutical industry. They are inconsistent with the requirements of various individual company compliance and ethics codes.

I would, with all due respect, suspect that there has been some change in your brother's experience in the restaurant in recent years, because I know that there have been changes in the kinds of behaviors. Pharmaceutical representatives, when they are buying meals for physicians, are buying them in a place where it is

quiet, and they can focus on communication of information. I don't believe that there are lots of examples of the type you describe, and if there are, I would certainly encourage you to forward them to the companies involved, because I think those are now inconsistent with both the AMA and the PhRMA code.

Senator MCCASKILL. So they are not allowed to buy alcohol for doctors anymore?

Ms. POWELL. The code says that they may buy a meal in a reasonable setting at a reasonable price——

Senator MCCASKILL. That wasn't my question.

Ms. POWELL [continuing]. Which I would——

Senator MCCASKILL. Are they allowed to buy alcohol for doctors anymore, yes or no?

Ms. POWELL. Our code does not explicitly go to that level of detail——

Senator MCCASKILL. So they can?

Ms. POWELL. If a company were to decide that a glass of wine was reasonable, yes, I think they could. But the purpose of the interaction would be communicating information to the physician, and that would more likely happen in a setting where you didn't have either food or alcohol, or perhaps you were bringing pizza so that not only the physician, but the nurse practitioner, who is actually dealing with the patient and telling the patient how to use the medicine, knows what information needs to be conveyed to the patient.

Senator MCCASKILL. I just don't have a sense that the enforcement—I mean, I know, Dr. Sade, that the AMA has done some in this area. But there is, I think, out there a real perception, and—as we do here in this body. We fight perception sometimes, not reality.

I don't think that lobbyists buying lunch for any individual congressman is necessarily polluting the process. But what has happened is because of abuses over the years and because of the prevalence of that kind of activity, we are now moving to cutoff that kind of activity and, therefore, doing something about the perception.

I just think that your industry has got your head in the sand if you think you have turned the corner on this, because I don't believe, in terms of the public's perception, that you have at all.

Mr. SADE. If I may comment——

Senator MCCASKILL. I am sorry. We have a vote, and——

The CHAIRMAN. I will give you 30 seconds, so go ahead, Dr. Sade.

Mr. SADE. OK, a 30-second comment.

Over the last 4 years, since the PhRMA code went into effect, we in my medical school have noticed a distinct change in the relationship of pharmaceutical representatives and physicians. Expensive dinners never have taken place all that much. Yes, they do take people to dinner, but they are always at modest prices and at restaurants in which actual real educational programs take place.

So I think that the perception lags the reality in this case. The perception will change when the reality becomes more obvious.

Senator MCCASKILL. Thank you.

Ms. POWELL. Senator McCaskill, we are working to educate not only our company sales representatives and, with the AMA physicians, but trying to change the perception. I agree with you that

there is a perception problem, but it is one we are working very hard to try and change.

Senator MCCASKILL. OK. Thank you.

Anyone who has anything they want to add, I am sure the Chairman will allow them to submit it to the record.

The CHAIRMAN. Thank you so much, Senator McCaskill.

Senator MCCASKILL. Thank you, Senator.

The CHAIRMAN. We thank our witnesses. You shed a lot of light on the issue and the topic, and it is really important.

We thank the first panel, also, and you can all look forward to some progress on this matter.

So thank you for being here.

Mr. SADE. Thank you very much.

[Whereupon, at 12:16 p.m., the Committee was adjourned.]

APPENDIX

DR. KASSIRER RESPONSES TO SENATOR KOHL'S QUESTIONS

Question. Four years ago, the Office of the Inspector General at the Department of Health and Human Services issued ethics guidelines, in an effort to enforce its mandate to investigate and prosecute illegal kickbacks to physicians from drug companies. Do you think these guidelines have been effective in curbing ethical conflicts?

Answer. In a highly unfortunate action, the Office of the Inspector General failed to take an opportunity to strengthen conflict of interest guidance. It merely accepted the recommendations of PhRMA and the American Medical Association. In my opinion, these recommendations are lax. They continue to allow gifts and meals as well as participation by physicians in industry speaker's bureaus and consultations on marketing issues. Since their pronouncements in 2002, there have been no apparent actions by the OIG on this issue. If these ethical conflicts are to be curbed, the OIG will have to promote new, more stringent guidance.

Question. The voluntary guidelines put into place by both the medical industry and pharmaceutical industry several years ago have done little to curb the excessive marketing to physicians. In fact, the problem seems to be getting worse. Since the guidelines were adopted, drug industry spending on physician marketing has increased roughly $7 billion. If the voluntary guidelines were mandatory and they were properly enforced, would that be a good first step in cracking down on the problem?

Answer. No. Because the voluntary guidelines of the "medical industry" and the pharmaceutical industry are so deficient, even making them mandatory would have little effect.

Question. We've heard testimony about efforts to tighten ethical guidelines in states, hospitals, and universities around the country, for example the University of Wisconsin Hospital banned free samples outright in 2001. What role should the federal government play in limiting these conflicts of interest and the troubling perceptions that they cause?

Answer. Free samples are ideally used for patients who cannot afford them, but they often get into the wrong hands. Nurses, technicians, and doctors often use them. In addition, free samples are fundamentally marketing gimmicks, allowing physicians to familiarize themselves with the newest and most expensive drugs, and then to prescribe them. I believe all free samples should be sent to a central repository and given out by a voucher method to those who would benefit most from them. The federal government could promote this practice.

Question. At the hearing, Dr. Lurie recommended a national disclosure law to provide transparency of gifts and payments physicians have received from drug companies, do you agree with his recommendation and would disclosure of these gifts and payments be an important first step in eliminating these conflicts of interest?

Answer. In my testimony, I agreed that a federal registry would be valuable, at least in identifying the physicians who receive the largest payments from industry. But a registry alone is not sufficient. We must have data that includes the industry money that goes to professional organizations and lay organizations, not just individual doctors. We need information on what influence industry money has on medical organizations.

Question. After hearing the testimony of Dr. Rosenthal, that these countless gifts and financial conflicts of every kind have caused a rift in his corner of the medical profession. At least some of his colleagues appear to be fed up with the negative effects that this money is having upon medical research. Do you perceive any evidence of a backlash or revulsion by younger physicians or medical students against accepting gifts, grants, trips, and honoraria of every description?

Answer. The American Medical Student Association (no connection to the AMA) has taken a strong stand against students accepting gifts and food from industry.

A Web site by New York physician Bob Goodman (www.nofreelunch.org) has taken a similar stand, and scattered across the country are students who regularly eschew free gifts.

Dr. Rosenthal's Responses to Questions From Senator Kohl

Question 1- How has pharmaceutical influence become so pervasive in the ophthalmic and retinal specialties?

The conquest of the research and development process in the retinal world is due to the coalescence of three trends. First, our area is simply representative of the broader phenomenon across medicine precisely detailed in Dr. Marcia Angell's book: "The Truth about the Drug Companies". This book analyzes what the pharmaceutical industry has accomplished in the last couple of decades to perfect their ownership of the drug development pipeline, including the control over the regulation of their activities. The second trend is the decreasing availability of administrative and research dollars available to academic medicine, and PHARMA's eagerness to fill this void and alter the process to their benefit. The third trend is the insidious acceptance among physicians of the idea that their motivations can appropriately be primarily financially motivated according to the accepted character of the for profit business. This change in attitude requires the abandonment of the long held imperative that the physician's primary role is one of advocacy for the patient and society. This is particularly true for physicians in a position to do research and medical education, since it is these physicians who are most attractive to pharmaceutical marketing departments in their efforts to control the research and education processes as coordinated piece-parts of the marketing of their products.

The process of infiltrating the retinal world is an illustrative microcosm of the medical industry in general. Pharmaceutical control of retinal medicine reached a watershed with the development and marketing of Visudyne in the late 90's and into the new millennium. This coincided with decreasing availability of federal funds for research and the emergence of pharmaceutical treatments for many retinal diseases. The details of this story and others that followed, and the perversion of research paradigms illustrated in various retinal vignettes can be found in the attached essay, "Climate Change in the Treatment of Exudative Maculopathies"[i]

The task of eliminating this influence must be comprised largely in dismantling the long history of corrupting the process. Since the majority of retinal doctors are still honest and desire to practice in their patients' and society's best interests, creating a true, credible registry of the pervasive conflicts of interests would be a first step. There is value in being able to prove one's independence from these conflicts. Data on payments and material relationships is available in drug company databases, and this information should be public. There is no credible argument that this type of data is in any way proprietary. Second, physicians themselves should be polled. Third, company sponsored studies should be exposed wherever studies are designed to serve marketing interests. We need to return to a system where study designs are generated from valid and independent scientific process. This is especially valid since companies are benefitting from the payment for many of their products with Medicare funds. They have perfected the process of literally draining large portions of CMS budgets into their coffers by having drugs paid out of Medicare Part B, and it is entirely appropriate for those drug studies to be under independent design, review, and federal oversight. Next, government agencies themselves, particularly CMS, the FDA, and the NEI should be cleansed of the pervasive pharmaceutical collusion that currently exists. We cannot have independence in research if these organizations are effectively co-opted by industry.

For further commentary on this first question, I am attaching a thoughtful analysis from Dr. Steve Kaufman, MD, one of my cofounders of Physicians for Clinical Responsibility.[ii]

Question 2- Would a national disclosure law and a registry of financial relationships help eliminate conflicts of interest?

As discussed above, this would be a very doable and excellent first step. There is marketing value for physicians in being able to claim and prove allegiance only to their patients and the society in which we must all live and function. This would only be a first step, because the most nefarious offenders have already proven their callous lack of conscience, and it would cause not great problem for them to lie to a registry just as they euphemize and conceal their current activities. As Dr. Kassirer has described in his testimony and his book, "On The Take", more concrete measures to expose and sanction malfeasance need to be developed. A congressional advisory committee comprised of Drs Kassirer, Angell, Dr. Howard Brody, Dr. Lurie, and others could provide authoritative and independent guidance in establishing appropriate laws.

Question 3-Would it help if voluntary guideline are made mandatory?

The problem with voluntary guidelines is that they tend to be developed with input from the very people who intend to ignore them anyway. In the collusion between the pharmaceutical industry and medicine, we have many very secretive and toxic dynamics. In order to have a meaningful set of mandatory guidelines, the current guidelines need to be thoroughly reviewed and revised to adequately and ***seamlessly*** address the egregious malfeasance and is currently so commonplace. For example, while we may have a guideline that proscribes a pharmaceutical company from directly hiring speakers for a "CME" meeting, the simple workaround is to simply hire or create an intermediary company to perform this task. This is made to seem independent, but is in fact under the complete control of the pharma company. Simply making current voluntary guidelines mandatory would do nothing to close loopholes that industry has had a hand in creating and which industry has perfected the process of exploiting.

Question 4- Thus far in the absence of much federal leadership, there has been a proliferation of state, local, and private guidelines to control financial conflicts. What role should the federal government play in this process?

First, the government should clean its own house. There are honest medical researchers and administrators at the NIH and within other agencies, but the level of industry influence in these institutions is nonetheless at an historical high. The Congress can and must reverse this regrettable trend through rigorous oversight. It would be a relatively simple technical matter to terminate permission for industry to retain those in positions of influence to promote their agendas. Second, the federal government needs to develop strong laws based in part on lessons that can be learned from state and private efforts, and the laws need to be structured such that they do not inadvertently circumvent or weaken existing controls.

Question 5- Do I anticipate criticism for my active role in calling for responsibility and transparency?

I am counting on it. Our specialty is rife with avarice and moral relativism, and if I do not incur any enmity or contempt from such individuals, then I will have failed. In my career, I have already walked away from many hundreds of thousands of dollars to avoid Medicare fraud (by former partners), inappropriate payment for influencing others, and various other remunerative misbehavior. I am materially poorer for it, but I have earned the respect of more altruistic doctors; respect that is of far greater value than anything I have missed. I actually think it has helped me materially by receiving referral cases specifically because of the values I espouse. Specifically in regard to this issue, while I have been warned "not to take this on" by some, my colleagues at Physicians for Clinical Responsibility (PCR) and I have literally received fan mail and many messages of encouragement, some examples of which are listed below.[iii] These e-mails were written in response to the essays that formed the basis for the formation of PCR. Some of these are reprinted below.[iv] These e-mails are evidence that there is a significant frustration with those who are happy to cash in for personal gain. This sentiment proves that we do have a legacy worth fighting to regain.

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[i] Climate Change in the Treatment of Exudative Maculopathies

There has been a revolutionary climate change regarding the treatment of exudative macular degeneration. "Conventional", i.e. PDT or Macugen, therapy is based on old, inaccurate assumptions. With PDT and Macugen therapy, the studies have defined a "successful" result to include continued and considerable loss of vision. With the advent of Avastin, and more recently Lucentis, we need to reconsider what is ethical and reasonable in our future treatment and study of AMD and related macular pathologies. This extends to consideration of combination therapies and also to the types of studies we can continue or design in the future. It may be helpful to take a look back at developments over the last 5 or 6 years and take a new, if iconoclastic, look at what is going on now, and where we need to go in the future. My intention here is not to be critical or to beat to death old horses, but to frame questions for more thorough discussion among the retinal specialists who fight these diseases everyday with no agenda or relationship other than to the patients they serve.

Lowered Standards

In recent years, although many in the retinal community have been disappointed by PDT, most have still considered it to be a mainstay of treatment for classic neovascular AMD. This has required that we lower our expectations as to what we consider acceptable success rates and cost-effectiveness. Our acceptance of PDT has come in spite of extreme cost, generally poor results, and some degree of systemic risk. Officially, PDT stands for "Photo-Dynamic Therapy", but a common joke in the retinal community is that it actually stands for "Pretty Dismal Therapy". There are legitimate reasons for this. Clinically, most patients continue to lose vision, especially with repeated sessions of treatment. Virtually all retinal surgeons who do PDT have had to field questions from patients about the "perfectly circular blind spot" that many notice after therapy. This calls into question the original claim that PDT was benign to normal tissue. We should have seen this coming. If Visudyne selectively acted on abnormal neovascular tissue and left surrounding normal tissue alone, why would patients need to stay out of the sun for 3 to 5 days to avoid severe burns to their normal skin. Between the unimpressive therapeutic

effect and the macular toxicity issue, the visual impact of PDT is for some patients not very different from direct thermal ablation of the macula.

Histologically, PDT does some very bad things that can explain why vision doesn't improve more often and in fact why PDT often causes significant visual harm. Although the original studies did not focus on histologic effects, subsequent work [1-3] shows that PDT with Visudyne causes immediate, nonselective devastation to the neovascular membrane ***and*** surrounding tissue. This actually stimulates release of more VEGF, and considerable inflammation and tissue damage. Although some of this reverses, especially with concurrent intravitreal triamcinolone, severe choriocapillaris destruction is permanent and additive with repeated sessions. Any surgeon who has performed ICG studies after PDT has seen the circular choroidal destruction exactly correlating to the patient's circular scotoma. Dynamic ICG videography provides particularly striking evidence of this problem. Even when Snellen acuity is relatively preserved, the scotoma can be documented with testing such as the Nidek Microperimeter and other instrumentation still under development. PDT may allow eventual histologic "normalization" of endothelial and pericytic growth, but the overall histology is still severely disturbed. The original lesion is actually widened by the treatment, eventual aggressive neovascular recurrence may occur, and through pericytic normalization, PDT may actually make the lesion less responsive to eventual anti-VEGF therapy.

Before nonselective VEGF inhibition, perhaps a case could be made for using PDT. Now, however, it is hard to imagine how anyone would ever recommend PDT as primary therapy or as anchor therapy in combination strategies. In fact, the recent ASRS survey indicates that only 0.7% of respondents still recommend PDT as primary therapy.

The original PDT studies were Corporate Sponsored prospective Randomized Controlled Trials (CSRCTs). Although OCT and ICG were both available at the time, histologic and choroidal vascular study with live patients was not reported originally. Visual results were sufficiently unimpressive that visual stability was redefined for the purposes of the study to include 15 standard letters of additional vision ***loss***. Cost utility measurements [4,5] show positive results, but this is based on less loss of vision, not upon actual visual improvement. The emphasis on counseling patients that less vision loss is gain persists today. A patient education presentation distributed by Novartis and PDT advocates in the summer of 2006 counsels us that it is important to advise patients to ***"lower their expectations"*** and to consider slowed vision loss as their desired outcome[6]. Drs. Lewis and Sternberg[7] make the point more directly :

> "we have the responsibility of providing our patients with accurate information and of explaining to them that, although the treatment is better than no treatment, it rarely results in improvement in vision and that most patients continue to lose vision."

In spite of the pragmatic study design and the underwhelming results, PDT has been promoted as a great advance by those who have a monetary and/or political stake in its success. Perhaps it was at the time, but if the original PDT studies had been done independently of the drug maker (as an Independent RCT (IRCT) one could wonder whether the treatment effect on macular histopathology would have originally been neglected and whether visual success would have been redefined from the MPS standard. Without these study modifications, one could also wonder whether PDT would have ever even been approved at all.

The Soft Underbelly of "Hard" Data

I don't mean to "beat the PDT horse to death", but this all calls some attention to certain "myths" that have been promoted since the Visudyne CSRCTs. I am not suggesting that everyone in the retinal community buys into these myths, but I do believe that they are promoted by many in the drug industry and sponsored research community in the hope that they will gain at least some traction. These issues are exactly those used by corporate advocates and parroted by a surprising number of doctors fearful of bucking the corporate sponsored party line. I do not use the "Myth vs. Truth" construction here to condescend to the reader but rather to point out issues that need to be discussed among the many intelligent and independent retinal specialists who must ultimately take back control of treatment standards from corporate marketing departments. Although I will use the term "myth" here, perhaps "mind set" or "marketing paradigm" are alternative concepts.

One example is the growing "myth" in recent years that ***only*** prospective randomized clinical trial data is ***real*** data. This, along with the more insidious myth that CSRCTs are just as legitimate and unbiased as IRCTs, seems to imply that retrospective data is useless. In other words, the myth implies that we can ***never*** learn anything useful or normative from past experience. Contrary to these myths, there are some basic truths about RCTs and retrospective or experiential data that we need to consider. Frankly, it is easier to follow the crowd. It is easier to assume that any data from an RCT is unimpeachable and that any other data is useless, but we cannot afford to be that lazy. We are professional caregivers and with that responsibility, we need to consider and critically evaluate ***all*** data and recommend to our patients treatments based on ***all*** evidence. I am not suggesting that we consider retrospective data in preference to prospective data, only that we are responsible for critically analyzing ALL data according to its strengths and weaknesses. ***That*** is what evidence-based medicine requires.

We therefore need to take a hard look at the soft underbelly of RCT data:

Myth #1- All RCT data is equal and inherently unchallengeable.

Truth #1- RCTs are only as good as the premises upon which they are based and the questions that they ask. If insightful, honest, non-leading questions are designed, it is more likely that useful, normative data will be gained. If uninsightful, or worse, self-serving questions or premises are employed, then it is easy to manipulate RCT data and alter the apparent outcome. The data, although statistically legitimate, can be made to only answer the questions and suggest the outcomes that you want it to. One example of course is found in of the ***absence*** of questions about histopathology in the original PDT studies and the decision to redefine "visual success". As another example, the experiential data on Avastin is so strong that it is virtually impossible to imagine that the brilliant, creative, and careful people at Genentech could have missed its utility unless they intended to. This makes the parallel Lucentis development *look like* a contrived effort to circumvent the pricing of 1 mg. of Avastin for ophthalmic use, when the price of hundreds or thousands of milligrams had already been fixed for oncologic use. It is now abundantly clear that the ***premise*** upon which Lucentis was developed, that Avastin would not work in the eye because the molecule was too large, is wrong. Whether intended or not, this false premise abrogates the need to develop Lucentis at all. Ironically, the only value of the Lucentis trials is to indirectly suggest that its analog Avastin is probably also safe and effective. The unintended implication of the Lucentis trials, and particularly the PIER trial[9] which shows poor utility of Lucentis in dosage frequencies that seem to work with Avastin, is that Lucentis may indeed be inferior to Avastin regardless of price. A senior Genentech officer and one of their sponsored researchers have carefully explained to me that they consider Avastin to be a "temporary stop gap" measure that they now consider unnecessary and unworthy of study now that Lucentis is available. They

explicitly argued that Avastin should be irrelevant although they both freely admitted believing that it is just as safe and effective at 1/100th the cost per case.

Myth #2- Any treatment can be evaluated in an RCT.

Truth #2- Only simple standardized and relatively non-skill-intensive treatments lend themselves easily to an RCT. Treatments that cannot be easily standardized, particularly skill intensive procedures, are difficult to study in an RCT. There are many treatments that have become standard care without the benefit of a prospective trial, such as insulin, penicillin, and now Avastin, where experiential data decisively removes doubt as to safety and utility. There are other examples of therapies, especially surgeries, for which trials span generations of surgical refinement and end up not recommending techniques that had subsequently became unequivocal standards of care because of refinements not included in the study design. The evolution of diabetic vitrectomy in spite of marginal DRVS data stands as one example.

Myth#3- Pathologic conditions are nonvariable and therefore the spectra of severity and pathologic character do not affect the quality of prospective studies.

Truth #3- Pathologic conditions are highly variable, and RCTs are actually only useful in studying very specific conditions within a disease spectrum. Beyond that, we as physicians have a longstanding tradition and a very legitimate responsibility to use our insight, best judgment, ***and past experience*** to apply what we have learned from data available to us, whether from an RCT or elsewhere, as we treat patients suffering from a wide variety of disease types. ***In point of fact, RCTs can only provide basic direction , and individual and reported past experience is far more valuable and far more appropriate data to use in addressing the wide variability of disease that we encounter, variability that is not specifically addressed in the RCT.***

Myth #4- RCT data is valid and retrospective data simply is not. We should therefore only consider prospective data (uncritically) and ignore retrospective data (categorically). This is a myth that drug companies have fought hard to promote in regard to CSRCTs in recent years, and incredibly, it is the most common argument I hear from those who choose Lucentis over Avastin.

Truth #4- RCT data when critically analyzed for its strengths ***and weaknesses*** is valuable, ***as is*** retrospective data. We simply need to critically analyze and use data for what it is, not giving it greater weight than is deserved (as by those who uncritically accept RCT data and only RCT data), and not ignoring ***any*** data that is carefully collected. The whole subdiscipline of Bayesian analysis considers the validity of outcomes based on the application of conditions retrospectively. Our most legitimate use of RCT data is to use it within its limitations and to use our best judgment and experiential experience to make treatment decisions for our patients. A compelling recent example of course is again the situation with Lucentis and Avastin. The limited RCT data that is available says that Lucentis is safe and useful in the treatment of exudative AMD. The drug company, its minions, and those unwilling to accept the responsibility of practicing true evidence-based medicine would seem to like us all to leave it at that. The problem of course is that we know that Avastin exists and that it is in fact the "parent" analog of Lucentis and therefore might be expected to act similarly. We have individual and reported experiential data that says not only that it works but that it works astonishingly well with no sign of unexpected adverse effects. We have the further burden of knowing that it works so well as to raise the possibility that the antibody's developer should have been able to know this before pronouncing it useless, legitimizing a multimillion dollar development that in retrospect seems like little more than a strategy to circumvent pricing regulations. We have the unsubstantiated but likely

possibility that the smaller molecular weight size of Lucentis may in fact be a liability, causing it to have too short a duration of effect compared to Avastin, possibly allowing a disease to smolder and that this may promote fibrosis and less durable treatment effect. Finally, we have the knowledge that many patients have significant financial exposure with Lucentis, when ***all*** available clinical data suggest that they can have the same or better effect with Avastin at a miniscule fraction of the cost and with, in our best judgment, the same degree of safety. Theoretically, Avastin might even be safer, since the smaller Lucentis molecule has more rapid and higher peak clearing ***into the systemic circulation. We are responsible for ALL of this data. Morally, we do not have the luxury of letting those with a financial interest do our thinking for us.*** Reasonable people may conclude that the best evidence-based decision is to use Avastin over Lucentis, unless comparative studies, prospective or retrospective, suggest otherwise.

Ironically, Genentech may be the strongest believer of all in the retrospective Avastin data. It is only on the basis of this data that they could reasonably refuse to study Avastin head to head with Lucentis, believing (as seems reasonable) that Avastin would be shown to be at least as good and possibly superior to Lucentis at about 1/100th the cost per case. This is of course only my speculation.

Myth #5- Independent RCTs (IRCTs) and Corporate Sponsored RCTs (CSRCTs) are identically nonbiased and provide identically unimpeachable data.

Truth #5- RCTs in general are limited by the quality of the questions that they ask and the elegance of the studies used to answer them. Consequently, no RCT is above analysis. Furthermore there is growing evidence in multiple medical disciplines that CSRCTs are significantly prone to bias and should be subjected to even more diligent scrutiny, especially considering the financial pressure to produce profitable products,. This was recently reported in regard to psychiatric drug testing in BJM[12].We have already discussed the Visudyne example, where the pragmatic definition of visual success and neglect of now obvious macular toxicity were beneficial to the acceptance of a marginal therapy. To this, we should add the question of whether Lucentis ever needed to be developed at all. At this point, reasonable people have speculated that the only believable reason to develop Lucentis was to remarket an analog of an already approved compound at a vastly more profitable price.

A New Standard of Care

With the emergence of nonselective VEGF inhibition, the standard of care in the treatment of wet AMD and other exudative maculopathies has changed abruptly and decisively. Because of the volume of retrospective data and the ubiquity of experience throughout the retinal world, Avastin has become the *de facto* standard against which all other treatments, including Lucentis, must be compared. Why is that? Because the *de facto* Avastin standard was set first. To put it colloquially, by the time Lucentis came along, the Avastin cow was already out of the barn. There are many precedents for rapid adoption of *de facto* standards of care. These include aspirin, insulin, penicillin, and many surgical procedures, to name just a few. Although its own maker appears to have made a conscious effort to ignore and even suppress its use in the eye, Avastin's impact on various maculopathies is equal on an historic scale to these other examples.

Looking back on the various recent treatment developments for AMD, one of the things we have learned is that rapid and complete inactivation of the neovascular sequence seems to be extremely important for long term visual success. Without this, the neovascular and/or fibrotic processes continue, resulting in worsening vision and lower

success rates after conversion to more effective therapy. We have learned that PDT actually ***causes*** damage to the surrounding "normal" RPE and choriocapillaris on a scale comparable in some patients to thermal macular ablation, at least with infrared thermal laser. To this, we must add the risks of cataract and glaucoma associated with intravitreal triamcinolone, since "unprotected" PDT is even more clearly risky and inefficacious.

Like PDT, Macugen use is associated with continued visual loss in most patients and expansion of vascularity and fibrosis within the lesion[8]. The speculation is that this is due to the inability of $VEGF_{165}$ inhibition to completely stop the neovascular process. Early data on studies of Lucentis[9] suggest that decreasing the frequency of injection from 4 weeks to three months is associated with progression of the neovascular process. Perhaps because of its small molecular size and rapid clearing from the eye, its fairly brief duration of effect may allow progression of the neovascular/fibrotic process in the same way that Macugen's selectivity mitigates its effect.

The experiential data on Avastin suggest that it causes an extremely rapid and complete cessation of neovascular activity. Furthermore, this effect seems to last at least two months in most patients. Although this needs to be quantified, we have seen noticeably less submacular fibrosis on exam and OCT than has been typical in Macugen or PDT treated patients. Histologic, Dynamic ICG, and ERG studies, both reported and in our practice, show none of the anatomic or functional disruption that is now well documented with PDT. We have also seen none of the choriocapillaris devastation, central scotomata, or florid vascular regrowth after Avastin treatment that is common after PDT.

All of this supports nonselective VEGF inhibition as the new standard of primary care and of Avastin as offering the best combination of safety, efficacy, ***and*** cost-effectiveness. In spite of this, some payers continue to require that patients fail with the older, and now clearly inferior "conventional therapies" before they will cover Avastin. This needs to be rectified quickly. We also see suggestions to continue using Macugen as maintenance after nonselective anti VEGF "induction". This seems senseless, and appears to be a contrivance by Macugen advocates to find some use for a drug that is more likely to become an historical anecdote.

A Crossroads for Research-

In spite of this revolutionary change in our understanding of the neovascular process, and in spite of the recent adoption of Avastin, and secondarily Lucentis, as the *de facto* standard of care for exudative maculopathies, many continue to describe PDT and Macugen as "standard" or "conventional" therapies for AMD. Furthermore, some researchers have so far continued to recruit patients for studies that place PDT and Macugen as primary therapies or anchor therapies in combination protocols. Neither of these practices has any logical basis in the era of nonselective anti-VEGF therapy. These studies are based on a standard under which continued visual loss is acceptable. ***We simply cannot ethically continue to recruit patients into studies that we know will cause tissue destruction or indolent continuation of the disease process or where we expect vision loss to continue when we know that those same patients can receive treatment that causes no anatomic or functional harm and from which we can expect rapid and durable improvement in vision.***

We are at a crossroads that demands a complete re-evaluation of our investigational goals. Nonselective VEGF inhibition is not a cure for neovascular and exudative maculopathies, but it is vastly superior to any of the "conventional" treatments currently in use. This is not to say that those older therapies cannot have an adjunctive role, although that may not be likely especially for the more invasive and expensive ones. What it does mean is that the visual and anatomic effect of non-selective VEGF inhibition is no longer an unknown. The early

prospective data on Lucentis is definitive, and the retrospective data on Avastin is so strong that an RCT to evaluate its effect compared to natural history or the effect of PDT or Macugen would not be ethical. There are suggestions that Avastin may be superior to Lucentis as to its duration of effect, and of course it is obviously and vastly superior in its ***cost***-effectiveness. The relative utility of Avastin vs. Lucentis is still quantitatively unknown however, and since both have clearly similar safety and efficacy profiles, it would be scientifically reasonable and ethical to compare them in a prospective trial. If nothing else, the vast positive experience with Avastin far exceeds the pilot data on Lucentis patients that the company determined was adequate to mandate further study.

It appears that a head to head study will need to be done independently, without Genentech's assistance. Genentech has been quoted in the national press on three different continents now as saying that they 'need to make their money back on Lucentis' and that they 'will never support a comparative trial with Avastin'. Their business partner, Roche, has gone as far as using the structure of the national formulary in Australia to make Avastin completely unavailable there for ophthalmic use. Judging from the public reaction to this, it would appear that the company's plan to sweep Avastin under the rug may be blowing up in their face in the public eye, with the retina community, and with payers including many Medicare carriers. Given the recent concerns over bias in company sponsored RCTs, an independently funded and administered RCT would have more legitimacy, and Genentech's noninvolvement may actually be an advantage.

There are unknowns other than a head to head analysis that need to be explored. Combination therapy using nonselective VEGF inhibition as anchor therapy with various other treatments would be a very important type of study. Noting the status quo of extreme drug pricing deemed acceptable with Visudyne and Macugen, it would be ironic indeed if the inexpensive combination of intravitreal Avastin and triamcinolone was found to be a safe and efficacious treatment combination. Another question to be evaluated might be the combination of pharmacologics and laser surgery. The few surgeons in this country and the many more in Europe and Asia who have taken the time to become proficient with feeder vessel treatment (FVT) have found it to be extremely safe and effective and anecdotally superior to PDT in many patients. The main problems with feeder vessel therapy in my five years of experience with it is that it requires a very expensive camera, it requires a lot of work with a high learning curve, and there is a high initial recurrence rate (although stability once achieved can be long-lasting). We have found, again anecdotally, that combining FVT with IVTA can result in much better effect and duration of effect, and it seems quite reasonable to hypothesize that combining FVT with Avastin and/or IVTA in some sequence might offer significant synergies, especially considering that all three (with the exception of Kenalog's known risks) are individually quite safe. The role of siRNA, protein kinase inhibition, and other new agents should of course also be looked at in the context of the new nonselective anti-VEGF standard of care.

A study of another kind might be worthwhile at the congressional level or by independent investigative reporting. Given Genentech's obvious resistance to prospectively comparing Avastin to Lucentis, its resistance to even consider submitting Avastin for FDA approval for ophthalmic indications, and the transparently financial motivation for this intransigence, it might be reasonable to look not only into the Lucentis controversy, but also at the impact of company sponsored medical research on the public good.

New Imperatives-

So, what imperatives are we faced with? Many, it would seem. We clearly have a new standard of primary care in the treatment of exudative AMD. We should re-evaluate and possibly suspend ongoing studies based on therapies that are clearly inferior to the new standard or that accept continuing vision loss as a "successful" endpoint. We

should look at the design of new studies and define success endpoints based on what we know we can achieve in practice today rather than on the inferior standards set by PDT and Macugen. We should think hard about allowing research goals to be so strongly influenced by corporations. Corporate participation of course is vital to medical progress, but this needs to be focused on public welfare as well as shareholder welfare. Pharmaceutical companies have a public responsibility unlike, say, a textile maker. They should be held accountable to the public interest and not be free to consider only their shareholders' interests. Perhaps this needs to be regulated by better independent or governmental oversight. Finally and perhaps most importantly, ***we*** need to take more responsibility for the financial as well as clinical well being of our patients. Too many retina specialists have rationalized using expensive and sometimes inferior therapy by arguing that 'the government is paying for it anyway'. When we have good data that a vastly less expensive off-label therapy is as good or better in terms of safety and efficacy, that is irresponsible. The system is our system, and if we don't respect it, or worse, if we actively or passively assist corporations in manipulating the system for their financial benefit, then we have hurt our patients and the system in which we must all co-exist. The potential market cost of Lucentis used according to the RCT protocol is around 10.1 BILLION dollars per year for new AMD cases alone, over twice the Medicare Part B budget ***for all of ophthalmology!*** With the emerging discipline of evidence-based medicine, spear-headed by visionaries including our own colleague Gary Brown and others, we have useful tools that will help us to demonstrate what therapies are most effective ***in our patients' own estimation***, and also which are most cost-effective. Time-tradeoff techniques and QALY based effectiveness analysis are emerging as powerful tools that will place in stark perspective the actual value of therapies that are marginal in terms of effect or cost compared with those that are vastly more effective and cost-effective. The climate has changed forever, and it is time that we accept this and adapt.

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[ii] ***A letter from Dr. Steve Kaufman, of Physicians for Clinical Responsibility, to the Committee:***

Thank you for the opportunity to express my concerns, shared by many in my profession, about the growing influence of pharmaceutical companies on physician research, training, post-training education, and clinical decisions.

I will attempt to be brief, anticipating that Dr. Kassirer and others can elaborate in greater detail. While not an exhaustive list of problems, I raise what I regard as principal concerns, and I offer remedies, some of which may be outside federal jurisdiction.

1. There are incentives to prescribe more expensive medications.
The Medicare standard to reimburse providers 6% above Average Wholesale Cost for in-office medicine delivery virtually eliminates any incentives to control costs and actually provides strong incentives for physicians to either use more drug or to choose more expensive drugs. This problem is most pronounced in cancer treatment and dialysis centers. There are strong incentives to overuse of certain drugs whose use is optional, such as the white blood cell booster [I'll get the name, Greg] and to use excessive doses of drugs such as the red blood cell booster erythropoetin (and use of erythropoeitin for dialysis-related anemia is the single largest Medicare drug expenditure). The April 18 issue of the Journal of the American Medical Association reported, "Compared to patients in nonprofit dialysis facilities (n=28 199), patients in large for-profit dialysis chain facilities (n=106 116) were consistently administered the highest doses of epoetin regardless of anemia status." The accompanying editorial noted that there is no evidence that the target hemoglobin routinely set by the for-profit centers increases survival, and in fact there has been compelling evidence that it reduces survival [perhaps because people on dialysis have a

"hypercoagulable state" -- their blood clots more readily.]

As a retina specialist, I see this problem in the Avastin vs. Lucentis issue, because providers stand to make much more money by using Lucentis ($1950/dose) than Avastin ($50/dose).

Remedy: Change Medicare reimbursement arrangements such that there are no incentives to prescribe more expensive medications. Right now, reimbursement for drug infusion at cancer treatment centers is very low, and these centers' very survival depends on profits from drug sales. In order to keep these centers viable, fair compensation for infusion services much accompany elimination of physician drug profits. The result will be dramatically reduced drug costs and huge Medicare savings.

2. Kickbacks for physicians
An article entitled "Doctors Reap Millions for Anemia Drugs" in the May 9, 2007 issue of the New York Times reported how two companies that produce erthyropoeitin are legally paying hundreds of millions of dollars annually to physicians in return for prescribing their drugs. I am not sure how this avoids Stark anti-kickback laws, but evidently there is a loophole that has been exploited to the benefit of drug companies and to the detriment of public welfare.

3. Influence on CME

A. Many programs have a speaker hired by a drug company that pays for the speaker as well as many of the program expenses. Naturally, that speaker favorably reviews that company's products.
B. Many programs have "unrestricted grants" from drug companies. However, everyone knows who butters the bread, generating incentives to portray sponsors' products in a favorable light.
C. Programs often feature "leading" academics, who have impressive academic credentials and/or authorship of important textbooks. However, today nearly all such academic people are beholden to drug companies that sponsor their research and/or provide these academic leaders with generous speaker and consultation fees.

At the 2006 American Academy of Ophthalmology's Retinal Subspecialty Day conference (with about 1000 in attendance), every single speaker who talked about drug use in macular degeneration had a financial relationship with the companies that made the drugs about which they spoke, and one was a company employee with "patent and/or royalty" conflicts of interest!

Remedy: Programs that have pharmaceutical sponsorship should not be used for Continuing Medical Education credit.

5. Influence on the Literature

A. Drug advertising is a major source of income for professional journals. There are strong incentives to publish articles favorable to sponsoring drug

companies. I am not claiming that our journals are little more than mouthpieces for pharmaceutical companies, but it is reasonable to expect a journal not to publish articles of borderline scientific merit that have unfavorable conclusions about sponsoring companies' drugs, and to publish reports that are similarly scientifically borderline but that offer favorable conclusions about sponsoring companies' drugs.
B. Editors choose who will peer-review articles, who will write editorial reviews that discuss published articles, and, ultimately, which articles are published. The editor of the journal Retina, my principal sub-specialty journal, is a consultant for at least nine pharmaceutical companies.

Remedy: It may be possible for the federal government to reduce pharmaceutical influence on journals, because medical libraries often receive large grants from the federal government to purchase these journals. If these grants could be contingent on their purchasing journals that had low levels of conflict-of-interest, this would generate incentives for the journals to change their policies.

6. Influence on Research
A. Many drug companies offer lucrative contracts with researchers to collect data, which the company then controls. In this way, unfavorable data are never published, and favorable data are published with the name of respected researchers and research institutions giving the data legitimacy.
B. Many drug companies offer general support of labs, but again the researchers know not to bite the hand the feeds them.

Remedy: The government should not provide research support for any projects that also include private industry support. Also, the government should not sponsor a project on a drug any of the project's researchers is on the speaker panel or is a consultant for the company that makes that drug. (In essence, the government should not pay for research tainted by pharmaceutical influence.)

[iii] ***Unsolicited feedback on "Through the Avastin Looking Glass and/or Avastin vs. Lucentis: Why it Matters:***

Folks,

I read your monograph, Avastin versus Lucentis: Why It Matters, with great interest.

I am tired of being a Big Pharma biotch.

Please sign me up on the email list.

GC, M.D.

Fort Worth, Texas

How can I help in furthering the use of avastin?

Is it worth having every MD using it, speak with their Congressman?

Perhaps we should have a letter for every patient to sign and then fax to their Senator and Congressional Representative.

Please let me know how I might help.

MF MD

Ft Wayne IN

Your letter intrigued several ophthalmologists in my community. However, most retina specialists in NYC (I'm in Brooklyn, NY) are using Avastin as primary treatment. I gave 350 injections in 2006 all Avastin and have had no side effects and no inflammation. It seems that the larger high profile retina groups and those in the university settings have switched from Avastin to Lucentis.

It is becoming increasingly obvious to me that many speakers on the AMD circuit, the so called experts, are puppets serving their needs and the companies that pay them. An example of this is Macugen. I am happy that some ophthalmologists took an idea and made big money from it. However the hard sell at that time for a drug that had only minimal if any more benefit than PDT was amazing. Anecortave also is an example of a drug that almost got

pushed through the system despite its lack of success. As you know data can be manipulated - their sell was if you only look at the patients that didn't have reflux from the injection site (after they modified the

procedure) then there was evidence of benefit.

I'm happy Lucentis works. It should be a second line drug if patients are not responding well to Avastin. It is unfortunate that the so called experts won't admit that Avastin has a significant role in AMD. Yes, we don't know the long term effects of Avastin . But we really don't know the long term effects of Lucentis. What happens after 2 years? And if you were a patient would you really want 24 injections if you may only need half that number for a similar effect?

Let me know if I can be of assistance.

JR, MD

I agree 100% with your organization. It is ridiculous that the Federal government should pay thousands of dollars for an injection, while a similar injection that is just as effective costs just $50.

As I read your article- I am blown away that Lucentis could cost the healthcare system Billions of dollars.

Please let me know how I can help

Best regards

BT, MD

Thank you for the great pamphlet! It has been a source of frustration for many of us. I wrote carefully composed letters to the editor of one of my local papers (Omaha World Herald) and to the Wall Street Journal last Autumn

in which I came up with similar numbers. Of course, neither letter was published. It was refreshing to hear others were similarly upset.

MW, M.D.

Lincoln, NE

I greatly appreciated your article entitled Avastin vs. Lucentis...

>

> I agree wholeheartedly with your statements. In the beginning I was

> deeply troubled by the vulgar pricing of Lucentis. I used avastin

> predominantly. However, I have become concerned about the

> medical-legal aspects of using an off label med when an approved med is now available.

> Your article as well as others help to give us a basis to use avastin.

>

> However, is there anyway we can have our malpractice carrier and/or

> academy issue statements advocating the cost-effectiveness of avastin vs.

> lucentis.

>

> Thank you.

> JM, MD

>

> I enjoyed your newsletter on Lucentis vs. Avastin. Do you have a PDF

> version that I could email to my colleagues? I support your arguments!

> Thanks,

> Don Stewart, MD

> Charlotte Eye Ear Nose & Throat Associates Charlotte, NC First, let me

> applaud your efforts in putting forth a thoughtful and accurate

> assessment of the Avastin/Lucentis debate.

>

> I recently met with some Genentech reps who have been fervently trying

> to get me to convert from Avastin to Lucentis..they even flew out one

> of their "heavy hitters", a former pharmacist, from San Francisco .

> While the ridiculous price of Lucentis is the "Gorilla in the Corner",

> I had a lively debate with the Genentech reps about which medicine works
better.

> The pharmacist stated that Lucentis has gone through a controlled

> clinical trial and so should be preferred. I explained to her that I

> have done a sort of meta analysis on all available Avastin

> data...Avastin appears to have the same efficacy as Lucentis..I think

> the key element is that intravitreal Avastin studies are predominantly

> PRN dosing. PRN treatment is very attractive to patients and doctors

> alike. We have much MORE data on Avastin PRN than we do on Lucentis PRN.

>

> Currently, there is no convincing data that Lucentis works any better

> than Avastin.

>

> Currently, I believe there is convincing data that Avastin PRN works

> at least as well as Lucentis every 4 weeks.

>

> CH, M.D.

>

>

>

> I received your letter regarding Avastin vs Lucentis. You echoed my

> thoughts. I am a retinal specialist treating many patients with

> Avastin and I have held off treating with Lucentis.

>

> Please keep me informed

> RB, MD

> Brooklyn, NY

>

> Thank you for your newsletter on Avastin vs. Lucentis. I agree with

> your assessment, and I am concerned about the outrageous cost of these

> new therapies. Please keep me informed.

>

> Thanks,

>

> SR MD

>

>

>

> 1. We comprehensive ophthalmologists can use our influence to

> pressure our retinologists to use Avastin.

>

> 2. The cost of glaucoma medications are skyrocketing also. Maybe it

> is time for us to start a "grass roots" campaign against all

> unrealistic price increases.

>

> 3. Insurance companies essentially dictate how much I get for a

> particular procedure why on earth do they pay Genentech such

> outrageous amounts? Why not tell them it's going to be "x" take it or

> leave it?

>

> 4. Doesn't Genentech care about their PR? If I were the only

> ophthalmologist in town I would still charge a reasonable amount. I

> care what my patients think about me and I doubt Genentech would want

> to be synonymous with greed.

> Scott Richards MD

>

>

>

> As a group you should all be commended.

>

> I have been using Avastin almost exclusively. I would be very

> interested in getting involved with your effort. In addition to

> educating physicians on this matter, I strongly believe that patients

> also need to be enlightened.

> Sincerely,

>

> JE, MD

> 5 Franklin Ave. Suite 209 Belleville, NJ 07109

>

>

> I was very pleased to receive your recent communiqué and am in

> complete agreement with your views. I have long argued that we the
'community'

> doctors should forge and define the 'standard of care' and not the

> for-profit industry giants (who buy the ads and organize the sponsored

> meetings) or a small group of KOLs at various institutions (who

> control the media and podiums around the country, yet are more prone

> to be influenced by industry than independent sole proprietors). This

> conflict of interest was made quite obvious by the PDT saga, as has

> been brought out in the open by the AJO editorial authored by

> Sternberg and Lewis. With Lucentis, however, the stakes are higher.

> While many of us may not be Key Opinion Leaders, we are Key Care

> Leaders, and as such, it is up to us to promote the interests of our

> patients and society at large. Today, both are far better served by

> Avastin than Lucentis. The CATT will provide statistical significance

> to support what is presently the right thing to do. I encourage you to continue to lead us in this campaign.

>

> Sincerely yours, JS

>

> JS , MD , FACS, FRCOphth

>

>

>

>

> We are in receipt of your recent newsletter, which discusses Avastin

> versus Lucentis. I am writing to make you aware of the fact that our

> clinic, under the direction of Charles E. Lyon, M.D., FACS, is

> conducting an on-going, in-house study of our Avastin patients. We

> have several hundred patients enrolled, dating back to October 2005.

>

> If you have an interest, Dr. Lyon would be happy to discuss our data

> with you. Please feel free to contact me at your convenience, and I

> will put you in touch with Dr. Lyon.

>

> Thank you very much for your time, and please expect a check for $35

> for membership to your organization.

>

> Sincerely-

> TT

>

>

> 1) I am in receipt of your brochure "Avastin versus Lucentis: Why it

> Matters" and find that I agree in principle, personal experience, and

> in practice with all points made. I have previously spoken up in

> public at the 2005 AAO meeting predicting the same catastrophic

> economic impact of Lucentis/Macugen on Part B financial stability. Thus, count me in.

> 2) You may or may not be aware of the effort by uninvolved

> pharmaceutical companies to quash the "head to head" testing. See

> http://irvaronsjournal.blogspot.com/2006/11/avastinlucentis-update-8-r

> eport-of.html

> 3) The one point that keeps being missed in everything I have seen

> written about this quandry is the financial motivation differential

> that is being inflicted upon retina specialists by CMS and private

> payors in favor of Lucentis.

> The drug reimbursement policy of 5% over avg wholesale cost yields

> approximately $100/dose to the retina surgeon for Lucentis and
> $2.50/dose for Avastin. If he administers 10 doses a year to 100
> patients, that makes $100,000 net annually for Lucentis and $2,500 for
> Avastin , a differential that is difficult to ignore for a
> practitioner already caught in the vise of constantly rising overhead
> and lowering reimbursement, particularly in those cases wherein the
> patient in his care is not financially affected by drug choice. It is
> within the power of CMS to correct this part of the iniquity. Perhaps
> it just needs to be revealed more clearly.
> 4) The practical use of these drugs is a constantly changing scene,
> month by month. It has become clear to me and others that anti-VEGF
> therapy is effective not only against wet ARMD, but also CRVO, IJT,
> OHS, CSC, exudative DR, and as an adjunct in the treatment of BVO.
> Few payors will cover these uses, even after time-consuming individual
> appeals. Many patients can hardly afford even Avastin injection fees
> for this, out of pocket. If we all used Avastin and chose to forgo
> Lucentis entirely, all these conditions could be easily covered by
> private and federal payors, still leaving a huge net savings to the
> system. In view of the now-established safety of Avastin, the
> resistance to payment coverage can hardly be viewed as other than
> cost-control. Many Americans are losing vision permanently while we
dither.
> Sincerely,
> TH, MD
> PS If you have a digital version of your brochure please send it to
> me, to facilitate sharing with others.

iv *Slip Sliding Away*

At a recent local society dinner in our town, the speaker, a local retina guy, announced that he had no financial ties to any of his material, and then proceeded to give an infomercial for numerous company-sponsored "studies"/marketing ventures, each with financial relationships and some with the promise of consulting and speakers fees . When I pressed him on the point, he explained that he was "just an employee" of his practice, and therefore he had no disclosure obligation. The speaker's partner suggested that I should keep quiet because "everyone (including me??) is doing it anyway". That got me thinking again about the various conflicts of interest that have become so commonplace in the retina world today. I posted an essay about such ethical issues last year and received voluminous and unanimously encouraging feedback including a nice note from one of the patriarchs of the ASRS who decried "the pathetic slide of our profession into the hands of the drug companies".

It has been a slide. Like many "slides", it starts innocently enough. A T-shirt at the Academy booth for listening to the pitch. Later, maybe the company sponsors a dinner for you and your referrals, some nice CME, and of course you pick a topic that flatters the sponsor, or at least doesn't criticize them. Later they ask you to give a talk with an honorarium and travel expenses, and again the talk appropriately expresses your gratitude. Then maybe a trip to be on the advisory board, and finally the big time: you are asked to be on the "research team", but of course they own and control the analysis and presentation of the data. You don't like that, but what the heck. It's great for the practice, and "everyone is doing it anyway". It all seems okay, you guess. The only trouble is,

It's not.

It's often so hard to see where that line is and whether or when you've crossed it. Indeed, there is much discussion about "the line", but most seem to agree that there is one and our profession has slipped well across it. The Lucentis/Avastin drama provides an excellent case study. I had a long conversation a few months ago with an associate professor of a major eye institute and his corporate "handler". We discussed many of the ethical facets of the Lucentis/Avastin debate, and as they were both expressing their personal belief that the two drugs were equivalent, the doctor explained to me that, in any case, he was "only a scientist" and as such had no obligation to address "the business ethics". That was a real eye opener for me. He seemed oblivious to his glaring conflict of interest and only too willing to absolve himself of its very existence.

As I have been involved in the national discussion regarding the Avastin/Lucentis controversy, I have had conversations with various bioethics leaders on the role of the drug companies in affecting the independence of medical practice and research. This is not particular to the retina world. Here is how it often works (as summarized from "On the Take", by Jerome P. Kassirer, MD):

A company has a new product for which they need Phase III or Phase IV data. They recruit willing doctors to whom they pay up to several thousands of dollars just for signing up a patient and then more for collecting the data. The data BELONGS, by contract, to the company. The company takes the data, ghostwriters write what favors the company and they often conceal whatever data doesn't suit them. They then attach some or all of the names of the hired docs to the ghostwritten paper and have it published. Since the study is designed to favor the drug, and since negative data is often suppressed, it is often not true science but rather more of a marketing project that looks scientific. It's a win-win. The company gets their product out, marketed in a way that looks like legitimate peer-reviewed development, and the docs get money and a little prestige as well. After that, the docs may get more money to be on the speaker's bureau to promote the product. Since there are innumerable combinations of products out there now, there is virtually no limit to how many marketing projects can be made into such "research". The crux here is that docs are paid a sufficient premium that there is an inducement to go along with the company on care decisions and data management that *could* compete with patient welfare. Since over the last decade or more the government has stepped back from funding clinical research outside of the NIH, companies are only too willing to pick up the mantle and fit "research" into their marketing plans. As physician reimbursements have come under increasing pressure, it has become tempting to replace perceived lost patient care revenue with drug company revenue. And why not? "Everyone else is doing it anyway."

Don't take it from me. Consider the books "The Truth about the Drug Companies", by Marcia Angell, MD, and "On the Take", by Jerome P. Kassirer, MD, both former Editors in Chief of NEJM. The first considers the manipulation of the drug development and marketing process by the drug companies and the second deals with physician complicity in this process. Both books should be required reading for anyone who seeks to be informed about the conflicts of interest in clinical care, research, and medical education.

The ophthalmology and retinal specialties were not deeply explored in these books, but our issues are very much on the battleground that they discuss. It is virtually impossible to find a meeting where speakers' are not compromised by financial conflicts of interest. Many colleagues have written to me in the past year that it is hardly worth even going to meetings anymore since so much of what we hear is nothing more than advertisement for the speakers' various sponsors. It would be easier if the speakers just wore NASCAR style jackets emblazoned with their sponsors' logos. The drug companies' influence is pervasive even beyond overt sponsorship. I was recently to give a talk on some of these ethical issues, but five minutes before speaking I was asked to change my topic because one of the companies had just given a large sponsorship check for the meeting.

Call me sentimental, but I still admire research that is done to gain unbiased knowledge, and I miss the time when our academics and "opinion leaders" never needed to explain (or euphemize) their financial interests at meetings and in papers. The financial conflicts that Dr. Kassirer talks about in his book are rampant in the retinal world.

There is a very good reason for this growth of corporate sponsorship of physicians. Over the last five or more years, there has been increasing downward pressure on physician reimbursement. Simultaneously, since the precedent of obscenely priced retinal pharmaceuticals was ushered in with Visudyne, drug costs have been eating into the Part B revenue pie. This has come to a head with Lucentis. Few dispute that Lucentis and Avastin work

very nearly identically, and many suspect a primarily financial motivation for Lucentis' development. Nonetheless, by the company's own estimates quoted in the recent Wall Street Journal article, Lucentis should take close to 1 billion dollars from the Medicare Part B budget for eye care in 2007. This is about 20% of that budget ***right here and now***, and it creates a virtual certainty that physician reimbursement and patient benefits will suffer accordingly. One option for physicians is simply to sell out, jump on the bandwagon, and replace lost patient care revenue with Big Pharm payoffs. These are available in the form of payment for corporate controlled research, marketing, speaking engagements, and the like. There is even a $100.00 per dose inducement to use Lucentis over Avastin, since CMS pays 106% of AWP, which is about $100.00 more for Lucentis than Avastin. And why not just give in? "Everyone is doing it anyway".

And what about the patients? Well, they're on their own, aren't they?

What about research? Real research still happens; it's just obscured by ever increasing volumes of corporate research that is too often designed to serve marketing interests at the expense of scientific interests. Even if good research is done by those who accept compensation from drug companies, that financial conflict makes it impossible and impractical to discern which data is biased and which isn't. Even the good, nonbiased data is tainted by the possibility of undetected bias. Before all these financial intrusions, we didn't have this problem. Furthermore, research that doesn't support marketing interests is often spurned. Take the head to head CATT study. This is being done without any corporate help because Genentech publicly admits that it will support no research on Avastin because "it is not in their best financial interest" (personal communication with a Genentech executive who will remain unnamed). So much for bringing a vision of (true) science to the science of vision. Maybe Genentech should change its motto to "Bringing the Science of Marketing to the Marketing of Science".

What of our societies and our academic "leaders" and "opinion shapers"? It would be nice to think that biased research happens only in the less regimented world of private practice, but it doesn't. Many, though certainly not all, of our academicians and "leaders" are hugely affected by financial conflicts of interest. It is no longer possible to go to a website or even a journal that is not affected by the infamous "unrestricted grant" from one or more corporations. In this context, "unrestricted" too often means, "spend this grant on what you want, but if you ever want another one, don't displease us". This has made it difficult for doctors who want to practice good medicine with reliable information. There is still a significant quorum of our peers who want nothing more than this, to practice good, evidence-based medicine in the best interests of their patients. How do we find unbiased information and teachers? Who can we trust? How can we connect with government in a sincere attempt to provide good and cost effective care? How can we advocate for patients and keep our health system solvent?

We must find answers to these questions in the decade to come. In spite of the apparently impregnable fortress of "Big Pharma", I hope that we can decide that patients are more important than shareholders or various individuals' consulting deals. I think we need to speak up and act out. I have heard many, many insightful and deeply ethical thoughts from many colleagues since I first joined this discussion a year ago. I think we need to

make a stand and let the chips fall where they may. Truth tends to eventually bubble to the surface against all odds. New therapeutic development is vital, but unbridled marketing hubris has gotten out of control. "Opinions" that are crafted and purchased to serve corporate interests often just don't make sense for the public welfare. We need new opinions that serve the interests of patients and society, and if that means we need new "opinion leaders" who are willing to serve an ethic of truth over financial expedience, well that wouldn't be so bad.

In the spirit of providing a forum for discussion of these issues, several physicians have created a website and a grass roots organization called Physicians for Clinical Responsibility. This is meant for physicians who have decided ***not*** to enter into financial interests that might conflict with patient interests. This essay and several earlier ones as well as news articles and links to Dr. Kassirer's and Dr. Angell's books are on the www.clinicalresponsibility.org website. I invite you to take a look, sign up to be a member of Physicians for Clinical Responsibility and even leave a comment or cosign any of the pieces on the site. If you agree with the content, say so. If you disagree or have other input, say so. The independent literature there speaks for itself. The members' essays are not intended to be dogmatic and certainly are not intended to be inaccurately critical. If there are inaccuracies, please post corrections. The intent is simply to catalog opinions in a dedicated clearinghouse, stimulate input, and create a forum for concerned members of the medical profession.

Respectfully,

Greg Rosenthal, MD

May, 2007

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The following has been called "great", "very important", "right on the mark", and "the right thing to do" by several of the leaders in our specialty. It has been criticized as being "biased" by some who have financial relationships with one or more corporations. It has been submitted to several retinal publications, but rejected for being "too controversial" for their advertisers. It ***is*** controversial, but it reflects concerns raised many times and in many

forums in the retinal world. I have no desire to be a pariah or to disrespect the many fine doctors and researchers in the retinal field. Still, I do believe that these and future questions need to be raised and discussed. This is therefore an attempt to clarify rumors and innuendos that have been circulated about Avastin and to promote discussion about how we control or cede control of our practice of retinal medicine. I have no relationship of ***any*** kind with any pharmaceutical company.

Through the Avastin looking glass

I think I may have slipped through the looking glass and down the rabbit hole into a surreal world.

It seems that every time I turn around, I see an interview or a meeting or a flyer about how great PDT or Macugen is because patients ***lose*** fewer than 15 letters of vision. The participants seem to assume that Avastin doesn't exist or that AMD treatment needs a less effective but more expensive combination drug for "maintenance" when those same patients could have actually gained vision safely with Avastin monotherapy at a fraction of the cost. Then it struck me. Many of these speakers and interviewees are ***paid*** either by Novartis or Pfizer, both of whom might wish that Avastin ***didn't*** exist. Brief reference to financial relationships can be found in the fine print, but the façade is always that of an objective, scientific discussion impartially considering ***all*** of the facts. It is really no better in the equally surreal evolution of the Avastin/Lucentis controversy. Based on Genentech's apparent actions to increase price and limit availability of Avastin and the publicity for Lucentis which also seems to assume that Avastin never existed, one could speculate that even they would like ophthalmic use of Avastin to disappear as they promote its analog at an exponentially higher price.

It is the potential for marketing plans to guide the direction of medical care and our responsibility to maintain independence and objectivity as we provide care for our patients that concerns me. This is where we have begun to stray and where we need to refocus and guide corporate sponsorship of care rather than have that care guided by corporate interests. The Avastin story provides an opportunity to explore trends that have been growing for some time. I have no desire to disparage or disrespect any individual or corporation but rather to simply raise points of concern that have entered the world-wide retinal dialogue.

A good example of misinformation came across all of our desks this past summer: A glossy Pfizer flyer talking about thromboembolism in the elderly, written as if it is a foregone conclusion that nonselective VEGF inhibition causes stroke. Pfizer has based its recent promotional campaign on implicating Avastin (and Lucentis) for incidental, probably unrelated vascular disease common in the elderly patient population. As evidence for a causal relationship, this flyer referred to van Wijngaarden et al's [1] observation that if your instruments are sensitive enough, you might detect traces of systemic Avastin after a 1.25 mg intraocular injection. This is supposed to be the smoking gun. Are we to ignore the fact that oncologists infuse 500 mg or more of Avastin directly into the blood stream every 2 weeks with virtual impunity? They consider the therapy "very effective and very benign" (except for possible interference with wound healing). Of course, the cancer patients may have little to lose since

their options are limited, but contrary to the implication, the now sizable and ever-growing ophthalmic literature [2-12] on the safety and efficacy of intravitreal Avastin yields no provable adverse effect. The even more voluminous Avastin safety survey[13] also supports a high margin of safety.

As I understand it, the stroke story is based on advisory letters that Genentech released in August 2004 and January 2005. Based on a meta-analysis of cancer patients, they warned that in patients with disseminated colorectal cancer (and ***only*** in that prothrombotic patient population), the ***combination*** of high dose IV Avastin ***and*** high dose IV 5-Fluorouracil may increase the annual rate of all thrombotic events from a high 1.9 percent to a slightly higher 4.4 percent. At the time, Dr. Hal Barron, Chief Medical Officer for Genentech was quoted in Nature Biotechnology [14] saying, ***"It isn't absolutely known whether the effects seen with Avastin can be generalized beyond the population of metastatic cancer patients receiving 5-FU....The implications of it being unique to 5-FU or to colon cancer would be very important for clinicians to understand."*** The thromboembolism advisory was directed ***only to patients with disseminated colorectal cancer and only with the act of combining IV 5-FU with IV Avastin***. The message is now different. Genentech was cited on CNBC and elsewhere in December 2005 as indicating that physicians and patients should just wait for Lucentis because using Avastin in the eye is conclusively "unsafe". Could financial factors have had any role in this change of heart?

I am aware of no other evidence implicating Avastin in thromboembolism. I have been told by every oncology colleague I have asked that drawing an analogy from this single advisory and ignoring the volumes of safety data from the rest of the oncology literature is unreasonable, especially considering the differences:

- We are using 1.25 mg rather than 500 to 1000 mg or more
- We are injecting into the sequestered space of the eye rather than directly into the systemic circulation
- We are treating every 2 months or so rather than every 2 weeks
- We are not using 5-FU
- And of course, generally speaking our patients don't have disseminated colorectal cancer. Ironically, there are cases of patients' wet AMD improving during systemic Avastin therapy for cancer!

It is not surprising that the drug companies are fighting acceptance of Avastin for ocular use. They have worked hard to establish a status quo where we are all supposed to accept, even embrace, the concept of medicines in the growing field of retinal chemotherapy costing $1,000 to $1,500 (or even $18,250) ***per dose***. We are furthermore supposed to consider 3 lines of additional vision ***loss*** a "successful response". Unfortunately for this status quo, Avastin and its analog Lucentis have redefined "successful response" as one where most patients gain vision quickly and unequivocally, especially if we exclude patients who have already lost vision during Macugen or PDT therapy.

Then there is the question of cost-effectiveness. The cost differences between therapies are stark. According to published protocols, the baseline cost per case (just for the drug and not including triamcinolone combinations) is roughly:

- PDT- $1500.00 per dose every 3 months for 2 to 3 years = $12,000 to 18,000
- Macugen- $1000.00 per dose every 6 weeks for 2 years = $17,000
- Lucentis- $1950.00 per dose monthly for 2 years = $48,000!
- Avastin- ~$30.00 per dose every two months for two years (a frequency and duration that may be more than is necessary) = $**360**

As the saying goes, "you do the math". Of course, there are variables in comparing Lucentis and Avastin. Avastin sometimes results in stability after a single dose and other times may require multiple injections. Similarly, it might not be necessary to give Lucentis every month for long durations, although the PIER data demonstrates that decreasing to quarterly injections results in resumed progressive loss of vision. At least in the short term, Lucentis seems to have a beneficial effect similar to Avastin, but at potentially 133 times the cost per case, it would need to be greatly superior to be justifiable. Indeed, the question of whether there is any role for Lucentis at all can only be answered by a head to head comparison with Avastin. If this is not done prospectively, physicians will have the appropriate responsibility to make recommendations based on the data that *is* available. There is enough experience with both to be confident that they are similarly safe. The simple fact is that with volumes of data published by reputable sources, Avastin sets the de facto standard for the *combination* of safety, efficacy, and cost against which all future AMD treatments including Lucentis must be compared. Unless Lucentis is priced according to this standard, its release will become irrelevant to patient care and a step backwards in cost-effectiveness. Doubling the cost of Avastin and/or making it less accessible are hardly appropriate ways to make Lucentis seem more acceptable by comparison.

None of us want our patients harmed, but there is no current proof of adverse effects caused by intravitreal Avastin as compared to Lucentis or any other therapy. We must remember that losing vision from an inferior treatment and/or adding unnecessary additional cost is harm too. We don't know that Avastin (or Lucentis) ***never*** causes adverse effects, but the empirical data supporting the safety of both forms of this molecule are very compelling and reassuring. We certainly shouldn't ignore risk, but when those with a financial interest are willing to manufacture or distort data to wage a campaign of fear, we owe it to our patients to stand up and do our best to act on truth rather than "urban legend".

It is unfortunate that since the introduction of PDT, some of our colleagues have literally sold their support to corporations to promote certain treatments to the exclusion of newer and better alternatives. Whether it is stock options, money, funding for chaired professorships, or just travel expenses to exotic destinations, such remuneration can adversely affect credibility and perhaps objectivity as well. Paid endorsement, in any form, needs to be ***clearly and completely*** represented as such. There are many physicians of impeccable integrity who work with various corporations, and they adequately disclose those relationships. That is not the problem. The

problem lies with those willing to sell opinions and whose relationships are more nebulously described. Research bias in company-funded studies, even if not intended, is another concern. This is not unique to ophthalmology. Evidence of favorable bias in company-funded research was recently reported in the British Medical Journal.[15] Of course, we deeply appreciate the efforts of pharmaceutical companies to develop new drugs. We appropriately want to help with research and advice, and it is appropriate that such help be compensated. Compensation for services rendered is perfectly acceptable; however, the moment a physician assumes a *vested* interest in the success of a company or product (such as accepting stock options) or accepts compensation or reimbursement specifically to endorse a product or disparage a competitor, that physician can then act only as an agent for his or her "employer". They must recuse themselves from independent discussion. Many of us have been offered trips or stock options too, but most of us have declined when a vested or promotional interest is involved. We all make pretty good livings without it, and we need to be able to say what we believe to be true without having our motives questioned. The case of a physician being a principle in a company is of course above board, easily understood, and nonambiguous.

According to all available data, Avastin appears to be extremely safe and effective in the majority of patients. Judging from the Spring 2006 ASRS Avastin survey, this appears to be the strong consensus of the retina community. The retinadialogue.com surveys show over 80% of respondents continuing to use Avastin 2 months after the release of Lucentis, supporting the consensus that Avastin is a legitimate standard of care. We need to decide what to do; with Avastin of course but also with the broader questions that are raised by the Avastin issue. We should value the great work Genentech has done in developing Avastin; however, we should be mystified when, in the face of compelling data from reliable sources, the company's position continues to be that 'it doesn't work' (Miami 2006 Antiangiogenesis Meeting). We should wonder about the motivations for developing another version of the same drug. Was it to improve it, or was it to circumvent the "pricing problem"? We should consider our own responsibility in choosing between two forms of the same drug with similar safety and efficacy but radically different cost. We should be circumspect about taking corporate stock or money, especially if it leads us to do things like redefine "success" to include three lines of failure in order to make marginal treatments look acceptable. We should be alarmed when corporations wage a disinformation campaign based on data that a first year medical student could debunk. We should stand up for our patients and regain our credibility with them, with payers, with the government, and indeed with eachother by working with facts instead of spinning them. We should start acting like doctors again instead of corporate agents.

We need to decide.

J. Gregory Rosenthal, MD

Vision Associates Retinal Service

Toledo, Ohio

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Avastin versus Lucentis: Why It Matters

Although Lucentis is a remarkably safe and effective treatment for exudative macular degeneration, it could cost our health care system billions of dollars annually, which will be a significant burden on our strained health care system. Fortunately, it appears that Avastin is roughly equal to Lucentis in safety and efficacy, and Avastin's far lower cost makes it an attractive alternative. We encourage wider use of Avastin, which can help sustain the health care system that has benefited our patients medically and ourselves professionally.

Growing health care expenses (to which rapidly rising drug costs have contributed heavily) are unsustainable. In response to these growing costs, Medicare has been attempting to reduce all physician fees, a move Congress blocked at the last minute in 2006. Right now, ophthalmology faces annual cuts of 1% for four years, a 3% cut in 2007 for certain commonly used ophthalmology codes, and the prospect of further Medicare cuts in the future. Just as legislators targeted cataract fees as a way to reduce health care expenditures, it cannot serve the public's eye care needs if huge pharmaceutical expenses result in an explosive growth in federal expenses for ophthalmic care. Fortunately, there are things all ophthalmologists can do to address these challenges.

How Might Lucentis Affect

Physician Compensation?

Medicare Part B pays for physician services as well as drugs delivered in offices. In ophthalmology, Visudyne and Macugen have caused sharp increases in Medicare Part B expenses, and the impact of Lucentis is likely to far exceed that of Visudyne and Macugen combined. There are more than 200,000 new cases of exudative age-related macular degeneration (AMD) in the U.S. each year,1 and we estimate that about 85% are treatable. The cost of Lucentis is about $2257 per injection,2 and the MARINA study3 showed benefit from monthly Lucentis injections for two years. Therefore, after one year of full market implementation, Lucentis costs in the U.S. could, in theory, exceed $9 billion.4

Several factors temper this figure, and, based on Lucentis sales data, it appears reasonable to anticipate at least $2-3 billion in annual U.S. sales under current conditions. Some patients require less than 24 treatments, and some retinal specialists use fewer injections by using the PIER or PrONTO protocols.5 Also, many providers

currently treat exudative AMD primarily with Avastin. On the other hand, exudative AMD appears to be a recurrent condition, so many successfully treated patients may need additional rounds of therapy, just as many of our PDT patients have developed recurrences after initial closure of the choroidal neovascular membrane (CNVM).

To put this $2-3 billion figure in perspective, in 2006 the total Medicare Allowed Charges for all of ophthalmology was $4.77 billion. That total covers physician fees, practice expenses, malpractice Relative Value Units, and imaging. In 2004, total spending for all Medicare Part B drugs for all medical fields was about $12 billion. Compare the approximate $54,168 cost of treating one eye with Lucentis monthly for two years to the $46,326 median annual household income in the U.S. in 2005.

Avastin's Benefits

In contrast to Lucentis' cost, the drug cost for Avastin is only about $50 per dose. Further, many treating physicians have noted that Avastin seems to be longer-acting than Lucentis, perhaps because Avastin's larger size impedes clearance from the eye. Consequently, many clinicians use a less frequent dosing regimen with Avastin than Lucentis.

Why Would Ophthalmologists

Use Lucentis?

Although Avastin is a safe, effective, inexpensive treatment of exudative AMD, some ophthalmologists have offered the following reasons to use Lucentis:

1. Lucentis is FDA-approved for this indication.

2. Unlike Avastin, Lucentis has been studied with a randomized clinical trial, and the data for Lucentis are more long-term data than those of Avastin.

3. Lucentis may be safer than Avastin.

4. Lucentis has greater activity in vitro and Lucentis is a smaller molecule designed for better retinal penetration.

5. Physicians receive substantially more income by using Lucentis.

We'll address each of these reasons in turn. First, most prescriptions written in the U.S. are for off-label uses. There is compelling evidence of Avastin's safety and efficacy for CNVM in AMD based on published reports6

and current widespread clinical use. Consequently, the federal Medicare program offers coverage for intraocular Avastin for this indication.

Second, Avastin and Lucentis are structurally very similar, and ophthalmologists' collective short-term experience with Avastin has shown results comparable to those with Lucentis. The planned two-year National Eye Institute head-to-head study should clarify this issue.

Third, after thousands of applications, the ocular safety of both Lucentis and Avastin has been well demonstrated. In terms of systemic safety, thromboembolic events (such as angina, heart attacks, and strokes) have been the main concern. Preliminary long-term data indicate that Lucentis in the ocular dose of .5 mg (as currently prescribed) has a four-fold increased risk of stroke compared to a .3 mg dose, and this risk seems to involve primarily people with a history of prior stroke.7 There is less long-term data on ocular use of Avastin. Among patients using Avastin systemically for metastatic colon cancer, 4.4% who had Avastin in combination with other colon cancer chemotherapies had thromboembolic events, compared to 1.9% who received various colon cancer chemotherapies and no Avastin. However, this finding is of doubtful relevance to ocular use of Avastin. The ocular dose (1.25 mg) is about 1/300th of the systemic dose (5 mg/kg) used to treat metastatic colon cancer. Colon cancer patients receive treatment every two weeks, while intraocular injections of Avastin are generally at least 6 weeks apart. Therefore, ocular Avastin results in approximately 1/1000th of the systemic exposure compared to intravenous use. The increased risk of thromboembolic events occurred only in colon cancer patients who concurrently used other chemotherapies, so the increased risk may reflect drug interactions. Finally, colon cancer often leads to a hypercoagulable state, which predisposes the patient to thromboembolic events. As a smaller molecule, Lucentis has a shorter systemic half-life than Avastin, but it is unknown whether Lucentis has less systemic toxicity.8

Fourth, in practice Lucentis does not appear to be more effective than Avastin. It may be that the 1.25 mg Avastin dose effectively blocks all VEGF receptors, and any additional potency of Lucentis does not confer additional effect. Lucentis' smaller size may turn out to be a drawback, because Lucentis may clear the eye too quickly to work as well as, or as long as, Avastin.

Fifth, Medicare reimburses ophthalmologists 6% over the Average Wholesale Cost of Lucentis. Consequently, ophthalmologists who pay $1950 for Lucentis receive $2067 from Medicare, for a profit of $117 per dose given. In contrast, there is little, if any, profit generated by the $50 Medicare reimbursement for Avastin. A retinal specialist treating only 72 patients with monthly Lucentis injections, rather than treating these same patients with Avastin, will be paid an additional $100,000/yr by Medicare for the Lucentis drug. Further, retina specialist treating monthly with Lucentis, rather than treating patients with Avastin every 6-12 weeks, will likely generate additional income through injection fees.

Retinal specialists typically treat hundreds of exudative macular degeneration patients per year. While there are strong financial incentives to use Lucentis, we don't know whether these incentives influence treatment recommendations. We do know that, for every $100,000 of "profit" paid to ophthalmologists by the 6% "margin" from Lucentis sales, the cost of the drug to Medicare, insurers, and patients is $1.76 million. The 80% Medicare portion of this $1.76 million comes from the same Medicare Part B "pot" that also pays for physicians' medical services.

Are Medicolegal Concerns

with Avastin Reasonable?

We see no reason to infer that ocular use of Avastin poses significant risk of systemic toxicity or more such risk than other anti-VEGF ocular drugs. While some providers avoid Avastin in patients with a recent thromboembolic event,9 ocular Avastin has become a standard of care for most exudative AMD patients. A January 2007 Internet survey of the American Society of Retinal Specialists (ASRS) with 276 respondents found that 58.76% usually recommend Avastin for patients with subfoveal CNVM due to AMD when these patients have both Medicare and secondary insurance coverage (9.97% of these recommend Avastin plus PDT for such patients). For patients without secondary coverage, for whom the co-payment on Lucentis treatment is substantial, 79.20% of ASRS respondents usually recommend Avastin (2.77% of these recommend Avastin plus PDT).

What Other Factors Influence Pharmaceutical Use?

Pharmaceutical companies have always been eager to court "opinion-shapers," academic clinicians whom their colleagues trust to offer informed recommendations. The companies readily sponsor research by these academicians, hire them as consultants, and pay them for speaking engagements. These people deny that their objectivity has been compromised, but a general review of industry-sponsored research showed a bias in favor of the sponsoring company's products.10 Of course, many academicians do speak their minds, regardless of corporate relationships.

Who Is Paying for Lucentis?

For many years, growth in government expenditures for health care has exceeded the rate of inflation. Such growth is not sustainable. In an attempt to control rising costs, there are federally mandated restrictions on Medicare cost increases, effectively putting health care providers in direct economic competition with drug companies for limited Medicare Part B dollars. If we cannot control pharmaceutical costs, our patients will suffer, and we physicians will likely suffer as well. While it may be more politically expedient in the short term for Medicare to cut reimbursement to physicians than to reduce benefits, rising health care costs will eventually result in larger patient premiums, increased co-payments, or reduced access to care. Ultimately, our patients will suffer to the degree that the health care system is financially crippled.

What about Patients

Who Demand Lucentis?

Genentech's media blitz has encouraged many people to request Lucentis. We tell patients that Avastin appears roughly equal in safety and effectiveness. One reason we prefer Avastin is that it may require less frequent injections, which would help reduce the risks of anti-VEGF treatment. We also note that, for people without secondary insurance, the out-of-pocket cost of Lucentis is much higher. Then we leave the choice to our patients. When using Lucentis, we generally follow the PrONTO study guidelines. That protocol often results in significantly fewer than 24 treatments for each CNVM episode.

What Do We Recommend?

1. We think it is reasonable for general ophthalmologists to ask retinal specialists who use primarily Lucentis why they choose to do so.

2. Until the NEI's study of Avastin versus Lucentis is completed (not before 2009), we need to carefully monitor outcomes.

3. As professionals, we have obligations to society-at-large as well as to our patients. In this new era of extremely (we think outrageously) expensive drugs for macular degeneration, we should be mindful of the public-health consequences of our practice patterns.

4) As public health advocates, we should encourage legislators and regulators to remove financial incentives that might encourage physicians to treat patients with more expensive drugs.

1. Postgrad Med 1998;103(5):153-64.

2. $1950 (wholesale cost) + $117 (Average Wholesale Cost mark-up) + $190 (approximate injection fee).

3. New Eng J Med 2006;355:1419-31.

4. After one year, there could be 170,000 eyes receiving monthly treatments and another 170,000 added in the second year. Each eye would receive 12 treatments per year at $2257 per treatment.

5. Ophthalmol Clin North Am 2006;19(3):361-72.

6. Ophthalmol 2006;113:363-72; Am J Ophthalmol 2006;142:1-9; Retina 2006;26:383-90.

7. Genentech "Dear Health Care Provider" [physician advisory] 1/24/07.

8. New Eng J Med 2006;355:1409-12.

9. Ophthalmol 2006;113:363-72.

10. JAMA 2006;296:996-8; Br Med J 2006;333:782-6; Br Med J 2003;326:1167-70.

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Avastin versus Lucentis: Why It Matters

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RESPONSES TO SENATOR KOHL'S QUESTIONS FROM PETER LURIE

Question. In your testimony, you recommend a national disclosure law to provide transparency of gifts and payments physicians have received. Who should administer this program and be responsible for enforcing it?

Answer. We recommend that the database of payments to physicians be maintained by the Department of Health and Human Services (DHHS). The agency already has experience with a similar national database, the National Practitioner Data Bank. Moreover, the increased expenditures on drugs that ensue from the industry's heavy reliance upon marketing are borne by the Medicaid and Medicare programs, both of which are also housed under DHHS. We would urge stiff penalties for instances of non-compliance with any reporting requirement.

Question. Additionally, some states have exempted certain things, such as drug samples or gifts under $100. Do you think certain gifts or payments should be exempted from disclosure?

Answer. We believe that, as long as the nature of the payments is clearly part of each disclosure, the public is quite capable of distinguishing between, for example, payments for research and those for elaborate meals. Let the information be made public, in as detailed a fashion as is feasible, and let the public decide for itself what it deems objectionable. Sample, in particular, should not be exempted from disclosure, as these are the single largest item in pharmaceutical company expenditures on promotion. As noted in our testimony, three of the five states with disclosure laws (District of Columbia, Maine and Vermont) exempt payments under $25 and the remaining two (Minnesota and West Virginia) exempt those under $100. We would favor as low as exemption as possible. In Vermont, for example, only 23% of payments over $25 exceeded $100 (Ross, et al. JAMA 2007;297:1216–23), so high exemptions can result in the loss of information about the majority of payments.

Question. The voluntary guidelines put into place by both the medical industry and pharmaceutical industry several years ago have done little to curb the excessive marketing to physicians. In fact, the problem seems to be getting worse. Since the guidelines were adopted, drug industry spending on physician marketing has increased roughly $7 billion. If the voluntary guidelines were mandatory and they were properly enforced, would that eliminate the problem?

Answer. The underlying purpose of the medical and pharmaceutical industry guidelines on gifts to physicians was to preempt any federal or state legislation. We therefore have no confidence that these codes will ever be enforced. We would suggest that the Senate Special Committee on Aging ask the industries to list all the enforcement actions they have taken under their codes to date.

RESPONSES OF REP. SHARON TREAT TO QUESTIONS FROM SENATOR KOHL

QUESTION 1: Do you believe the Maine data mining law will have a detrimental effect on the education of physicians regarding prescription drugs?

The Maine law restricting the use of physician prescribing data will not have an adverse effect on the education of physicians regarding prescription drugs. Using individualized prescriber data, drug manufacturers and their salespersons or "detailers" use sophisticated techniques including data mining to target their marketing efforts to specific subsets of doctors who are most likely to be receptive to their sales pitches. Research has shown that sales representatives using prescribing data in this manner are not the most effective way to provide evidence-based information to prescribers -- although they are extremely effective boosting the sales of particular drugs.

The data mining industry itself focuses on the financial payoff. "Research has shown that winning just one more prescription per week from each prescriber yields an annual gain of $52 million in sales."[1] Medical experts who have studied drug marketing techniques agree. Dr. Jerry Avorn and Dr. Aaron Kesselheim of Brigham and Women's Hospital and Harvard Medical School and School of Public Health assert in a statement submitted in support of Maine's datamining legislation that the evidence demonstrates that "commercial sources play a disproportionate role" in shaping physician's knowledge and prescribing decisions, and "[t]his influence is aimed primarily at increasing sales of the drugs being promoted, rather than at providing a balanced presentation of all the medical evidence." Avorn and Kesselheim report that "A substantial number of physicians consider interactions with detailers to be their most influential source of information, and detailers' importance is greatest among physicians who issue more prescriptions. In one study, 60% of physicians named commercial sources, such as detailers, as most influential in their first decision to prescribe a drug."

According to Avorn and Kesselheim, "Another study showed that meetings with pharmaceutical representatives were associated with changes in physician prescribing practices as well as requests by physicians to add the drugs to their hospitals' formularies. Contact with detailers was shown to be the most consistent predictor of physicians' early adoption of new pharmaceutical agents." Overall, many experts agree that there is a "strong, consistent, specific, and independent" association between physicians' behavior and their exposure to detailers.[2] Avorn and Kesselheim state:

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[1] "Datamining at IMS Health, How We Turned a Mountain of Data into a Few Information-Rich Molehills," by Paul Kallukaran & Jerry Kagan, IMS HEALTH Paper 127, Plymouth Meeting, PA

[2] Statement of Dr. Jerry Avorn and Dr. Aaron Kesselheim of Brigham and Women's Hospital and Harvard Medical School and School of Public Health submitted to the Maine Legislature's Joint Standing Committee on Health & Human Services in support of legislation regulating use of prescriber data for marketing purposes (LD 838 and LD 4, attached). Studies referenced in the Avorn/Kesselheim statement include: Dana J, Loewenstein G,. A social science perspective on gifts to physicians from industry. JAMA 2003;290:252-255; Williams PA, Cockerill R, Lowy FH., The physician as prescriber: relations between knowledge about prescription drugs, encounters with patients and the pharmaceutical industry, and prescription volume. Health & Canadian Soc'y 1995; 3:135-64; Peay MY & Peay ER., The role of commercial sources in adoption of new drug. Soc Sci Med 1988;26(12):1183-9; Berndt ER, Bui L, Reiley

> *"The studies we have cited indicate that more physician-specific detailing will lead to more prescriptions of brand-name agents, often with no additional patient benefit but at much higher cost to patients and to state-based insurance programs, which will continue to drive up the cost of health care in Maine. More patients will be exposed to the risks of heavily marketed pharmaceutical agents whose side effect profile is not fully evaluated, as well as to the risk that detailers may mislead physicians about the risk/benefit profile of particular agents by providing distorted or even incorrect information."*

As noted above, these practices have public health implications, because studies have shown that the information provided by detailers using data mining techniques is not always reliable or evidence-based. One study of detailers' promotional brochures found that 15% of the pamphlets presented data that differed from the published studies on which they were based. In another study, 11% of the statements made by pharmaceutical representatives about drugs were scientifically inaccurate, and physicians generally failed to recognize the inaccurate statements.[3] Detailers are also key promoters of off-label use of drugs, a consistent finding of the Prescrire sales reps monitoring network in France. This Network was created in 1991 at the initiative of a group of subscribers. For 15 years, members of the Network compared sales representatives' claims with the information contained in the summaries of product characteristics. Results were remarkably consistent over the years - sales reps highlight the efficacy of the drugs they present, often for unapproved as well as approved indications. In contrast, adverse effects are not mentioned in three-quarters of visits.[4]

Thus, alternative mechanisms such as academic detailing and conflict-free continuing medical education programs are preferred methods to educate doctors and other prescribers. Coincident with its adoption of restrictions on data mining, the Maine Legislature enacted legislation to establish an independent education program for prescribers to insure that conflict-free, evidence based information will be widely available in the state.[5] Further, effective physician education programs can access other data that is better suited to studying physician prescribing patterns as part of an education effort. This data includes Medicaid data as well as state-based data collection and analysis such as the Maine Health Data Organization. The Maine law exempts the use of prescriber-identifiable data from restrictions where it is used for true health research as opposed to research used for marketing purposes.

DR, Urban GL. Information, marketing, and pricing in the US antiulcer drug market. Amer Econ Rev 100 1995;85:100-5.

[3] See studies referenced in Avorn and Kesselheim statement.

[4] A review of the Network's findings "Don't expect sales representatives to help improve healthcare quality" can be found at: http://www.prescrire.org/aLaUne/dossierVMbilanEng.php

[5] See Maine LD 839, Public Law 327 (2007), "An Act To Establish a Prescription Drug Academic Detailing Program."

QUESTION 2: Will a national registry disclosing gifts and payments to physician be an important first step in eliminating conflicts of interest?

A properly constituted federal gift and payment registry would be an excellent first step in eliminating conflicts of interest. When I say "properly constituted" I mean a registry free of loopholes such as "trade secret" and confidentiality exemptions, that includes medical devices as well as drugs and biomedical treatments, that permits public access to information concerning which doctors were paid and how much, that insures that information can be accessed electronically, and that includes educational seminars, speaking bureaus and other honoraria. I also recommend that any legislation establishing such a registry also provide for analysis and a report such as currently compiled annually by the Vermont Attorney General. This analysis is an important component of an effective law because it provides the public a user-friendly way to understand the raw data. It is only from that public understanding that we can hope to see an actual reduction in the underlying conflicts, as patients ask their medical providers about conflicts that are reported.

QUESTION 3: If voluntary guidelines were mandatory and they were properly enforced, would that eliminate the problem?

The current voluntary guidelines are inadequate, and not only because they are unenforceable. They have been in place for several years and have failed to achieve much. The PhRMA code is riddled with broad language and exemptions that makes it toothless. There is no disclosure at all under the PhRMA code. It would ban free golf balls to physicians but allow consulting fees and speakers bureau payment of hundreds of thousands of dollars without disclosure. Finally, how can the public have faith in simply enforcing industry-drafted standards when the industry has such an abysmal record of voluntary compliance?

QUESTION 4: What role could the federal government play in reducing conflicts of interest in hospitals and universities?

The federal government could have a significant role limiting conflicts of interest in hospitals and universities. Adoption of policies voluntarily has been spotty at best. Through its Medicare and Medicaid programs, hospital accreditation, support of teaching medical centers, and the Veterans Administration, the federal government could establish baseline requirements such as banning certain practices as a prerequisite for being reimbursed by the federal government for medical services.

QUESTION 5: What obstacles did you face passing legislation and what advice do you have for other states developing similar laws?

The major obstacle to passing disclosure and gift ban legislation is the opposition from the organized medical profession, eg, medical associations. We can expect the pharmaceutical industry to be opposed, and of course the industry's resources are immense and effective. But if the medical community itself were to get on board with these policies, passage would be much more likely. The recent emergence of the National Physician's Alliance as a resource and advocate for doctors who are concerned about conflicts of interest is an encouraging

development, as is the advocacy of the medical students' association. Many doctors are very concerned about conflicts of interest, but their voice is not heard through the American Medical Association and many of its state affiliates. The other obstacle states face is lack of money to launch and sustain measures to counter these conflicts, for example funding to pay for an academic detailing program, or even for staff to analyze data collected in a gift and payment registry.

QUESTION 6: What is your response to the argument that limiting gifts will have a negative impact on the availability of continuing education programs and clinical research?

It may be that limiting gifts will reduce funding for continuing education. If so, that fact reveals that the CMEs receiving industry funding are more about marketing than evidence-based education, so I am not sure how much of a loss that would be. Certainly, there is a need for objective educational programs, and that may mean that the federal and state governments and the medical profession itself will need to step up their funding of these programs. With respect to clinical research, I see no valid reason for a link between gifts to doctors and the conduct of research. In fact, it would seem to be more likely to contaminate the design and results of studies, leading to the conclusion that limiting conflicts will improve such research.

Brigham and Women's Hospital

Division of Pharmacoepidemiology and Pharmacoeconomics
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March 26, 2007

Members of the Joint Standing Committee on Health & Human Services
Maine Legislature
100 State House Station
Augusta, ME 04333-0100

Dear Members:

Jerry Avorn, M.D., Chief of the Division of Pharmacoepidemiology and Pharmacoeconomics, and I would like to submit this statement in support of Representative Sharon Treat's recent bill, "An Act Protecting the Confidentiality of Prescription Information" (LD 838). It is important for physicians to learn about the risks and benefits of the drugs they prescribe. However, numerous studies have shown how promotion of drug products to physicians by pharmaceutical manufacturers can have important negative effects on public health. For example, such promotion may encourage use of newer, more expensive products where the side effects may not be fully understood, rather than adherence to evidence-based treatment guidelines. For the reasons explained in the attached statement, we feel that commercial sale of physician identified prescription data greatly supports the harmful aspects of pharmaceutical promotion at the expense of its possible educational value. We also describe how we have used physician-identified prescription data to promote positive patient outcomes and more efficient use of health care resources, and LD 838 will continue to allow drug safety researchers like ourselves to use such data for these purposes outside the commercial context.

Feel free to contact us with further questions.

Sincerely,

Aaron S. Kesselheim, M.D., J.D.

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Responses of Marjorie E. Powell, Senior Assistant General Counsel, PhRMA, to Senator Kohl from the June 27, 2007 Hearing

Question: How does PhRMA enforce its code of conduct and what evidence can PhRMA provide that all of our member companies have been following the guidelines?

Answer: PhRMA's Code on Interactions with Health Care Professionals ("the Code"), like the AMA Code and many other association codes, is voluntary. However, the 2002 update to the PhRMA Code, and the 2004 addition of Questions and Answers, were adopted by PhRMA's Board of Directors, senior leaders of our member companies, after full consideration of the concrete rules contained in the Code and Q&As and their application in particular situations. The Code also states explicitly that each PhRMA member company is strongly encouraged to adopt procedures to assure adherence to the Code, and we are confident that member companies have done so. In addition, other trade associations in the health care community, associations which include different operating units of many of the PhRMA member companies, have also adopted codes of interaction with their customers throughout the health care community. In each instance, the senior leadership of the member companies has considered, and committed the trade association and, by implication, its members, to the principles set forth in that code.

It is important to remember that, while PhRMA can establish a voluntary code, provide education about its code in a variety of settings, and encourage its application among all members of the health care community, other organizations fill different roles, and have different obligations, within the health care system. For example, the Office of the Inspector General of the Department of Health and Human Services has an obligation to investigate situations that might involve violations of the federal anti-kickback statute, 42 U.S.C. § 1320a-7b(b) (2003). The OIG has issued a Compliance Program Guidance for Pharmaceutical Manufacturers,[1] in which the OIG provides guidance about conduct that would, and would not, raise concerns about the relationships between pharmaceutical companies and health care professionals. Based on information contained in numerous public statements by member companies, presentations of lawyers who work with the pharmaceutical industry, and the OIG's publication of redacted requests for advisory opinions, PhRMA is confident in saying that pharmaceutical companies interacting with health care professionals in the United States about FDA-approved medicines have adopted compliance policies that would be consistent with the PhRMA Code and the Guidance provided by the OIG.

Indeed, as I said in both my written and oral testimony, the OIG indicated in its Compliance Program Guidance that the OIG viewed the PhRMA Code positively.

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[1] Department of Health and Human Services, Office of Inspector General. OIG Compliance Policy Guidance for Pharmaceutical Manufacturers. Fed. Reg. 2003; 68 (86):23731-43.

Answers to Senator Kohl from June 27, 2007,hearing
from Marjorie E. Powell
PhRMA

While the written testimony said that the OIG had endorsed the Code, as I tried to communicate in my oral testimony, I did not mean that the OIG had formally approved the PhRMA Code in any way or that the Code created a safe harbor. The testimony rather was intended to indicate that the OIG had viewed the Code favorably, and had referred to it in the OIG's Compliance Program Guidance for Pharmaceutical Manufacturers, indicating that the PhRMA Code was "practical and useful" and although the PhRMA Code will not protect a manufacturer as a matter of law under the anti-kickback statute, it will substantially reduce the risk of fraud and abuse and help demonstrate a good faith effort to comply with the applicable federal health program requirements." (emphasis added.)

The educational efforts by PhRMA, the American Medical Association and other medical groups, and the medical educators, as well as the guidance provided by the OIG Compliance Program Guidance have had an effect. According to a New England Journal of Medicine study published in 2004, since the PhRMA Code and other regulatory activities have been put in place, the pharmaceutical industry, among others, has "engaged in defining the boundaries of acceptable behavior."[2] The authors reached their conclusion because they found that, "The amount of regulatory, self-regulatory, and prosecutorial activity that is currently focused on conflicts of interest in the interactions between physicians and pharmaceutical companies is remarkable. Four years ago, this area was chiefly of interest to medical ethicists and others concerned about the threat posed to clinical decision making by the growing influence of drug companies. Today, professional organizations, the pharmaceutical industry, the Department of Health and Human Services, and a cadre of federal prosecutors are all actively engaged in defining the boundaries of acceptable behavior."[3] The authors affirmed the importance of the PhRMA Code when they say that, "Because the [PhRMA Code] is one of the most detailed statements available on acceptable practices in industry-physician relations, physicians and researchers should be aware of it."[4]

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[2] David M. Studdert, LL.B., Sc.D., M.P.H., Michelle M. Mello, J.D., Ph.D., M.Phil., and Troyen A. Brennan, M.D., J.D., M.P.H. , "Financial Conflicts of Interest in Physicians' Relationships with the Pharmaceutical Industry — Self-Regulation in the Shadow of Federal Prosecution," New England Journal of Medicine <http://content.nejm.org/cgi/content/full/351/18/1891>; 1898.
[3] Id. at 1899.
[4] Id. at 1899.

Answers to Senator Kohl from June 27, 2007,hearing
from Marjorie E. Powell
PhRMA

Question: Many academic medical centers have banned drug company reps and gifts on their campuses. If this practice is purely educational, why would medical schools prohibit it?

Answer: PhRMA does not have information about the underlying views or motivations of those academic medical centers that have taken these steps. However, in considering the effect of such policies, we believe it is important to consider the facts about prescribing patterns that were discussed in our testimony.

First, approximately 63% of all prescriptions used in the United States are generic.[5] This is one of the highest generic market shares of any developed country, clearly indicating that the regulated information conveyed through pharmaceutical company marketing of brand medicines is only one of many factors that physicians consider when making prescribing decisions.

Second, academic medical center bans on drug representatives do not ban all activities from outside the medical center that may have an impact on physicians' prescribing practices. For instance, health plans may strongly influence prescribing through formulary design and utilization management strategies, among other factors. As discussed in our testimony, research published in *Health Affairs* reports that one-third of physicians do not always discuss treatment options when those options would not be covered by the patient's insurer.[6] A physician survey by the Boston Consulting Group found that 14 percent of physicians reported that pharmaceutical representatives had a major impact on prescribing decisions, compared to 54 percent identifying formularies as having a major impact, 50 percent identifying peers and 47 percent identifying clinical guidelines.[7]

Third, bans on interactions between medical center staff and pharmaceutical company representatives do not offer a solution to sub-optimal patterns of using medicines that, if improved, would lead to better health outcomes and more efficient delivery of health care. For instance, a landmark RAND study published in the *New England Journal of Medicine* in 2003 reports underuse of medicines for 7 of 9 conditions studied (asthma, cerebrovascular disease, congestive heart failure, diabetes, hip fracture, hyperlipidemia and hypertension) and on 83 of the 103 indicators where the recommended treatment was prescription medicines or vaccines.[8] Likewise, a 2007 study published in *Health Affairs* estimates that if all

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[5] Generic Pharmaceutical Association, "Statistics," http://www.gphaonline.org/Content/NavigationMenu/AboutGenerics/Statistics/default.htm (Accessed 1 August, 2007).
[6] M. Wynia et al., "Do Physicians Not Offer Useful Services Because of Coverage Restrictions," *Health Affairs*, July/August 2003.
[7] 2002 BCG Proprietary Physician Survey, n=399.
[8] E. McGlynn et al., "The Quality of Health Care Delivered to Adults in the United States," *New England Journal of Medicine*, 2003. See also K. Gilberg et al., "Analysis of Medication Use Patterns: Apparent

patients with hypertension were treated to guideline, 89,000 premature deaths and 420,000 hospitalizations could be avoided annually—in addition to the 86,000 premature deaths and 833,000 hospitalizations for heart attack and stroke already avoided through use of antihypertensive medicines.[9]

Overuse of Antibiotics and Underuse of Prescription Drugs for Asthma, Depression, and CHF," *The Journal of Managed Care Pharmacy*, May/June 2003.

[9] D. Cutler et al., "The Value of Antihypertensive Drugs: A Perspective on Medical Innovation," *Health Affairs*, January/February 2007.

Answers to Senator Kohl from June 27, 2007,hearing
from Marjorie E. Powell
PhRMA

Question: In 2005, pharmaceutical manufacturers spent, in aggregate, $7.2 billion on pharmaceutical promotion. Specific questions about those expenditures are:

1. What activities are included in the $7.2 pharmaceutical promotion number? Drugs? Continuing medical educations?

Answer: According to IMS Health, the company that collects and publicly reports on pharmaceutical marketing and promotion spending, the $7.2 billion figure includes office promotion, which includes costs associated with sales activities of pharmaceutical representatives that are directed to office-based physicians; hospital promotion, which captures the costs associated with sales activities of pharmaceutical representatives that are directed to hospital-based physicians and directors of pharmacies; and journal advertising, which reflects advertising expenditures for prescription products appearing in medical journals. IMS does not collect data on spending for continuing medical education.

2. Could you provide a consistent series of expenditures on pharmaceutical promotion over the past ten years?

Answer: PhRMA does not collect data from its members on pharmaceutical promotion. Data on promotion spending are publicly available from IMS Health, dating back to 1996. Below we provide professional promotion figures using the publicly reported IMS data drawn from the attached tables. For consistency, we exclude the value of free samples from 1996 to 2001, as during this time period IMS included the value of samples in pharmaceutical promotion spending but did not do so from 2002 on. The publicly available IMS data can be accessed at http://imshealth.com/ims/portal/front/articleC/0,2777,6599_80402580_81493254,00.html (this shows the newer data, but 1996-2001 is no longer available online); or in the attached screen captures which show the original IMS tables.

Answers to Senator Kohl from June 27, 2007,hearing
from Marjorie E. Powell
PhRMA

Year	Professional Promotion Spending in millions (excluding value of free samples and DTC)
1996	$3,469
1997	$3,875
1998	$4,555
1999	$4,790
2000	$5,287
2001	$5,916
2002	$6,637
2003	$7,383
2004	$7,835
2005	$7,206
2006	$7,203

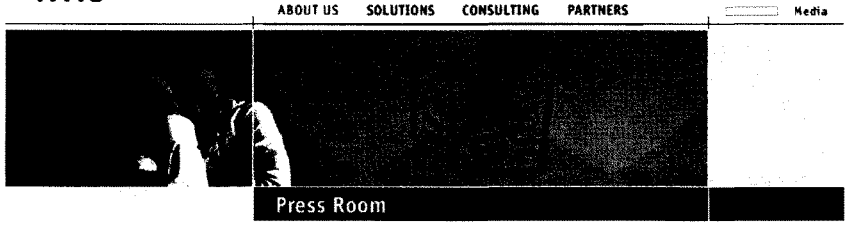
3. Can you break down those figures for each of your member companies?

Answer: PhRMA does not collect data from its members on pharmaceutical promotion. The publicly reported IMS Health data series referenced above is shown only at the industry level and does not include company-specific spending.

Attachments
IMS Health screen capture

ims

ABOUT US SOLUTIONS CONSULTING PARTNERS Media



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Total U.S. Promotional Spend by Type

Promo Spend Type	1996	1997	1998	1999	2000	2001	2002
Total Professional Spend $	8,373	9,922	11,157	12,020	13,241	16,380	18,546
Direct-to-Consumer (DTC) $	791	1,069	1,317	1,848	2,467	2,679	2,638
Total Promo	**$9,164**	**$10,991**	**$12,474**	**$13,868**	**$15,708**	**$19,059**	**$21,184**

Total U.S. Professional Promotional Spend by Type

Professional Promo Spend Type	1996	1997	1998	1999	2000	2001	2002
Office Promo	2,458	2,785	3,386	3,607	4,038	4,789	5,327
Hospital Promo	552	579	671	713	765	702	873
Journal Advertising	459	510	498	470	484	425	437
Retail Value of Samples	4,904	6,047	6,602	7,230	7,954	10,464	11,909
Total Professional Spend $	**$8,373**	**$9,922**	**$11,157**	**$12,020**	**$13,241**	**$16,380**	**$18,5**

The sampling figure represents, in millions, the retail value of the product sampling activities of pharmaceutical representatives that are directed to office-based physicians, as reported by members of their front office staff. DTC promotion represents the expenditures for direct-to-consumer pharmaceutical advertising for prescription products on television, magazines and newspapers, on radio and outdoors. Office promotion includes costs associated with sales activities of pharmaceutical representatives that are directed to office-based physicians. Hospital promotion captures the costs associated with sales activities of

pharmaceutical representatives that are directed to hospital-based physicians and directors of pharmacies. Journal advertising reflects advertising expenditures for prescription products appearing in medical journals.

Source: IMS Health, Integrated Promotional Services™ and CMR, 3/2003

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Total U.S. Promotional Spend by Type, 2006

(US $ Millions)	2002	2003	2004	2005	2006
Professional Promotion	6,633	7,383	7,835	7,206	7,203
Consumer Promotion	2,651	3,279	4,026	4,240	4,803
Promotion (total)	**$9,284**	**$10,662**	**$11,861**	**$11,446**	**$12,006**

	2002	2003	2004	2005	2006
Professional Journal Advertising	437	448	499	429	463
Sales Rep Details	6,196	6,936	7,336	6,778	6,740
Professional Promotion (total)	**$6,633**	**$7,384**	**$7,835**	**$7,207**	**$7,203**

	2002	2003	2004	2005	2006
DTC Advertising	2,651	3,279	4,026	4,240	4,803
Consumer Promotion (total)	**$2,651**	**$3,279**	**$4,026**	**$4,240**	**$4,803**

Journal Promotional Dollars includes:
Journal advertising reflects advertising expenditures for prescription products appearing in medical journals.

Contact Promotional Dollars includes:
Office/hospital promotion, which include costs associated with the sales activities of pharmaceutical representatives that are directed to office-based physicians, hospital-based physicians, and directors of pharmacies.

DTC Promotion includes:
DTC promotion represents the expenditures for direct-to-consumer pharmaceutical advertising for prescription products on television, radio, magazines and newspapers, as well as outdoor advertising. Professional promotion includes office and hospital promotion as well as journal advertising. Office promotion includes costs associated with sales activities of pharmaceutical representatives that are directed to office-based physicians. Hospital promotion captures the costs associated with sales activities of pharmaceutical representatives that are directed to hospital-based physicians and directors of pharmacies. Journal advertising reflects advertising expenditures for prescription products appearing in medical journals. Joint-ventures are assigned to product owner.

STATEMENT FOR THE RECORD
OF THE
AMERICAN COLLEGE OF PHYSICIANS
TO THE
SENATE SPECIAL COMMITTEE ON AGING
ON THE HEARING
PAID TO PRESCRIBE?: EXPLORING THE RELATIONSHIP
BETWEEN DRUG COMPANIES AND DOCTORS
JUNE 27, 2007

Thank you for the opportunity to submit written testimony on the important issue of physician-industry relations. The American College of Physicians (ACP) represents 124,000 internal medicine physicians and medical students, and is the largest medical specialty society and second largest medical organization in the United States. Our mission is to work on behalf of patients and their physicians to enhance the quality and effectiveness of health care by fostering excellence and professionalism in the practice of medicine.

The College commends the Special Committee on Aging for holding this hearing. Hardly a week goes by without a feature article in a major newspaper shining the spotlight on interactions between doctors and the pharmaceutical industry in clinical or research settings, or regarding continuing medical education or the publication of medical research. The American College of Physicians continues to evaluate relationships between physicians and industry and physician organizations and industry and to work to emphasize relationships that maximize the interests of the patient.

Physicians and the pharmaceutical industry share a mutual interest in advancing medical knowledge. But the primary goal and responsibility of the physician is to promote the patient's health, welfare and best interests.[1, 2] Partnerships between physicians and industry can lead to medical advances and improved care of our patients, but they can also create opportunities for conflicts of interest, bias and the appearance—or reality—of impropriety. While many physicians and physicians-in-training may think they are immune to commercial influence on prescribing, studies show that accepting industry hospitality and gifts can compromise judgment about medical information and subsequent decisions about patient care.

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[1] American College of Physicians Ethics Manual, 5th ed. Ann Intern Med. 2005;142:560-582.

[2] ABIM Foundation, ACP-ASIM Foundation, European Federation of Internal Medicine. Medical professionalism in the new millennium: A physician charter. Ann Intern Med. 2002;136:243-246.

ACP Positions on Physician-Industry Relations

In 1989-90, the College was the first medical society to develop and publish guidance to address ethical issues in relationships between the pharmaceutical industry and the medical profession.[3] That position paper was updated in 2002 and split into two papers—one addressing individual physicians[4] and one, physician organizations.[5] This year, the College approved a revision to position #1 on gifts of our position paper for individual physicians.[6] The revision was developed by the ACP Ethics, Professionalism and Human Rights Committee to clarify and strengthen the statement.

The revised position is:

Position 1: Industry Gifts, Hospitality, Services and Subsidies

The acceptance by a physician of gifts, hospitality, trips, and subsidies of all types from the health care industry that might diminish, or appear to others to diminish the objectivity of professional judgment, is strongly discouraged. As documented by some studies, the acceptance of even small gifts can affect clinical judgment and heighten the perception and/or reality of a conflict of interest. Accordingly, physicians need to gauge regularly whether any gift relationship is ethically appropriate and evaluate any potential for influence on clinical judgment.

- *In making such evaluations, it is recommended that physicians consider such questions as: "What would the public or my patients think of this arrangement?"; "What is the purpose of the industry offer?"; "What would my colleagues think about this arrangement?"; and "What would I think if my own physician accepted this offer?"*
- *In all instances, it is the individual responsibility of each physician to assess any potential relationship with industry to assure that it enhances patient care and medical knowledge and does not compromise clinical judgment.*[6]

In testimony by Peter Lurie, MD, MPH, Deputy Director of Public Citizen's Health Research Group at your June 27, 2007 hearing, the questions in the text above were

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[3] Goldfinger SE for the American College of Physicians Ethics Committee. Physicians and the pharmaceutical industry. Ann Intern Med. 1990;112:624-6.

[4] Coyle SL for the American College of Physicians-American Society of Internal Medicine Ethics and Human Rights Committee. Physician-industry relations. Part 1: individual physicians. Ann Intern Med. 2002;136:396-402.

[5] Coyle SL for the American College of Physicians-American Society of Internal Medicine Ethics and Human Rights Committee. Physician-industry relations. Part 2: organizational issues. Ann Intern Med. 2002;136:403-6.

[6] Turton FE, Snyder L for the American College of Physicians Ethics, Professionalism and Human Rights Committee. Letter to the editor, physician-industry relations. Ann Intern Med. 2007; 146: 469.

highlighted as potential theoretical underpinnings for disclosure laws. Dr. Lurie said, "Payment disclosure laws in effect put these theoretical questions to the test." The College's positions are intended solely as guidelines for physicians to continually evaluate their relationships with industry, and as such, ACP has not taken a position on enacting legislation to require that physicians disclose such relationships. Policies that may be appropriate and necessary for physicians to evaluate their own relationships are not necessarily applicable to legislative mandates. Indeed, ethical guidelines and policies can be an effective way of achieving desired changes in relationships between physicians and industry without requiring federal or state legislation.

The additional positions from the two papers published in 2002 are:
Position 2
Physicians who have financial relationships with industry, whether as researchers, speakers, consultants, investors, owners, partners, employees, or otherwise, must not in any way compromise their objective clinical judgment or the best interests of patients or research subjects. Physicians must disclose their financial interest in any medical facilities or office-based research to which they refer or recruit patients.[4]

Position 3
Public and private GME and CME providers that accept industry support for educational programs should be aware of potential conflicts of interest and should develop and enforce explicit policies that maintain complete control of program planning, content, and delivery.[5]

Position 4
Medical professional societies that accept industry support or other external funding should be aware of potential bias and conflicts of interest and should develop and enforce explicit policies that preserve the independent judgment and professionalism of their members and maintain the ethical standards and credibility of the society.[5]

The section on conflicts of interest in the ACP Ethics Manual reinforces these positions.[1] Clearly, as all of these positions illustrate, a bright line between the patient's interests and other interests, and between education on the one hand, and marketing/promotion on the other, must be maintained. Toward these goals, we would encourage exploration of other approaches to enhancing quality care and maintaining professionalism that emphasize data-based approaches to drug review and interactions based on that information.

Conclusion
Physicians must critically evaluate all medical information and its source in putting the interests and welfare of their patients first. The ACP commends the Special Committee on Aging for examining, on behalf of patients, issues arising from interactions between the pharmaceutical industry and physicians. We appreciate the opportunity to offer comments. If you have any questions regarding our comments, or on ACP policy in this area, please do not hesitate to contact Lois Snyder, Director, ACP Center for Ethics and

Professionalism (215/315-2835) or Patrick Hope, Legislative Counsel (202/261-4541). We look forward to working with you in the future.

Submitted July 10, 2007

For More ACP Information
ACP policy on industry relations: http://www.acponline.org/ethics/phys_inds.htm
ACP Ethics Manual statement on financial conflicts of interest, including a brief discussion of industry relations:
http://www.acponline.org/ethics/ethicman5th.htm#conflict .

Testimony of Anthony Fleg,
American Medical Student Association
National Coordinator on Pharmaceutical Policy, Committee on Medical Education
UNC-Chapel Hill Medical Student

Bad Medicine: The harmful effects of pharmaceutical industry-physician interactions to patients, physicians, and the U.S. healthcare system

U.S. Senate Special Committee on Aging

June 27th, 2007

Chairman Kohl, Senator Smith, and members of the Committee:

It is with great pleasure that we come before this esteemed body on the issue of physician-pharmaceutical interactions. I represent the future physicians of the American Medical Student Association (AMSA), the largest medical student organization in the U.S. and the first professional organization in the U.S. to disavow itself from drug companies as a funding source (quote the Appendix). Within AMSA, I am the National Coordinator for the Pharm-Free campaign, whose work revolves around changing the culture of medical education in order to create a new generation of physicians who are Pharm-Free (see appendices 2 and 3). In essence, this work involves three R's:

(1) Reclaiming the ethics of medicine
(2) Removing the conflicts of interest, and
(3) Restoring the sanctity of the patient-provider relationship

Unfortunately, today, medicine is practiced in a climate that is far from the Hippocratic ethics our profession is based upon. We seek the three R's as a way to return to what is right for our patients, ourselves, and the U.S. healthcare system. Pharm-Free, a campaign within AMSA initiated in 2001, is a critical component to this endeavor, as much of what needs to be reclaimed, removed, and restored is found in the single issue of physician-industry relationships.

Moreover, I feel compelled to express, before this Committee, that the current practices are simply "bad medicine". On one hand, medical students are taught to practice evidence based medicine, using objective data to make informed clinical decisions, with a purpose of protecting patients and eliminating un-needed costs.

Meanwhile, medical students like me across the country are offered promotional sales pitches and gifts from pharmaceutical companies, often under the guise of "education" by our schools and mentor physicians. The implications of the latter reach far further than the conscience of medical students, with patients, physicians, and healthcare system of the United States paying for the unchecked, unrestricted influence of pharmaceutical companies in medicine today (See Table 1).

As our nation turns to proposals to fix a healthcare system that we all know is sick and in need of treatment, it is essential that we address the "bad medicine" seen in the current physician-pharmaceutical relationship. We must re-capture the 3 R's and truly practice what we preach: evidence-based-medicine.

Figure 1: Unrestricted Physician-industry relationships: modes of advertisement and effects at three levels

PATIENTS

Modes of advertisement:

Direct-to-consumer advertising, advertising in the clinic

Effects on patients:

1) Increased, unnecessary use of medications
2) Increased, unnecessary use of higher cost medications
3) Increased risk for side effects due to (1) and (2)
4) Decreased time spent with physician
5) Decreased patient-physician relationship

PHYSICIANS

Modes of advertisement:

Lunches, seminars, conferences, continuing medical education, promotional cabinets, ads in medical journals

Effects on physicians:

1) "Dual loyalties" that interfere with patient-physician relationship
2) Medical professionalism is compromised
3) Inability to practice evidence based medicine

U.S. HEALTHCARE SYSTEM

Modes of advertisement: lobbying to lawmakers, professional organizations

Effects on the U.S. healthcare system

1) High, ever-increasing, and un-necessary cost of prescription drugs

2)	Numerous opportunity costs, as funds are shifted to pay for prescriptions medications
3)	Access to care jeopardized
4)	Increased health disparities

Before elaborating on the effects listed above, I will cite examples of the unrestricted nature of physician-industry relationships from the current culture of medicine. We will briefly look at the realms of medical education, academic medical centers, and private practices to illustrate this point.

Medical Education

- A JAMA article in 2005 showed that medical students are heavily targeted to receive promotional items, averaging one gift per week per medical student[1]. Interestingly, the primary forces encouraging this behavior were residents and attending physicians: 93% of students said they had been asked or required to attend at least one pharmaceutical company-sponsored lunch by a physician responsible for their education.
- Meanwhile, until very recently, amidst growing public concern over the ties between drug company salespeople and physicians, no medical school in the United States had a school-wide policy restricting or banning pharmaceutical representatives from the medical centers and clinics where students are trained. The vast majority also have no curriculum teaching medical students about the ethical and professional issues that arise when physicians interact with drug reps. These two realities are in stark contrast with the conclusions of the aforementioned study by Sierles et al:

  > Student experiences and attitudes suggest that as a group they are at risk for unrecognized influence by marketing efforts. Research should focus on evaluating methods to limit these experiences and affect the development of students' attitudes to ensure that physicians' decisions are based solely on helping each patient achieve the greatest possible benefit[2].

- Using an objective grading criteria employed by AMSA's recently released Pharm-Free Scorecard (see appendix 2); only 5 of the more than 125 medical schools received an "A". ("A" grades were

[1] Sierles, Broadkey, Cleary et al. Medical students' exposure to and attitudes about drug company interactions: a national survey. JAMA. 2005 Sep 7;294(9):1034-42.
[2] Ibid., p. 1040.

awarded for a "Comprehensive policy that restricts pharmaceutical representatives' access to both the medical school campus and the Academic Medical Center.")

- Grants, fellowships, and awards offered to medical students continue to have drug company sponsorships. As a personal example, I have ethical issues on whether or not to submit a proposal for a local conference in the fall of 2007 on "sustainable community development" or to apply for a community service award for my work in American Indian communities, as both are advertised and titled with a drug company's name. Regarding the former, my university is a co-sponsor[3]; more egregiously, the latter award is offered through the Association of American of Medical Colleges, an entity that should set a standard for eliminating conflicts of interest[4].

Academic Medical Centers (AMCs)

- Until recently, coinciding with the aforementioned medical school policies, there were no AMCs that banned drug companies and their salespeople from their premises. The lack of policies to eliminate conflicts of interest is critically important when considering that AMCs are an important source of medical knowledge and practice guidelines. At AMCs the majority of medical studies and clinical trials are performed, while the "thought leaders" of medicine, those who hold great clout regarding clinical guidelines for their respective fields are also found at AMCs. Thus, whereas meetings with pharmaceutical salespeople has been linked to smaller-scale changes (e.g. increased physician requests for adding drugs to hospital formularies[5]) we can only imagine the potential effects for physicians with these same relationships, in leadership positions, at flagship institutions, to create industry-friendly policies and guidelines for the U.S. healthcare system.
- A 2006 JAMA article called on academic medical centers to "take the lead in eliminating the conflicts of interest" involved in accepting gifts from the health care industry[6]. The article, which merely reveals the "why" and "how" of moving toward less-biased, more evidence-based, medicine, sparked a national conversation on the issue, revealing the current culture of unrestricted interactions between AMCs and industry.
- AMCs invent/develop the majority of the molecules and pathways that are then turned into incredibly profitable drugs. The ethical issue here is that this

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[3] 2007 Sustainable Development Conference. Accessed 7/1/07 at http://www.sph.unc.edu/ogh/2007_sustainable_development_conference_4729_4221.html.
[4] AAMC. Accessed 6/2907 at http://www.aamc.org/about/awards/cfc.htm.
[5] Wanzana, A. Is a gift ever just a gift? JAMA. 2000;283:373-380.
[6] Brennan TA, Rothman DG, Blank L et al. Health industry practices that create conflicts of interest: a policy proposal for academic medical centers. JAMA. 2006 Jan 25;295(4):429-33.

initial research is done largely with public funds, often from the National Institutes of Health (NIH). Therefore, AMCs have begun to profit off of selling compounds and molecules to industry, hoping to make both parties profits off of public-funded bench/lab research.

Private practices

- The majority of private practices continue to invite drug company salespeople into the clinics to give lunches, "educate" clinicians about their products, and leave promotional items that range from drug samples to clocks, and pens to posters, despite the fact that research consistently shows the effect of such modes of advertisement on physician prescribing behavior (e.g. away from evidence-based-medicine). A literature review of these studies, looking at the realms of industry sponsored trials, CME, and pharmaceutical salespeople revealed that "all three types of interactions affect physicians' prescribing behavior and, in the case of obtaining information from detailers, physicians' prescribing practices are less appropriate as a result of the interaction[7].
- Shahram Ahari, a researcher at UCSF and former drug rep, describes the tactics used by drug reps to manipulate physicians to change their prescribing habits. "It's my job to figure out what a physician's price is…for some it is dinner at the finest restaurants…for others it is my attention and friendship." He also points out that the recently adopted Pharmaceutical Research and Manufacturers of America Code for Gifts has many loopholes, the biggest of which are "unrestricted educational grants" and the fact that it is a self-regulated, self-enforced code[8].
- Even for those interested in not interacting with industry, the AMA sells the Physician Master File to information companies, who then link this with pharmacy data and sell it to pharmaceutical companies. The pharmaceutical companies then use the information to help direct their sales pitches to doctors. It was only in 2006, amidst physician concern over this practice, that the AMA allow for an "opt out" clause, where physicians could remove their names from this list.
- Further hindering access to unbiased sources of information, medical journals may have 20 or more ads for drugs, while more than half of the continuing medical education (CME) courses for U.S. physicians are funded by drug companies,[9] despite the fact that attending sponsored CME courses has a direct influence on physicians' prescribing habits[10]. .

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[7] Lexchin J. Interactions between physicians and the pharmaceutical industry: what does the literature say? CMAJ. 1993 Nov 15;149(10):1401-7

[8] Fugh-Berman A, Ahari S. Following the script: how drug reps make friends and influence doctors. 2007. *PLoS Med* 4(4): e150

[9] Angell, M. The truth about drug companies: how they deceive us and what to do about it. 2004. Random House.

[10] Wanzana, p. 373.

Having given examples of the unrestricted access that industry has to medical education, AMCs and private practices, we will now consider the effects that drug company-physician interactions have at the level of patients, the level of physicians, and at the larger U.S. healthcare system level. To do so, I would like to use an approach medical schools are fond of: a case study.

Mrs. Smith, a 35 year old woman, comes to the primary care clinic complaining of "a burning down in my throat, especially at night and after eating spicy foods." Her doctor, Dr. Jones has had recent lunches sponsored by AstraZeneca, the makers of Nexium and Prilosec. As the doctor enters the patient's room, she immediately asks about "the purple pill" she has seen advertised on television.

How does unrestricted physician-industry interactions affect the patient?

First, we might consider the ways in which this patient will pay more for her health and healthcare. Because of the ubiquitous nature of direct-to-consumer (DTC) advertising, she may be more likely to visit the doctor in the first place. DTC, permitted only in the U.S. and New Zealand has promotes a culture of the "worried well" in the U.S., making Mrs. Smith more likely to visit the doctor. In addition, once at the clinic, Mrs. Smith is more likely to ask for the brand-name pill she has just seen advertised, in this case Nexium. Because she asks for the purple pill, she is more likely to walk out of the office with a prescription for a medicine that she may not need and a medicine for which there may be a cheaper alternative.

Finally, because the doctor has recently been "educated" on the benefits of AstraZeneca's drugs for reflux disease, he/she is more likely to prescribe a medicine (versus trying non-medical therapy, including lifestyle changes), and to prescribe one that is a "brand name" drug as opposed to a generic. A fourth factor affecting the physician's decision and patient's wallet, is the 2001 marketing campaign by AstraZeneca to convince physicians that Nexium was superior to Prilosec despite the fact that they have the same active ingredient. This occurred as Prilosec was coming off patent, with the

convenient introduction of Nexium, a drug that costs up to ten times more than Prilosec, but which has no data to back its superiority to its older counterpart.

As a net effect of the physician's and patient's influence, the patient may very well spend more on treatment than she would have in the absence of the pharmaceutical milieu surrounding this case. Sources of increased costs include the visit itself, the patient's and physician's bias toward using medicine, and the physician's bias toward using more expensive medicines.

Second, Mrs. Smith may also pay in the currency of side effects, should she take unnecessary prescription medicines. Nexium and Prilosec have side effects that include abdominal pain, drug-drug interactions._____.

Third, Mrs. Smith may also see the effects of the drug industry's sales reps in the patient-doctor relationship she values with Dr. Jones, through a decreased amount of time spent with the doctor and the "dual loyalties" he is pursuing. Regarding the former, since this clinic is heavily profitable, there are many drug reps making visits on a given day, thus taking the time of doctors when they would otherwise be seeing patients. In my personal experience, there is a range here, with some physicians taking up to an hour of clinic time to talk with drug representatives throughout the day; not surprisingly, these same physicians were the ones most rushed in their patient encounters. Regarding the latter, if Mrs. Smith is one of the 70% of patients that believe that gifts from pharmaceutical companies to physicians affect their prescribing behavior[11], but not one of the minority (27%)[12] of the patients that believe that their doctor takes industry gifts, she is likely to be misled during this clinic visit, as doctors rarely reveal their gift-taking and lunch-eating practices to their patients.

How do unrestricted physician-industry interactions affect the physician?

First, Dr. Jones is inevitably faced with "dual loyalties" that will compromise his ability to do what is best for Mrs. Smith. On one hand, he wants to honor the sacred nature of the doctor-physician relationship, pursuing what is best for her. At the same time, he is consciously and subconsciously influenced by the pharmaceutical reps

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[11] Blake RL, Early EK. Patients' attitudes about gifts to physicians from pharmaceutical companies. J Am Board Fam Pract. 1995 Nov-Dec;8(6):457-64.

[12] Gibbons RV et al. **A Comparison of Physicians' and Patients' Attitudes Toward Pharmaceutical Industry Gifts. J Gen Int Med. 1998;**13 (3), 151-154.

he has recently met with, usually in a direction toward prescribing more medicines, especially those higher priced medicines. He is more likely to prescribe "the purple pill" (Nexium) over Prilosec, having just received "free" samples of Nexium along with a convincing sales-pitch for the drug. The loyalty he feels toward AstraZeneca may be in direct conflict with Mrs. Smith's health and wallet, resulting in cognitive dissonance that Dr. Jones will likely dispel by the common notion amongst physicians that "I am not influenced by the promotional attempts of the drug companies." (Interestingly, a study that looked at physicians' attitudes found that 61% felt they were not influenced by pharmaceutical gifts, while only 16% felt that other physicians were similarly "immune" to being influenced[13]) Bottom line: Dr. Jones' interactions with industry compromise his ability to act in the interest of Mrs. Smith, resulting in a scar to their patient-physician relationship.

Second, in addition to hindrances to honoring the patient-physician relationship, Dr. Jones will have difficulty in honoring the ethics and edicts of medicine, often termed *medical professionalism*. Hippocrates, one of the grandfathers of medical ethics, states in the Hippocratic Oath that, "In every house where I come I will enter only for the good of my patients, keeping myself far from all intentional ill-doing and all seduction." Thus, the very core of being a medical professional, grounded in values that are a large reason for the status and respect physicians receive, is jeopardized by Dr. Jones because of the close ties to industry that he and the medical organizations he belongs to maintain.

Finally, the ability of Dr. Jones to practice evidence based medicine, the gold-standard for quality medical care, is severely hampered. The pharmaceutical salespersons who he relies on to "keep up-to-date on the new medicines" will provide evidence and sales tactics to sell their product, not to provide him objective education. In essence, it will be nearly impossible for him to cater to industry and simultaneously make clinical decisions not influenced by that industry. (It is worth noting that the peer-reviewed medical literature that Dr. Jones reads as another way to keep abreast on medical knowledge, along with the CME courses he attends, increasingly involve pharmaceutical sponsored researchers and speakers, making it that much harder for him to practice evidence-based-medicine.)

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[13] Steinman MA. et al. Of principles and pens : Attitudes and practices of medicine house staff toward pharmaceutical industry promotions. 2001; 110(7): 551-557

How do unrestricted physician-industry interactions affect the U.S. healthcare system?

While we have considered the harmful effects of drug companies on patients, physicians, and the relationship between the two, we have not dealt with the, larger effects on the U.S. healthcare system.

Using this example, let us look at the financial costs of the marketing campaigns employed by AstraZeneca to doctors, and to a lesser extent, patients. AstraZeneca, facing the expiration of its patent on Prilosec, a drug that earned the company $6 billion annually, created Nexium. The truth is that the two drugs have the same active ingredient, and accordingly, are equally effective. However, AstraZeneca launched a huge advertising campaign in 2001 to convince doctors and patients that Nexium was superior to Prilosec, successfully converting the majority of patients to the "purple pill," at a price tag up to 10 times higher for the same medication. Thus, the U.S. healthcare system pays billions of dollars annually for patients like Mrs. Smith to have the "purple pill," despite the fact that a cheaper, less advertised version is available.

We will look at three of the many consequences of increased spending on name-brand drugs like Nexium: cuts in other health programs, and decreased numbers of insured Americans, and potential for increasing health disparities. In terms of opportunity costs, the ever-increasing amount spent of prescription drugs diminishes what is left to spend on other health programs. As the U.S. population increasingly ages, with more elderly persons on more medications, drug costs will continue to tap the healthcare system's resources. As a rule, preventive and health-promoting programs (e.g. enhanced emphasis on teaching doctors and patients ways to address reflux disease through behavioral change) will go under-funded in order to pay for more, and higher priced medicines.

A second consequence of the "Nexiums" of the market is that private health insurance becomes more expensive, to the point that it is either unaffordable (for out-of-pocket buyers) or dropped as a benefit (for those relying on their job for health insurance); indeed, rising prescription drug costs are directly related to the millions of uninsured Americans and the ever-decreasing numbers of employers able to purchase health insurance for their employees. The Nexium/Prilosec story, therefore, influences the healthcare system in ways that reach far beyond those with acid reflux, taking resources from other health programs and serving to make access to healthcare more difficult through harder to afford health insurance.

Third, the practice of industry-friendly medicine undermines much of the current work being done to reverse health disparities. As medicines become more expensive, those with lower paying jobs, more financial insecurity, and less financial or health literacy will be disproportionately affected. Some in this vulnerable group will even see their prospects for health paradoxically worsen through seeking medications, sinking further into debt, and even into bankruptcy (medical debt being the #1 cause of personal bankruptcy in the U.S.). Though the pharmaceutical industry insists that its programs will cover the costs for indigent patients, this assistance is temporary, often hard-to-obtain, and can be altered or terminated at any moment. Therefore, for the *Mrs. Smiths* in the U.S. without financial security and who are not in the minority of patients able to receive free medicines, the current climate puts their health at risk.

The real trouble is that there are countless examples that run the same theme as the "purple pill" story, all with a common storyline –pharmaceutical companies un-satiable drive for profits. Dr. Angell, former New England Journal of Medicine editor, states,

> Americans now spend a staggering $200 billion a year on prescription drugs, and that figure is growing at a rate of about 12 percent a year (down from a high of 18 percent in 1999). Drugs are the fastest-growing part of the health care bill—which itself is rising at an alarming rate. The increase in drug spending reflects, in almost equal parts, the facts that people are taking a lot more drugs than they used to, that those drugs are more likely to be expensive new ones instead of older, cheaper ones, and that the prices of the most heavily prescribed drugs are routinely jacked up, sometimes several times a year[14].

Therefore, Mrs. Smith and Dr. Jones are not the only ones who will feel the consequences of AstraZeneca's sales strategies, as the effects of the unrestricted influence of pharmaceutical companies make for "bad medicine" for every citizen that relies on the U.S. healthcare system. Moreover, we cannot expect to improve the larger healthcare system, whether it is to insure the uninsured or reduce health disparities, until we address the problem of physician-industry relationships.

CONCLUSION

Therefore, esteemed members of Congress, I am convinced that our current practice of unrestricted industry-physician relationships is "bad medicine" for patients, doctors, and our country's healthcare system. We all have a responsibility to make changes to curtail the current practices, including physicians, medical students, physician organizations, pharmaceutical companies, and policymakers. In our Pharm-Free campaign at AMSA, we have begun to work on solutions to the reliance on pharmaceutical funding, finding innovative ways to

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[14] Angell, Ibid.

raise money for programming, partnering with the Medical Letter (a source for information on prescription drugs that has no ties to the pharmaceutical industry), using student activism to push for changes in medical education and in our AMCs, and getting the doctors of tomorrow to commit to being Pharm-Free.

I am hopeful that this testimony inspires this Committee to make similar changes within you power to find cures for the "bad medicine" currently practiced. More specifically, policymakers have great opportunity for creating change through your power to regulate a largely unregulated industry. Price controls on medicines, stricter rules on the products of research from NIH funds, and bans on practices like direct-to-consumer advertising and "data mining" of physicians' prescribing information are all examples of steps that Congress can take to treat this condition. I ask this with a very simple vision: that I will practice medicine in an environment that is patient-centered, not pharmaceutical-centered, for the good of my patients, myself, and this country.

Appendix 1: Pharm-Free Scorecard

AMSA's 2007 Pharm-Free Scorecard

A ranking of U.S. medical schools' policies on pharmaceutical company access and influence

A Note about AMSA's Pharm-Free Scorecard

The American Medical Student Association (AMSA) and its 68,000 members believe in providing the highest quality care through evidence-based medicine. The aim of AMSA's Pharm-Free campaign is to remove the influence of pharmaceutical companies from the practice of medicine.

As the next generation of physicians, we consider it our responsibility to educate our fellow medical students about the steps their schools have taken, or too often not taken, to limit the access and influence of pharmaceutical companies and their representatives. The result of our efforts is this scorecard.

The **AMSA 2007 Pharm-Free Scorecard** is a new metric for students to use when choosing a medical school. An institution's Pharm-Free policies are indicative of the ethical, professional and practical foundation in medical education it can offer. As you will note, many of America's institutions are failing in their duty to put into place the mechanisms that separate those who would influence practice for the sake of profit and those whose practical concern is for the patient.

AMSA envisions a day when pharmaceutical companies are able to dedicate their resources to creating drugs that physicians choose to use because they are effective in treating disease, not because they are effectively marketed. We envision a day when every medical student and physician is aware of the professional, ethical and practical complications of the current relationship with pharmaceutical company representatives. We envision a day when physicians demand integrity, honesty, and education (not biased information) from members of their profession, for the sake of our patients and their trust in us.

Jay Bhatt	Justin Sanders	Anthony Fleg
National President 2006-2007	*AMSA Pharm-Free Coordinator 2006-2007*	*AMSA Pharm-Free Coordinator 2007-2008*

AMSA's 2007 Pharm-Free Scorecard Grading System

A	Comprehensive policy that restricts pharmaceutical representatives' access to both the medical school campus and the Academic Medical Center (AMC)
B	Limited policy that sets guidelines for the AMC, but makes little or no mention of the medical school and/or medical students
C+	No formal policy, but pharmaceutical representatives are not allowed to interact with students according to the administration
C	School is in the process of drafting a policy
C-	School is discussing the formation of a policy, and/or students and the faculty are receiving some education regarding industry interactions
D	

	No policy, but there have been discussions about creating a policy
F	No policy, no discussion or school has decided not to form a policy Students encouraged to interact with industry representatives

Summary of Findings

- **12** schools currently have pharmaceutical influence policies in place.
  Of those:
  - 5 schools received an A grade, 4 schools received a B grade, 1 received a D grade and 2 did not respond.
- Of all U.S. medical schools*:
  - **5** schools received a grade of **A**: Stanford University School of Medicine, UC-Davis School of Medicine, University of Michigan Medical School, University of Pennsylvania School of Medicine and Yale University School of Medicine.
  - **8** schools received a grade of **B**
  - **23** schools received a grade of **C+**
  - **13** schools received a grade of **C**
  - **8** schools received a grade of **C-**
  - **18** schools received a grade of **D**
  - **40** schools received a grade of **F**

** 40 colleges have not been graded because they did not respond*

Conclusion

AMSA and the future physicians of America recognize the insidious influence of the pharmaceutical industry in medicine. We want the medical profession to reclaim its role as patient advocates through an awareness of the real effects of pharmaceutical marketing.

Our clinical judgment isn't for sale. We look forward to Pharm-Free policies at all institutions.

AMSA's 2007 Pharm-Free Scorecard Complete Survey Results

A Comprehensive policy that restricts pharmaceutical representatives' access to both the medical school campus and the Academic Medical Center (AMC)

- Stanford University School of Medicine
- University of California, Davis, School of Medicine
- University of Pennsylvania School of Medicine
- University of Michigan Medical School
- Yale University School of Medicine

B Limited policy that sets guidelines for the AMC, but makes little or no mention of the medical school and/or medical students

- Columbia University College of Physicians and Surgeons
- Duke University School of Medicine
- Johns Hopkins University School of Medicine
- University of California, San Diego, School of Medicine
- University of Chicago Pritzker School of Medicine
- University of Hawaii Burns School of Medicine
- University of Kentucky College of Medicine
- University of Pittsburgh School of Medicine

C+ No formal policy, but pharmaceutical representatives are not allowed to interact with students according to the administration

- East Tennessee State University Quillen College of Medicine
- Harvard Medical School
- Jefferson Medical College
- Kansas City University College of Medicine*
- Lincoln Memorial University DeBusk College of Medicine
- Loyola University School of Medicine
- Mount Sinai School of Medicine
- Nova Southeastern University College of Medicine*
- State University of New York Upstate Medical University
- Tufts University School of Medicine
- Tulane University School of Medicine
- University of Arkansas for Medical Sciences College of Medicine
- University of Buffalo State University of New York School of Medicine and Biomedical Sciences
- University of Florida College of Medicine
- University of Illinois College of Medicine
- University of Iowa Carver College of Medicine
- University of Medicine and Dentistry, New Jersey – School of Osteopathic Medicine*
- University of North Dakota School of Medicine and Health Sciences
- University of South Alabama College of Medicine
- University of South Dakota Sanford School of Medicine
- University of Utah School of Medicine
- Vanderbilt University School of Medicine
- Washington University in St. Louis School of Medicine

C School is in the process of drafting a policy

- A.T. Still University College of Osteopathic Medicine – Mesa*
- Boston University School of Medicine
- Emory University School of Medicine
- University of California, Los Angeles, David Geffen School of Medicine
- University of California, San Francisco, School of Medicine
- Universidad Central Caribe School of Medicine
- University of Missouri – Columbia School of Medicine
- University of New England College of Medicine*
- University of New Mexico School of Medicine
- University of Puerto Rico School of Medicine
- University of South Florida College of Medicine
- University of Washington School of Medicine
- University of Vermont College of Medicine
- Touro University College of Osteopathic Medicine, Nevada*

C- School is discussing the formation of a policy, and/or students and the faculty are receiving some education regarding industry interactions

- Chicago Medical School at Rosalind Franklin University of Medicine and Science
- Creighton University School of Medicine
- New York University School of Medicine
- University of Massachusetts Medical School
- University of North Carolina at Chapel Hill School of Medicine
- University of Nebraska College of Medicine
- University of Rochester School of Medicine and Dentistry
- Wayne Sate University School of Medicine

D No policy, but there have been discussions about creating a policy

- Des Moines University College of Medicine*
- Florida State University College of Medicine
- Loma Linda University School of Medicine
- Northwestern Ohio University School of Medicine
- Northwestern University Feinberg School of Medicine
- Rush Medical College
- St. Louis University School of Medicine
- Temple University School of Medicine
- University of Alabama School of Medicine – Birmingham
- University of Alabama School of Medicine – Tuscaloosa
- University of California, Irvine, College of Medicine
- University of Colorado School of Medicine
- University of Kansas School of Medicine
- University of Miami Miller School of Medicine
- University of Virginia School of Medicine
- University of Wisconsin School of Medicine and Public Health
- The Warren Alpert Medical School of Brown University
- West Virginia School of Medicine

No policy, no discussion or school has decided not to form a policy

F Students encouraged to interact with industry representatives

- A.T. Still University College of Osteopathic Medicine – Kirksville
- Albany Medical College
- Brody School of Medicine at East Carolina University
- Chicago College of Osteopathic Medicine*
- Drexel University College of Medicine
- George Washington University School of Medicine
- Georgetown University School of Medicine
- Howard University College of Medicine
- Indiana University School of Medicine
- Joan C. Edwards School of Medicine at Marshall University
- Keck School of Medicine of the University of Southern California
- Lake Erie College of Medicine, Bradenton
- Louisiana State University School of Medicine, New Orleans
- Medical College of Georgia School of Medicine
- Medical College of Wisconsin
- Meharry Medical College
- Mercer University School of Medicine
- Michigan State University College of Medicine*
- Morehouse School of Medicine
- Oklahoma State University College of Medicine*
- Philadelphia College of Osteopathic Medicine, Georgia*
- Pikeville College School of Medicine
- Southern Illinois University School of Medicine
- University of Texas Southwestern Medical School
- University of Alabama School of Medicine, Huntsville
- University of Arizona College of Medicine, Phoenix
- University of Arizona College of Medicine, Tucson
- University of Connecticut School of Medicine
- University of Illinois College of Medicine, Peoria
- University of Illinois College of Medicine, Urbana/Champaign
- University of Illinois College of Medicine, Rockford
- University of Louisville School of Medicine
- University of Mississippi School of Medicine
- University of Oklahoma College of Medicine
- University of Oklahoma College of Medicine, Tulsa
- University of Texas Medical Branch at Galveston
- University of Texas Medical School at Houston
- University of Maryland School of Medicine
- Virginia Commonwealth University School of Medicine
- Western University College of Medicine of the Pacific*
- Wright State University Boonshoft School of Medicine
- West Virginia University School of Medicine

** denotes osteopathic medical school*

We received no response from the following schools: Albert Einstein College of Medicine of Yeshiva University; Baylor College of Medicine; Case Western Reserve University College of Medicine; Dartmouth Medical School; Eastern Virginia Medical School; Edward Via Virginia College of Osteopathic Medicine*; Lake Erie College of Osteopathic Medicine; Louisiana State University School of Medicine in Shreveport; Mayo Medical School; Medical University of South Carolina College of Medicine; Michigan State University College of Human Medicine; New York Medical College; Ohio State University College of Medicine; Ohio University College of Osteopathic Medicine*; Oregon Health and Science University School of Medicine; Pennsylvania State University College of Medicine; Ponce School of Medicine; Stony Brook State University of New York School of Medicine; State University of New York Downstate University College of Medicine; Texas A&M Health Science Center College of Medicine; Texas Tech University Health Sciences Center School of Medicine; Touro University College of Medicine*; UMDNJ – New Jersey Medical School; UMDNJ – Robert Wood Johnson Medical School; University of Cincinnati College of Medicine; University of Missouri, Kansas City, School of Medicine; University of Nevada School of Medicine; University of Tennessee College of Medicine; University of Minnesota Medical School; University of South Carolina School of Medicine; Wake Forest University School of Medicine; Weill Medical College of Cornell University.

There was no information on the AMSA chapters' schools at the time this Scorecard was published: Arizona College of Medicine of Midwestern University, CUNY Sophie Davis School of Biomedical Education, Kirksville College of Medicine*, McGill University Faculty of Medicine, New York College of Medicine of New York Institute of Technology, Sanford School of Medicine of University of South Dakota, UMDNJ – Robert Wood Johnson Medical School at Camden, Uniformed Services UHS F Edward Herbert School of Medicine, University of Illinois College of Medicine at Peoria, University of North Texas HSC Texas College of Medicine, University of South Alabama College of Medicine, University of Texas Medical School at San Antonio, University of Toronto Faculty of Medicine, University of Utah School of Medicine, Vanderbilt University School of Medicine, Washington University in St Louis School of Medicine

Appendix 2: History of the Pharm-Free Campaign

AMSA's Pharm-Free Campaign is a national movement to limit the access and influence of pharmaceutical companies and their representatives at medical schools and academic medical centers. Throughout its history, AMSA's leaders and members have taken pride in fostering honesty and integrity, and promoting the interests of our patients and communities. Affordable and quality health care for all is an issue that tugged on the heartstrings of AMSA's founders in the 1950s, and it continues as AMSA's rallying cry today.

In 2002, AMSA launched the nationwide Pharm-Free Campaign as an educational effort targeted at medical students in order to continue teaching the qualities of honesty, humility and accountability in undergraduate medical education and beyond. Without these qualities, both the credibility of the medical community-and the public trust given to it-will erode.

While AMSA recognizes that pharmaceutical companies provide a valuable resource for research and development of new and potentially lifesaving medications, we also realize that the industry has sales representatives deliver sales pitches to doctors. We encourage all physicians-in-training and health-care providers to seek out evidence-based and unbiased sources of information rather than to rely on pharmaceutical industry representatives for "education." AMSA banned pharmaceutical advertising and sponsorships at regional and national conferences, in AMSA's magazine, The New Physician, on the organization's Web site (www.amsa.org) and as a source of corporate donations. AMSA remains one of the few national organizations to completely eschew all pharmaceutical advertisements and sponsorships.

Appendix 3: AMSA's Pharm-Free Pledge

AMSA's Pharm-Free Pledge

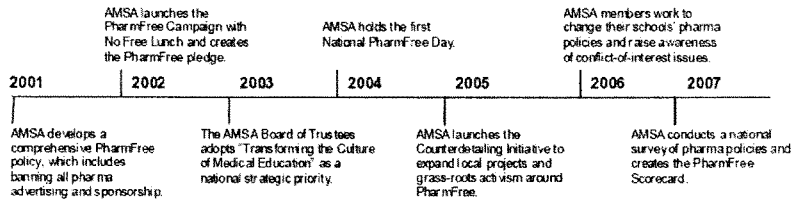
I am committed to the practice of medicine in the best interests of patients and to the pursuit of and education that is based on the best available evidence, rather than on advertising or promotion.

I, therefore, pledge to accept no money, gifts, or hospitality from the pharmaceutical industry; to seek unbiased sources of information and not rely on information disseminated by drug companies; and to avoid conflicts of interest in my medical education and practice.

AMSA's PharmFree Campaign

A national movement to limit the access and influence of pharmaceutical companies at medical schools and academic medical centers

PharmFree Campaign Timeline



Go PharmFree. **PharmFree** because the practice of pharmaceutical gifting to students and physicians increases the costs of health care for patients and does not primarily serve patient interests. **PharmFree** because medical students want to be honest with future patients about why a particular medication was prescribed without compromising personal and professional integrity. **PharmFree** because medical students want to treat future patients using modalities supported by the best existing clinical evidence, not carefully packaged advertising. Patients rightly expect and deserve this from the medical community.

— from AMSA's 2002 PharmFree launch statement

The History of the PharmFree Campaign

AMSA's PharmFree Campaign is a national movement to limit the access and influence of pharmaceutical companies and their representatives at medical schools and academic medical centers. Throughout its history, AMSA's leaders and members have taken pride in fostering honesty and integrity, and promoting the interests of our patients and communities. Affordable and quality health care for all is an issue that tugged on the heartstrings of AMSA's founders in the 1950s, and it continues as AMSA's rallying cry today.

In 2002, AMSA launched the nationwide PharmFree Campaign as an educational effort targeted at medical students in order to continue teaching the qualities of honesty, humility and accountability in undergraduate medical education and beyond. Without these qualities, both the credibility of the medical community—and the public trust given to it—will erode. While AMSA recognizes that pharmaceutical companies provide a valuable resource for research and development of new and potentially lifesaving medications, we also realize that the industry has sales representatives deliver sales pitches to doctors. We encourage all physicians-in-training and health-care providers to seek out evidence-based and unbiased sources of information rather than to rely on pharmaceutical industry representatives for "education."

Cont'd on reverse

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The History of the PharmFree Campaign, cont'd.

AMSA banned pharmaceutical advertising and sponsorships at regional and national conferences, in AMSA's magazine, *The New Physician*, on the organization's Web site (www.amsa.org) and as a source of corporate donations. AMSA remains one of the few national organizations to completely eschew all pharmaceutical advertisements and sponsorships.

The initial PharmFree effort was based on educational tools, like PowerPoint presentations and projects-in-a-box designed both by AMSA and No Free Lunch (www.nofreelunch.org). These tools were meant to inform medical students and empower them to educate their fellow medical students and other health-care professionals, and to make well-formed decisions regarding evidence-based medicine and PharmFree. These educational efforts were supplemented by a bi-weekly newsletter on pharma issues, an ethics primer for AMSA members and a presentation designed specifically for first-year medical students about pharma issues and how to change medical school curricula.

In 2003, the AMSA Board of Trustees adopted "Transforming the Culture of Medical Education" as one of the organization's four national strategic priorities. The PharmFree Campaign, with its call to revitalize professionalism, remains a central component of that priority. The next year, AMSA's Annual Convention centered on "Revitalizing Professionalism: Physicians Worthy of the Public Trust" and introduced AMSA members to PharmFree issues through keynote speakers, special programming and awareness-building information sessions.

The first National PharmFree Day was held on December 8, 2004. AMSA members held a "pen drop" and dumped thousands of pharma-branded pens and paraphernalia outside of the Pfizer headquarters. The next year, National PharmFree Day included chapter-based activities, such as lectures, debates, drug pen collections and policy discussions with clerkship directors and school administrators. "PharmFree Liberated" stickers showed up on medical school campuses across the country. National PharmFree Day has become a premier AMSA event.

The next step in the PharmFree Campaign was 2005's Counterdetailing Initiative. This effort took the PharmFree campaign to the next level by drawing on the knowledge base already established and introducing a focus on local projects and grassroots activism. Counterdetailing focused not only on physicians-in-training, but also on current healthcare professionals and encouraged the practice of evidence-based, rather than industry-influenced, medicine.

In 2006, with the backing of AMSA's 66,000 members, AMSA leaders undertook a national survey of medical school pharma policies. The result is AMSA's 2007 PharmFree Scorecard, which ranks U.S. medical schools based on their policies to limit the access and influence of pharmaceutical companies and their representatives at schools and academic teaching centers.

The PharmFree movement will revitalize professionalism in medical education and healthcare provision. All medical students should learn about the ethics of drug company interaction with health professionals and make the rational, informed decision to eschew "free" gifts from the pharmaceutical industry throughout their training careers. Every practicing physician should practice evidence-based medicine using modalities supported by the best existing clinical evidence—not carefully packaged advertising—and continue to uphold personal and professional integrity.

AMSA's PharmFree Pledge

I am committed to the practice of medicine in the best interests of patients and to the pursuit of an education that is based on the best available evidence, rather than on advertising or promotion.

I, therefore, pledge to accept no money, gifts, or hospitality from the pharmaceutical industry; to seek unbiased sources of information and not rely on information disseminated by drug companies; and to avoid conflicts of interest in my medical education and practice.

To sign the AMSA PharmFree Pledge, visit: http://www.amsa.org/prof/pledge.cfm

Updated April 2007.
Based on the history of AMSA's PharmFree Campaign introduced by 2005-06 AMSA National Leaders: President Leana Wen, PharmFree Coordinator Yavar Moghrim and Legislative Affairs Director Chris McCoy. Additional information provided by 2006-07 National Leaders: President Jay Bhatt and PharmFree Coordinator Justin Sanders.

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Appendix 4. AMSA's Principles Regarding Pharmaceuticals and Medical Devices

AMSA's PRINCIPLES REGARDING PHARMACEUTICALS AND MEDICAL DEVICES

The American Medical Student Association:
1. Regarding Government Policy:

a. URGES increased funding and regulatory power for the Food and Drug Administration (FDA) to enable it to ensure that pharmaceutical, diagnostic and other medical products are of the highest quality and safety; (2006)

b. SUPPORTS legislation that provides for the classification, testing and pre-market clearance of medical devices and encourages the development and use of new, approved devices; (2006)

c. SUPPORTS the incorporation of the National Drug Code into various drug compendia, SUPPORTS the mandatory utilization of the National Drug Code, its imprintation with barcoding on all drug rug containers and
solid dosage forms, and ENCOURAGES the increased use of automated barcode systems at point of dispensation to reduce drug errors; (2006)

d. URGES adequate funding of the FDA or a federal agency to be charged with:
1. coordinating and reviewing evaluative testing of bioequivalence and bioavailability of products and requiring it where indicated; (2006)
2. requiring and reviewing comparative testing between new products and existing products in addition to placebo when such products already exist within the same class to determine if the new product is superior or equivalent to existing therapy; (2006)
3. publishing lists of products it judges to be bio-equivalent or comparatively efficacious; (2006)
4. receiving and evaluating challenges to previous bio-equivalency and comparative efficacy decisions. (2006)
e. URGES the FDA and pharmaceutical manufacturers to make widely available to physicians and pharmacists definitive reports on bio-availability and therapeutic equivalence and bulletins indicating current trends where studies are not yet conclusive;
f. OPPOSES efforts to allow the use of uncertified or unapproved drugs in the treatment of a medical condition without emergency approval; (2006)
g. SUPPORTS government programs or legislation to encourage innovation of new pharmaceutical products especially new molecular entities (NME), biologics, and medical devices, particularly for neglected, communicable, or life-threatening diseases in the United States and worldwide. (2006)
2. Regarding physician/industry interaction:
a. SUPPORTS the concept that the physician's role in pharmaceutical product selection remain primary;
b. ENDORSES the objective sources of therapeutic information on pharmaceuticals, such as the "Medical Letter of Drugs and Therapeutics," "Facts and Comparisons," "The American Hospital Formulary," and ENCOURAGES all institutions to provide independent sources, rather than relying upon industry sponsored sources such as the *Physician's Desk Reference*;
c. OPPOSES the use of promotional gimmicks and inappropriate gifts serving no educational or informational purpose to influence medical students or physicians; (1992)
d. OPPOSES the process by which the AMA's guidelines on gifts to physicians from industry were adopted by members of the medical community and its related industries; (1992)
e. OPPOSES the policy of giving training institutions sole control over the allocation of industrial funds for the purpose of physicians'-in-training participation in extracurricular educational activities; (1992)
f. ENCOURAGES the pharmaceutical industry, in cooperation with AMSA and other organizations representing
physicians-in-training, to begin a continuing dialogue on the role of industry in medical education and in supporting legitimate medical education activities; (1992)

g. BELIEVES that practicing physicians should maintain an independent financial posture vis-a-vis the

pharmaceutical industry to avoid the potential of conflict of interests in prescribing for and treating their patients; (2002)
h. URGES all physicians, residents and medical students not to accept as end recipients any promotional gifts from the pharmaceutical industry. (2002)
i. URGES all hospitals and residency programs to discontinue the practice of pharmaceutical company funded lectures and lunches. (2002)
j. URGES all hospitals and residency programs to discontinue the practice of disseminating information about off-site drug-company sponsored events. (2002)
k. OPPOSES granting CME credit for pharmaceutical company-sponsored events. (2002)
l. URGES all physicians not to accept honoraria on behalf of pharmaceutical companies for speaking at educational conferences and not to accept compensation for token consulting or advising. (2002)
m. OPPOSES the tracking of prescriptions by commercial entities and SUPPORTS legislation to limit access to individual prescription patterns of physicians by the sales and marketing departments of pharmaceutical companies. (2006)
n. SUPPORTS including curricula in medical school education concerning the ethics of physician-industry interactions, particularly in relation to pharmaceutical research and marketing. This curriculum may include:
(2004)
1. the research and development process for new drugs, including the cost of creating new medications and the role for physician-researchers; (2004)
2. the decision-making process for prescribing medications, as it relates to the economics and bioequivalence of using brand name versus generic drugs; (2004)
3. the impact of direct-to-consumer and direct-to-physician marketing practices employed by the pharmaceutical industry, as they relate to the physician-patient relationship; (2004)
4. a review of the various guidelines concerning gifts from the pharmaceutical industry, including those issued by AMSA, AMA, and the Pharmaceutical Researchers and Manufactures of America (PhRMA). (2004)
o. Strongly ENCOURAGES physicians and physicians-in-training to refuse pharmaceutical samples in cases in which equally effective, low-cost alternatives exist and utilize samples only in cases in which other lower cost therapies have been unsuccessful or are contraindicated. (2007)
3. Regarding Pharmaceutical and Medical Device Pricing:
a. SUPPORTS efforts to reduce the cost of medications and medical devices for patients. Possible mechanisms to achieve lower prices include: (2006)
1. Bulk purchasing by federal and state governments to allow the negotiation of lower prices; (2006)
2. Compulsory licensing of pharmaceuticals and devices under patent protection; (2006)
3. Re-importation of medications from industrialized countries, when the medications are approved for use in the United States; (2006)
4. Maximum Allowable Cost (MAC) programs, only if all the following provisions are met:
a. that the physician be able to get a brand-name drug simply by certifying that it is his/her opinion that a specific product is needed; (2006)
b. that the pharmacist be reimbursed for a prescribed brand name-drug if he/she cannot reach the physician for permission to substitute; (2006)
c. that stringent quality controls be instituted regarding all substituted products to ensure they are, indeed, as safe and efficacious as the standard product. (2006)
5. Mechanisms to encourage research and development through government grants and awards, including rewards for innovation with one-time monetary compensation in exchange for open patents on novel medications. (2006)
b. AMSA OPPOSES any limitations on bulk purchasing, especially for public healthcare agencies. (2006)
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c. SUPPORTS legislation to require physicians to prescribe pharmaceutical products by generic name and then to note in parentheses the name of a specific brand name or company whenever the physician will not allow substitution, and which requires pharmacists to pass along to the consumer any wholesale price differences between generic and brand-name drugs when the generic drug is dispensed;
d. ENCOURAGES physicians to consider and make students aware of cost-effectiveness when recommending

or prescribing commonly used drugs and to educate about affordable alternative therapies for patients who have financial limitations to pharmaceutical access; (2006);
e. SUPPORTS legal action against pharmaceutical companies to mandate fair pricing in cases where essential
medications are unaffordable to the general public and pricing is disproportionate compared with other national or international prices. (2006)
4. Regarding pharmaceutical advertisement:
a. URGES that the advertising of all pharmaceutical and OTC products be maximally educational for both the public and physicians and meet the following criteria:
1. medications should be portrayed as medicines with a specific purpose and not as cure-all panaceas;
2. the advertising should not define a need that does not exist in a medical sense nor create a new need;
3. the advertising should be factual and without pictorial or verbal representations which appeal to emotions rather than intellectual reasoning;
4. patients and providers should be portrayed in a respectful and humane manner and not in a stereotyped or demeaning fashion with respect to age, sex, sexual orientation and gender identity, race and disability;
5. the promotional content should be clearly identifiable as such and be as separate from the educational content as possible;
6. a suggested retail price should be included in all detail advertisements;
7. the statement, "If you are presently taking any other medicines, consult your pharmacist or doctor before using our product," should be included in all OTC drug advertisements. (2006)
b. SUPPORTS required labeling of all cosmetic ingredients;
c. OPPOSES drug industry-sponsored direct-to-consumer (DTC) advertisements. (2005)
5. Regarding pharmaceuticals and international health:
a. CONDEMNS pharmaceutical companies that produce and export dangerous and controlled drugs to countries in quantities much greater than is used in those countries, and other parties contributing to illicit smuggling and sale of these drugs. (2006)
b. SUPPORTS the use of the World Health Organization (WHO) Model List of Essential Drugs as a reference base which countries may use in developing national essential drug policies. (2006)
c. URGES the pharmaceutical industry to adopt policies of research, development, manufacture and pricing that support developing countries in making essential drugs and vaccines available to their peoples, without promoting use of drugs and vaccines not included on the WHO List of Essential Drugs. (2006)
d. SUPPORTS worldwide efforts, such as the Global Fund, to increase access to essential medicines to all people of the world suffering morbidity or mortality due to treatable life-threatening or disabling diseases without discrimination due to gender, race, nationality, sexual orientation and gender identity, age or socioeconomic status. (2006)
6. Regarding research, intellectual property and access to essential medicines in resource-poor settings:
a. RECOGNIZES that Universities, as intellectual property holders, play a crucial role in the development of
new medicines and medical technologies, and that how they patent and license these technologies can help determine whether individuals in developing countries have access to the end products of university research. (2003)
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b. URGES Universities to utilize the following Principles, suggested by the institutional ethos of universities,
when making patenting and licensing decisions that have potential impacts on access to essential medicines and medical technologies worldwide:
1. University research is intended to advance the common public good, a primary element of which is the advancement of health.
2. Global public health concerns need to be an important part of patenting and licensing decisions.
3. The success of patenting and licensing programs should be measured according to their impact upon public health.
4. University intellectual property policies should be implemented in a manner supportive of developing countries' right to protect public health and, in particular, to promote access to medicines for all.

5. Technology transfer to develop capacity in developing countries is an important part of universities' mandate to advance knowledge and the social good. (2003)
c. URGES Universities to consider different strategies to implement these Principles, including not patenting or allowing their licensees to patent in developing countries, and issuing non-exclusive licenses for
developing country markets. (2003)
d. RECOGNIZES that changes in University practices, with regards to intellectual property, will require collective action and leadership amongst Universities world-wide. (2003)
e. URGES Universities to act together to establish norms and implement strategies and best practices to promote access to essential medicines in developing countries. (2003)
f. URGES the pharmaceutical and medical device industry to respect the scientific process of research and discovery, including the following:
1. SUPPORTS the right of researchers to freely publish their results without prior approval from sponsoring entities; (2006)
2. OPPOSES publishing partial and incomplete results of studies, using ghost-writers and otherwise bypassing the peer-review process; (2006)
3. OPPOSES the use of Contract Research Organizations (CRO) to conduct research outside of academic institutions; (2006)
4. STRONGLY OPPOSES attempts by industry to retaliate against and/or intimidate individuals and groups working to improve pharmaceutical safety or government pharmaceutical policies. (2006)
7. Regarding Prescription Drug Re-importation: (2004)
a. BELIEVES that Canadian pharmacies, which are subject to similar quality control and chain of custody standards as the United States have the ability to ensure the safety of prescription drugs. (2004)
b. RECOGNIZES that the re-importation of drugs from Canada is a temporary step towards improving access
to affordable drugs from pharmaceutical companies within the United States. (2004)
c. SUPPORTS the re-importation of drugs from Canada as a temporary solution, until equivalent pharmaceuticals
are available at equal or lower prices in the United States through bulk purchasing and price negotiation. (2006)
8. Regarding Liability of Pharmaceutical Companies:
a. SUPPORTS increasing the enforcement of pharmaceutical regulation and penalties on pharmaceutical companies for failing to disclose to the FDA any information concerning harmful effects of their products. (2006)
b. OPPOSES legislation that would exempt pharmaceutical manufacturers from legal liability stemming from known harmful effects of their products. (2005)

Statement of:
Lewis Morris
Chief Counsel to the Inspector General
Office of Inspector General, U.S. Department of Health and Human Services

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I appreciate the opportunity to submit this statement for the record, as requested, in connection with the Senate Special Committee on Aging's June 27, 2007, hearing on the relationship between doctors and the pharmaceutical industry.

There is growing concern that pharmaceutical manufacturers' aggressive marketing and sales practices are leading to increased health care costs and improperly influencing the medical judgment of the physicians targeted by these practices. The Office of Inspector General (OIG) for the Department of Health and Human Services shares these concerns and is at the forefront of the effort to pursue cases of fraud involving pharmaceutical manufacturers and to provide guidance to the pharmaceutical industry to steer it away from abusive and illegal practices. OIG also conducts audits and program evaluations to identify systemic vulnerabilities related to prescription drug coverage under the Federal health care programs.

This statement will review two important components of OIG's multifaceted approach to combating pharmaceutical fraud. First, I will discuss OIG's outreach efforts to promote the industry's voluntary compliance with program requirements. In particular, the discussion will focus on OIG's Compliance Program Guidance for Pharmaceutical Manufacturers (Pharmaceutical CPG), which OIG issued in 2003. The Pharmaceutical CPG describes the relevant fraud and abuse authorities, identifies major risk areas under these laws, and provides an armature around which drug manufacturers, prescribers, and other parties involved in the provision of prescription drugs can design effective compliance measures. Second, I will summarize OIG's enforcement accomplishments in the area of pharmaceutical manufacturer fraud. A comprehensive discussion of the enforcement work undertaken to combat fraud in the pharmaceutical industry is set forth in my February 9, 2007, testimony before the House Oversight and Government Reform Committee (http://oig.hhs.gov/reading/testimony. html). In conclusion, I will touch on future guidance OIG may promulgate to address the interactions between physicians and pharmaceutical and medical device manufacturers.

OIG Outreach Efforts to Promote Program Integrity

OIG engages in a variety of outreach efforts to foster a culture of compliance within the health care industry. We cannot protect the Federal programs alone. Therefore, we collaborate with industry stakeholders to promote the integrity of the Federal health care programs through voluntary industry compliance efforts. As part of our outreach effort, OIG issues advisory opinions, special fraud alerts, special advisory bulletins, and compliance program guidance (CPGs) to assist health care providers, suppliers, and others in guarding against fraud and abuse and in structuring lawful business arrangements.

CPGs are among OIG's most significant means of engaging the private sector in a systemic approach to preventing and reducing fraud and abuse in Federal health care programs. CPGs give the various health care sectors standards, principles, and analytical frameworks by which to establish and maintain effective internal compliance programs. OIG develops CPGs based on information from OIG oversight, enforcement, and outreach activities; consultations with Federal and State agencies; and communications with the health care industry. OIG solicits input from the regulated community and others through a public comment process, which increases the likelihood that good compliance practices will be adopted. By identifying business practices and arrangements that we believe are subject to serious abuse, we hope to encourage self-correcting behavior by the affected industry sector. Over the past 10 years, OIG has issued 13 CPGs covering virtually all major health care industry sectors. These CPGs can be found on OIG's Web site at http://oig.hhs.gov/fraud/complianceguidance. html.

CPGs are not regulations – they are voluntary guidance that can be adapted to the particular needs of the health care entity or organization. OIG has no statutory authority to dictate the elements of a voluntary compliance program. Consequently, CPGs are, by their terms, advisory and not compulsory. Nor does OIG have legal authority to deem certain types of activities to be *per se* violations of the fraud and abuse laws. The Federal anti-kickback statute, for example, is an intent-based criminal prohibition against the knowing and willful offer, payment, solicitation, or receipt of remuneration to induce or reward the referral or generation of Federal health care program business. (Social Security Act § 1128B(b); 42 U.S.C. § 1320a-7b(b)) The statute requires a case-specific analysis of the facts and circumstances to determine when a violation has occurred. OIG cannot proscribe particular categories of business arrangements or expand the scope of activities that the anti-kickback statute prohibits. OIG's regulatory authority at 42 U.S.C. § 1320a-7b(b)(3)(E) extends to promulgating regulations describing categorical practices that are *permissible*; these practices are described in "safe harbor" regulations at 42 CFR 1001.952. OIG also administers a statutory advisory opinion program through which individuals and entities can seek binding legal opinions about the application of certain fraud and abuse laws to specific existing or proposed business arrangements. (Social Security Act § 1128D; 42 U.S.C. § 1320a-7d)

The Pharmaceutical CPG

On June 11, 2001, OIG published a notice in the Federal Register soliciting comments and recommendations on what should be included in the Pharmaceutical CPG. 66 FR 31246 (June 11, 2001)) Following our review of comments received in response to the solicitation notice, on October 3, 2002, we published draft compliance guidance in the Federal Register and solicited further comments and recommendations. (67 FR 62057 (Oct. 3, 2002)) In response to the draft guidance, OIG received 142 written comments from a diversity of stakeholders, including pharmaceutical manufacturers, physicians, nurses, health plans, governmental entities, and trade associations representing an array of interests.

In addition to considering the public comments, in finalizing the Pharmaceutical CPG we reviewed previous OIG publications, including advisory opinions, safe harbor regulations, special fraud alerts, and reports relevant to the pharmaceutical industry. We also met with four groups of industry stakeholders: Pharmaceutical Research and Manufacturers of America (PhRMA) and pharmaceutical manufacturer representatives, health plan and health plan association representatives, representatives of pharmacy benefit managers (PBM), and representatives of the American Medical Association (AMA) and its member organizations. The process we used for finalizing the Pharmaceutical CPG was consistent with the process used in the development of other CPGs.

OIG published the final Pharmaceutical CPG on May 5, 2003. (68 FR 23731 (May 5, 2003)) This guidance provides detailed information for drug manufacturers on establishing and operating an effective internal compliance program and identifying fraud and abuse risk areas. It also suggests concrete ways manufacturers can mitigate their risks. Although the guidance is targeted at manufacturers, much of its content pertains to physicians, pharmacies, PBMs, and other parties involved in the provision of prescription drugs to Medicare and Medicaid beneficiaries. It also offers important guidance for participants in the new Medicare Part D prescription drug benefit.

The Pharmaceutical CPG describes certain specific risk areas in detail, including integrity of data used to establish Government reimbursement, drug samples, and kickbacks and other illegal remuneration. With respect to kickbacks paid by manufacturers to purchasers of products, for example, the Pharmaceutical CPG discusses risks associated with manufacturers providing discounts, product support services, educational grants, research funding, and various formulary support services in connection with the sale of a manufacturer's products. Similarly, with respect to kickbacks to physicians and other persons in positions to make or influence referrals of drugs, the Pharmaceutical CPG addresses risks associated with manufacturers providing payments under switching arrangements, consulting and advisory payments, payments for detailing, business courtesies and other gratuities, and educational and research funding. The Pharmaceutical CPG also discusses potential risks associated with compensation arrangements for sales agents. As noted in the Pharmaceutical CPG, many of the potential risk areas for pharmaceutical manufacturers are equally applicable to medical device manufacturers.

Although the Pharmaceutical CPG identifies specific suspect marketing and sales practices, it is not a static list of all potentially problematic practices. The health care industry is rapidly evolving, as are the fraud schemes that exploit the Federal health care programs. The Pharmaceutical CPG offers guiding principles and illustrative factors that manufacturers can use to identify and avoid potentially abusive arrangements. For example, the Pharmaceutical CPG identifies a process for analyzing business practices under the anti-kickback statute that applies to a wide range of industry conduct. This approach ensures that the Pharmaceutical CPG will continue to be relevant in a dynamic industry.

In PhRMA's written testimony for this hearing, it suggested, erroneously, that OIG "endorsed" the Code on Interactions with Healthcare Professionals, a voluntary code adopted on April 18, 2002 by PhRMA (the "PhRMA Code"). OIG does not endorse the PhRMA Code or any industry codes. Rather, OIG views the PhRMA Code, like some other industry-promulgated codes of conduct, as a useful starting point for evaluating compliance. As stated in OIG's Pharmaceutical CPG, the PhRMA Code "provides useful and practical advice for reviewing and structuring these relationships," and compliance with the PhRMA Code "will substantially reduce the risk of fraud and abuse and help demonstrate a good faith effort to comply with the applicable health care program requirements." (68 FR at 23737) As the Pharmaceutical CPG makes clear, compliance with the PhRMA Code does not protect a manufacturer as a matter of law under the anti-kickback statute or other fraud and abuse authorities.

Pharmaceutical Fraud Enforcement by OIG

Industry guidance is just one facet of OIG's substantial, ongoing effort to combat fraud and abuse by pharmaceutical manufacturers. While CPGs and other OIG guidance documents focus on preventing fraud, OIG, together with its Government partners, plays a substantial role in enforcing the fraud and abuse laws through criminal, civil, and administrative actions. OIG has participated in the investigation and/or resolution of pharmaceutical fraud cases that have resulted in about $4.8 billion in recoveries and fines since 1999. (This figure includes criminal and civil resolutions with pharmaceutical manufacturers, PBMs, retail pharmacy chains, and institutional pharmacies.) In addition, OIG is increasingly using its administrative authorities to sanction individuals and entities engaged in fraudulent and abusive practices in the pharmaceutical and medical device industries.

A series of significant settlements of cases under the False Claims Act illustrates law enforcement's successful pursuit of cases involving alleged wrongdoing by pharmaceutical manufacturers in connection with marketing and promotion of drugs to physicians.

- In May 2007, Purdue Frederick Company, Inc., and Purdue Pharma L.P. entered a global $600 million settlement relating to allegations that the companies engaged in fraudulent marketing of Oxycontin. The companies will pay the settlement amounts and implement other settlement-related obligations following a criminal sentencing that is expected to occur in July 2007.

- In April 2007, the Government settled a civil case against Medicis for $9.8 million in connection with allegations that Medicis caused false or fraudulent claims to be submitted to Medicaid as a result of off-label promotion of Loprox to pediatricians.

- Also in April 2007, the Government settled for $10.5 million civil allegations that Cell Therapeutics illegally promoted Trisenox for off-label uses and that its sales force misrepresented the side effects of Trisenox to physicians.

- In October 2006, the Government entered into a settlement of a civil and criminal case with InterMune, Inc., for $36.9 million. The Government alleged that InterMune improperly promoted Actimmune for off-label uses, resulting in false or fraudulent claims to the Medicare and Medicaid programs.

- In August 2006, the Government entered into a global settlement for $435 million to resolve criminal and civil allegations that Schering-Plough Corporation engaged in a variety of fraudulent price reporting and sales and marketing practices with regard to several drugs.

- In October 2005, the Government entered into a $704 million global settlement with Serono, Inc., and related companies, of civil and criminal allegations, two aspects of which involved off-label promotion of Serostim and alleged kickbacks in the form of an all-expenses-paid trip for a select group of high-prescribing physicians (and their guests) to a conference in Cannes, France.

- In May 2004, the Government settled a civil and criminal case against Pfizer, Inc., and Warner-Lambert Company, LLC, for $430 million involving a variety of allegations, including allegations that Warner-Lambert promoted Neurontin for off-label uses and provided kickbacks to physicians, including kickbacks in the form of sham consulting fees and trips to Florida, Hawaii, and the 1996 Olympics.

- In 2001 and 2003, respectively, the Government settled civil and criminal cases with TAP Pharmaceutical Products, Inc. and AstraZeneca Pharmaceuticals LP, involving a variety of allegations, including allegations that sales representatives gave physicians free samples of the prostate cancer drugs in question in return for ordering their products. The physicians who billed Federal health care programs for the samples were reimbursed between $400 and $500 for each unit of the drug, which should have been given to patients for free.

The Government is currently investigating numerous additional allegations of fraudulent marketing and promotional practices in the pharmaceutical industry and is reviewing over 100 sealed qui tam complaints involving pharmaceutical fraud and abuse.

OIG administrative sanctions complement criminal and civil enforcement by providing an additional avenue for Government enforcement. OIG has the authority to exclude individuals and entities from the Federal health care programs and to impose civil monetary penalties (CMP) for a range of abusive practices, including kickbacks and false claims. (See Social Security Act §§ 1128, 1128A; 42 U.S.C. §§ 1320a-7, 1320a-7a)

In recent years, OIG has increasingly used its CMP authority to sanction the payers and recipients of kickbacks. OIG's settlement in July 2007 with Advanced Neuromodulation Systems, Inc. (ANS), a device company specializing in spinal cord stimulation, is illustrative. As previously noted, many of the same schemes that OIG has encountered in the pharmaceutical sector are present in the medical device manufacturing sector. In this

matter, OIG alleged that ANS engaged in a marketing program in which it paid a number of physicians $5,000 for every five new patients tested with an ANS product. OIG alleged that ANS's program did not have any significant clinical value but rather served as a marketing tool to increase ANS's sales. In addition, OIG alleged that ANS's sales and marketing personnel provided physicians with sports tickets, free trips, free dinners, grants, and other gifts. ANS paid $2.9 million and entered into a three-year Corporate Integrity Agreement with OIG to resolve allegations that it paid kickbacks to physicians in violation of the CMP law.

In the past, criminal prosecutors targeted their limited resources on companies paying kickbacks and generally did not focus on physicians receiving kickbacks. This may have created the misimpression by some physicians that they can demand kickbacks from drug, device, and other companies with impunity. However, OIG has stepped into this breach and is using its authority to impose program exclusion and significant monetary penalties to target these kickback recipients. It is our intention that OIG administrative enforcement will prompt physicians to think twice before accepting kickbacks from pharmaceutical and other companies.

OIG has entered into CMP settlements with recipients of alleged kickbacks from pharmaceutical companies. For example, in 2004, a California physician and a Texas physician agreed to pay $57,500 and $38,941, respectively, and to enter into Integrity Agreements with OIG to resolve their respective liability under the CMP provisions applicable to false claims and kickbacks. In each case, OIG alleged that the physician received free samples of the prostate cancer drug Lupron from TAP Pharmaceutical Products, Inc. and billed at least some of those samples to Medicare and other payers. In 2003, an Ohio urologist agreed to pay $42,224 and to enter into an Integrity Agreement to resolve his liability under the CMP provisions applicable to false claims and kickbacks. OIG alleged that the urologist conspired with AstraZeneca Pharmaceuticals LP employees to receive free samples of the prostate cancer drug Zoladex and then billed at least some of those samples to Medicare and other payers.

Looking Forward

Federal and State law enforcement agencies continue to investigate many fraud schemes similar to those outlined above. Criminal and civil investigations are resource intensive, time consuming, and require extensive coordination between Federal and State agencies. Furthermore, the parties engaged in these frauds are adept at modifying schemes in response to Government efforts to strengthen program integrity. The large and growing size of Federal expenditures for prescription drugs will continue to attract those intent on defrauding Medicare and Medicaid.

Accordingly, we intend to enhance our existing fraud prevention and detection efforts to meet new challenges as they arise. For example, OIG is constantly evaluating the need for additional, updated guidance for different segments of the health care industry. OIG is currently taking a hard look at the area of pharmaceutical and device company relationships with physicians in order to determine whether any additional guidance

would help promote compliance and minimize fraud and abuse. Like the Pharmaceutical CPG, any such forthcoming guidance from OIG will complement the comprehensive guidance and enforcement efforts already in place.

OIG shares the Committee's commitment to protecting the integrity of Federal health care programs and the health and safety of beneficiaries. We will continue to fight fraud in Medicare and Medicaid and promote compliance by the pharmaceutical industry and those who do business with the industry.

Thank you for the opportunity to discuss OIG's work on this important matter.

Testimony Submitted to the Senate Special Committee on Aging
July 3, 2007

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Dear Senator Kohl and Members of the Special Committee on Aging:

On behalf of the National Physicians Alliance (NPA), thank you for this opportunity to share our views on the importance of the relationship between physicians and the drug industry. As Chair of the NPA's Prescription Privacy Task Force and as a member of the NPA's Board Of Directors, I want to begin by emphasizing our organization's support for the strong arguments presented to this committee by Dr. Jerome Kassirer, Ms. Sharon Treat, and Dr. Peter Lurie.

The National Physicians Alliance was founded in 2005 with a mission to restore physicians' primary commitment to the core values of our profession: service, integrity, and advocacy. We have grown to represent 10,000 physicians across medical specialties and across the United States. Unlike the vast majority of physician organizations, we accept no money from pharmaceutical companies. Our first concern is the health of patients and communities.

The National Physicians Alliance believes that the public health is directly threatened by the commercial influences that now pervade medical education and practice. It has become increasingly difficult for physicians to find and distinguish legitimate, evidence-based sources of medical information from sources either sponsored or produced by companies with a financial stake in the information presented. Pharmaceutical companies have found myriad, powerful ways to market their products and bias the medical literature—and our members are concerned about the degree to which our profession has become complicit in this work.

The relationship between physicians and the drug industry is complex and intertwined. Recently the *New England Journal of Medicine* revealed that 94% of physicians have some sort of relationship with the pharmaceutical industry; 83% receive free food from pharmaceutical detailers; 78% receive free medication samples; 35% receive reimbursement for costs associated with professional meetings or continuing medical education; and 28% receive direct payment for consulting, giving lectures, or enrolling patients in trials. [i]

Are gifts really gifts?

Though commonly referred to as "gifts," these expenses are rightly budgeted by the pharmaceutical industry as marketing costs. They are investments, not gifts. Examples of these expenses range from branded pens and post-it notes to generous speaking fees. During training,

one of our members personally witnessed that is was commonplace for some teachers to beef up their salaries with honoraria for dinner talks sponsored by pharmaceutical companies, receiving in excess of $1,000 dollars per talk.

It is well established that "gifts"—large or small—can affect how physicians behave.[ii] Physicians are no more immune to inducements than anybody else. When a pharmaceutical sales representative brings lunch to the office staff, the free food is generally appreciated. When she befriends a beleaguered and overwhelmed doctor-in-training, the support is generally welcome. These courtesies extend to other health-care providers as well, including nurses and nurse practitioners, who often have influence over what prescriptions are chosen.

As borne out in the literature and recently highlighted in the *Baltimore Sun* (6/03/07), medical students—who may be considered the most vulnerable or impressionable—are strongly targeted as well. They are provided dinners in restaurants they normally could not afford and are offered expensive software and textbooks emblazoned with company logos. The cheerful, solicitous friendship and material offerings of drug detailers have become an everyday part of medical culture. Changing this culture is not easy. Some of us who have been made to feel guilty by their own front-office staffs for "taking away" the free Starbucks coffee or Chinese lunches by limiting visits from sales reps, others regularly buy pizza or other meals for his staff to offset their resentment at his refusal to take free food from drug reps.

One NPA member worked hard to remove pharmaceutical marketing influences from his rural practice in Oregon. He and his partners stopped accepting visits and lunches from drug reps. They threw away all branded items from the office and even received media coverage for these "radical" steps. Nearly 16 months later, this family practitioner still receives glossy promotional mail from the drug companies, most recently a package that included a hand-written note from a rep stating, "please try to get more people on our therapy."

The pressures put on doctors by pharmaceutical salespeople take many forms. Though clearly outside the published ethical guidelines of the industry, there have been situations reported by NPA members where pharmaceutical sales representatives provided free birth control samples to OB/GYN residents for their personal use, and others where they have befriended student physicians to the point of attending their private parties or even taking them to strip clubs.

Along with the food and friendship comes a flood of "educational" material—some for physicians but much that is targeted for patients. It is dangerous for both groups to rely on sales representatives for medical information; the glossy materials provided by industry representatives are likely to be incomplete—selectively including results of all relevant studies—and are likely to compromise patient safety by downplaying reference to known side effects.[iii]

What do medication samples achieve?

The pharmaceutical industry asserts that free medication samples enable physicians to begin needed therapies without delay and to provide treatment otherwise unaffordable for many patients. There is no doubt that many doctors recognize these benefits. While we understand

that prohibiting samples would be an unpopular endeavor, we ask the committee to take the following into consideration:

- Drug samples influence prescribing behavior (Adair & Holmgren, *Am J Med*, 2005)
- Prohibiting free medication samples leads to more appropriate prescribing (Boltri, et. al., *Fam Med*, 2002)
- Drug samples may be taken by physicians and office staff themselves, without prescription (Westfall et al, *JAMA*, 1997)
- Most samples are for medicines that need to be taken long term; if a patient cannot afford a particular medicine, it is not necessarily the best choice to introduce it as a free, short-term sample because the result can only be a dependency on the samples (and the doctor)—which warrants an ethical discussion—or the ultimate discontinuance of that medication, which may have side effects (for example, a heart attack resulting from the abrupt discontinuation of a blood- thinning drug after a stent procedure). The patient may be better off with the initial prescription of an affordable prescription that is not "free."
- Most patients have access to a pharmacy that is open on weekends and sometimes 24 hours and immediate commencements of therapy is seldom necessary for medicines that need to be taken chronically.

There is also some evidence that pharmaceutical sales representatives consciously distribute or withhold medication samples in response to physicians' willingness to have their personal prescribing habits available for the reps to view. Shortly after the launch of the American Medical Association's Physician Data Restriction Program (AMA PDRP)—a program which enabled physicians to "opt-out" of having their prescribing data available to reps—the following posts appeared on the online bulletin board "Cafepharma.com," where drug detailers share their experiences anonymously. (And I realize that the original sources are not verifiable, but I think these opinions are unlikely to come to light in public. Here is an exchange that appeared on September 1st, 2006, shortly after the PDRP started (www.cafepharma.com/boards/showthread.php?t=108100):

> POST: "My latest cut of data now is showing a couple of doctors as opt outs, no rx[Prescription] data, just a new line item on the report saying they do not report, anyone else see this yet?"
>
> REPLY: "I've got a couple. I am cutting their samples by 75%." [...]
>
> POST: "No data submission - no samples. Because my company will not give us credit for docs who don't report [...] In a way I don't blame them because those who write a lot of scripts get hounded by too many reps [...] I get [mad] at my manager always having me come up with some sort of action plan and counterdetail against the products they write most of.

This example (which is not the only one on that site) illustrates that samples are indeed intended to increase prescriptions of a particular brand.

In this context it should be noted that the NPA is opposed to the sale of physician prescribing records for pharmaceutical marketing purposes. We further believe that the AMA's PRDP is an insufficient measure, as the physicians' prescribing data is still sold to pharmaceutical companies with the expectation of industry self-regulation.

Should the pharmaceutical industry be a major supplier of physician education?

The National Physicians Alliance is deeply concerned that drug companies now spend well over one billion dollars annually to support continuing medical education (CME) courses for physicians. [iv] Even more distressing is the fact that drug company sponsorship now accounts for *more than half* of the CME courses available to physicians, who rely on these courses both for licensure and to maintain professional competency.

While it is true that doctors need to be educated about new medicines, education should come from qualified, independent scientists, not those with a stake in any particular drug's profit margin—and definitely not from salespeople who lack scientific training. Promotional materials from industry encourage the use of new, brand-name drugs that come at a much higher price than well established generic medications which are often of comparable efficacy and which have a longer record of safety.

In the case of CME, a common method used by pharmaceutical companies to influence prescribing is anointing "key opinion leaders"—physicians who are richly paid to lecture to peers about "best practices." These talks often open with a quickly flashed slide that discloses the fact but not the extent of the speaker's financial relationships. Any omissions are unknowable to the audience. Indeed, sometimes it is not only the speaker who is being paid, but the audience as well. One NPA member shamefully recalled an all-expense 2 day paid trip he took to Las Vegas during his training, where he left with a $750 check for attending a 4-hour "consulting session" with 20 to 30 other doctors. To call this practice a "consulting service" is a real stretch.

These marketing practices have proven to be good investments for the industry and they have concerning consequences for patients and doctors alike. Physicians can afford to pay for their own CME courses. They can afford nice meals. There is no ethical place for the industry influence wrought through gifts or sponsorship.

The more we know about these investments and relationships, the better we will understand their direct impact both on how physicians make their prescribing choices and on the collective cost and clinical appropriateness of those choices. Disclosure laws, as considered or enacted by many states, are an important step in the right direction. We also hope that increased public attention to the need for doctors to have industry-free sources of medical data may lead to greater public investment in continuing medical education, with great benefit for patients.

Conclusion

Understanding pharmaceutical marketing practices will help guide future efforts to distinguish advertising from evidence-based, scientific data. The National Physicians Alliance believes the Congress should require the disclosure of all "gifts" and honoraria to health care providers—even those below the arbitrary limit of $25—as research has shown that even inexpensive gifts have surprisingly large influence. Such a law would respect the public's and the medical profession's right to know how drug manufacturers are trying to influence what should be clinically focused decisions. Disclosure laws are very helpful:

- They pressure both physicians and drug makers to reflect on the ethics of their entanglements.
- They will help lawmakers evaluate the impact of marketing on prescribing practice, revealing trends with major implications for health-care costs and patient safety.
- They may lead to some changes in marketing practice—a possibility most likely to happen if disclosures are made available to the public.

Professional standards and guidelines are essential to restoring integrity to the practice of medicine. Journalists, lawyers, and lawmakers all have stricter expectations for gift-refusal than do physicians. The National Physicians Alliance is encouraging members and colleagues to become more thoughtful about these influences and more circumspect about the sources of their medical information.

In closing, there is risk in trusting that guidelines or ethics codes alone will restore integrity and science to a field overrun by marketing. Where both lives and enormous financial profit hang in the balance, industry should not be expected or allowed to police itself. Transparency will help all of us do what's best for patients. The National Physicians Alliance welcomes this public attention to the nature of pharmaceutical marketing practices and we look forward to working with Congress and others on these issues. The NPA is eager to help achieve a safe, affordable, and effective health care system for all patients.

Respectfully submitted,

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