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THE IMPACT OF DIRECT-TO-CONSUMER DRUG ADVERTISING ON SENIORS' HEALTH AND HEALTH CARE COSTS

HEARING

BEFORE THE

SPECIAL COMMITTEE ON AGING
UNITED STATES SENATE

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THE IMPACT OF DIRECT-TO-CONSUMER DRUG ADVERTISING ON SENIORS' HEALTH AND HEALTH CARE COSTS

THURSDAY, SEPTEMBER 29, 2005

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

The committee met, pursuant to notice, at 10 a.m., in room SH–216, Hart Senate Office Building, Hon. Herb Kohl, presiding.

Present: Senators Smith, Talent, Kohl, and Wyden.

OPENING STATEMENT OF SENATOR HERB KOHL

Senator KOHL [presiding.] Good morning and we welcome everyone to this hearing where we will examine today the effects of direct-to-consumer advertising of prescription drugs on patients, doctors, and health care spending. As always, we thank our Chairman, Gordon Smith, for working with us in a bipartisan manner to examine this important issue affecting seniors.

We all know that Americans pay the highest prices in the world for medicines that are largely researched and manufactured here in our own country. Starting in January, the American taxpayers will pay hundreds of billions of dollars for drugs through the new Medicare benefit. So now, more than ever, we have a responsibility to ensure that those dollars are being spent wisely.

As we look to the reasons why drug costs are so high, one contributing factor is the widespread advertising of drugs directly to consumers. Spending on advertising of prescription drugs more than quadrupled between 1996 and 2003 in this country. Companies have the right to spend as much as they choose to promote their products, although it should be noted that, aside from New Zealand, the United States is the only country in the world that allows direct advertising of drugs to consumers. We should consider whether there is a message there that we should think seriously about.

But as the largest payer of prescription drug costs, the Federal Government has an obligation to examine the impact of these drugs on drug choices and health care spending. Today's ads often steer consumers toward newer, costlier drugs when older, less expensive drugs may be more appropriate. This leads to higher health care spending as patients demand and doctors prescribe more expensive medicines.

The reason that these ads are so powerful is because they often are the only source of information that patients have about a drug.

The ads paint a picture of a healthy life that can be theirs only if they just "ask their doctor." Unfortunately for consumers, this is not always the complete picture as most patients have no idea whether the new drug is better than the older one that they have been taking for years.

It should not be left solely to the drug industry to educate patients and doctors about new medicines. We need more unbiased research, perhaps through the NIH, that will compare new and old drugs to help doctors and patients determine which is the best, most cost-effective medicine for them.

We also need to give doctors time to fully understand the benefits and risks of a new drug once it reaches a market. Ads for newly approved drugs hit the airwaves immediately, sending patients to their doctors to request what they have seen. We should consider a moratorium on advertising for newly approved drugs to provide doctors enough time to fully understand their effects.

Finally, we also know the FDA has limited enforcement measures at their disposal to crack down on misleading advertising. Providing stronger enforcement tools to the FDA will help prevent unnecessary utilization costs and potentially harmful outcomes to patients.

I am working on legislation to address some of these issues, and I know that other Senators, including Senator Wyden, who is here today, have also begun working on legislative answers. I have also joined with Senator Frist to ask the GAO to study the effect of DTC advertising on drug costs and utilization. I look forward to working with all of my colleagues on this important issue. Clearly, companies have the right to advertise their products, but with the new Medicare drug benefit starting soon, taxpayers are about to foot the bill for billions of dollars in drug costs. They deserve to know that doctors and patients have the best information available to choose the most appropriate and the most cost-effective medicines.

We thank everybody for their participation here today. Before we turn to Senator Smith, I want to mention that we have a roll call vote at 11:30 which requires all Senators to be in the chamber. I hope we can move forward with this hearing and maybe conclude so that we will not have to recess for an extended period of time and return.

So now we turn to our esteemed chairman, Gordon Smith, for his opening remarks.

OPENING STATEMENT OF SENATOR GORDON H. SMITH, CHAIRMAN

The CHAIRMAN. Thank you, Senator Kohl. It is a pleasure to work with you. This hearing is very appropriate, very timely, and it was your idea, and we thank you for your leadership.

Also, my colleague in the Senate, Senator Wyden, thank you for your service on this committee as well. Ron Wyden's commitment to seniors and the elderly is legendary in my State, and appropriately so.

We welcome all of you and wish you a good morning. While national health care spending has slowed in recent years, it is projected that total national spending on health care goods and services will reach 18.4 percent of the Nation's gross domestic product by 2014. How the Government and individual citizens spend their health care dollars will continue to be an important policy discussion on Capitol Hill.

One area of health care in which spending is projected to increase significantly in coming years is prescription drugs. Advances in pharmaceutical sciences have provided millions of Americans with the opportunity to live longer, healthier lives, but often at a significant cost.

Over the last several decades, the pharmaceutical industry has spent billions of dollars to promote new prescription drugs to both doctors and consumers. Direct-to-consumer advertising is just one component of a larger marketing effort. But given that spending on such ads has quadrupled since 1998, it is an area that deserves further exploration, especially in connection to how it affects consumer safety and overall prescription drug consumption.

From a positive standpoint, direct-to-consumer drug advertising may encourage individuals who might otherwise not seek health services to see their doctors. This is especially true for individuals who may be suffering from a mental illness, such as depression or bipolar disorder.

A 2003 study showed that approximately 25 percent of surveyed individuals who had discussed an advertised drug with their physicians reported receiving a new diagnosis. Evidence would suggest that advertising can encourage individuals to learn more about symptoms they might suffer from and get treatment for undiagnosed conditions.

Beyond advertising's ability to prompt individuals to seek out health care, there are many other issues that should be explored further by policymakers, industry representatives, and health care advocates. For instance, does the content of direct-to-consumer advertisements appropriately inform individuals of the benefits and risks of new prescription drugs, or are they aimed more at building product loyalty? This is an especially important question to ask in regard to new products entering the market, whose effect on the general population may not be fully known. I am hopeful some of the discussion today can address this concern, as well as other issues relating to better informing consumers through direct-to-consumer ads.

In terms of physician prescribing behavior, it is still unclear how direct-to-consumer advertising affects the decision to prescribe a certain type or brand of prescription drug. We will hear today

about recent research that suggests patient requests for specific drugs may influence doctors' prescribing behavior. However, while such findings highlight an interesting dynamic of the patient-physician relationship, it may be more difficult to explicitly link drug requests to direct-to-consumer advertising.

I should also note that in considering the issue of prescribing behavior, we should not ignore other types of promotional activities, especially those targeted towards physicians and their office staffs.

I invite all witnesses to share their thoughts on the relationship between direct-to-consumer advertising and overall health care consumption. Additionally, I would appreciate any suggestions witnesses might have to offer that improve the process by which information regarding prescription drugs is communicated to the public.

I look forward to a thoughtful exchange today, and I hope this hearing will prompt a broader discussion of the steps interested parties can take to further ensure a more consistent balance between promotional and education content in all forms of prescription drug advertising. Ultimately, we should all be working toward the goal of keeping consumers well informed of important developments in pharmaceutical science so that they can improve their overall health and well-being.

Thank you, Senator Kohl.

Senator KOHL. We thank you, Mr. Chairman, and now we would like to hear from the very fine Senator from Oregon, Ron Wyden.

OPENING STATEMENT OF SENATOR RON WYDEN

Senator WYDEN. Well, thank you, and I guess I should thank all the chairmen that are here today, and I think it is terrific, Senator Kohl, that you developed this idea, but these hearings don't just happen by osmosis. They happen because the Chair wants them to, and I commend Senator Smith, and I very much share his view about the need to educate consumers as well.

I have come to the conclusion on this that the people of this country think prescription drug advertising has just gotten completely out of hand, and that much of the advertising—not all of it, but much of it goes way beyond the legitimate interest in educating the consumer and is primarily used to increase demand and increase profits for the pharmaceutical companies. I have been struck and have actually asked the pharmaceutical representatives why it is that if education is the primary interest here, why is it that only the blockbuster drugs seem to be the ones that get advertised. You don't seem to see the ones, the orphans that can't generate much profit. They don't seem to be the ones that get advertised.

So the question then becomes: What would be an appropriate approach to deal with this issue that particularly is consistent with the Constitution? There is a First Amendment right to communicate, and certainly the companies have asserted it. The companies also get a tax break for using that First Amendment right, so when those purple pills dance across somebody's television set, there is already a taxpayer subsidy for that particular activity. But in fairness to the companies, it is also correct that if somebody advertises for their pizza parlor or some other business, they get a tax break for that as well.

So the question that I have said at least ought to be the start of this debate is: Should there be a double subsidy for these prescription drug ads? The pharmaceutical people already get one subsidy. Should they get a second one? Senator Sununu of New Hampshire and I have concluded that that is where we would draw the line. We would say let us now take the advertising expenses out of the costs at least of Government programs like Medicaid.

Senator Smith in particular has done extraordinary work on the Medicaid program. It is clear that there are going to have to be reforms. The Congressional Budget Office has told us that given the fact that we are going to spend $4 billion a year on prescription drug ads—not my figure; that is from the Wall Street Journal. According to the figures from the Congressional Budget Office, we could get close to half of the savings that are needed for the Medicaid budget target just if we stop the companies from getting a double subsidy and took advertising expenses out of the cost of Government health programs like Medicaid.

So Senator Sununu and I are going to continue to work on that legislation. It is S. 1128, the Pharmaceutical Advertising and Prudent Purchasing Act. It was introduced in May. I want to wrap up just by giving a couple of comments on some charts that we have developed. We have put together some charts that outline the advertising situation.

The first shows the most advertised drugs in our country as of 2003, and you can see many drugs that the consumer and the public is familiar with.

The second chart is the one that I think is particularly troubling. It shows the drugs that are most used by the Medicaid program. These are the top ten drugs that Medicaid pays for with taxpayer dollars for low-income people at a time when the Medicaid program faces the draconian cuts. You can see that of the ten most commonly used drugs in the Medicaid program, four of them are paid for with this double subsidy that I think is so troubling.

The last chart I brought is an indication that highlights the point Senator Kohl made of what is to come. We, of course, are starting very shortly a Medicare prescription drug benefit. We are now talking here about the ten most commonly used drugs in the Medicare program, and virtually all of them are advertised. So, once again, Medicare, like the other programs—the VA, the Public Health Service, and other programs—Government health programs will pay a double subsidy. It seems to me that if the companies get to exercise their First Amendment rights, they get a tax break for exercising their First Amendment rights, at some point you ought to draw the line and say we are not just going to subsidize them again and again and again. Senator Sununu and I have drawn that line in S. 1128 where we would take the advertising expenses out of the cost of government health programs.

I thank the two Chairs, and particularly for giving me a little extra time to walk through our legislation, and I look forward to working with both of them and thank them both for their kind words.

Senator KOHL. Thank you, Senator Wyden.

At this time we will call our first witness, Dr. Rachel Behrman. Dr. Behrman comes from the Food and Drug Administration. She

is the deputy director of FDA's Office of Medical Policy, which oversees the Division of Drug Markets, Advertising, and Communications.

Dr. Behrman, we are very pleased that you are here today, and we welcome your testimony.

STATEMENT OF RACHEL E. BEHRMAN, MD, MPH, DEPUTY DIRECTOR, OFFICE OF MEDICAL POLICY, CENTER FOR DRUG EVALUATION AND RESEARCH, AND DIRECTOR, CROSS-CENTERS INITIATIVES TASK FORCE, OFFICE OF THE COMMISSIONER, U.S. FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Dr. BEHRMAN. Thank you, Senator Kohl, Senator Smith, and Senator Wyden. Good morning. As you mentioned, I am Dr. Rachel Behrman, deputy director of the Office of Medical Policy and director of the agency's Cross-Centers Initiatives Task Force.

Thank you for this opportunity to discuss FDA's role and experience in overseeing the promotion of prescription drugs to consumers. Today I will briefly discuss some of the issues behind the ongoing debate about DTC advertising, many of which have just been touched upon, and then summarize several agency initiatives.

One of our top priorities is ensuring that Americans are educated about their health and treatment options with clear and accurate information. We have all been exposed to DTC ads in print and on television, for example, and perhaps have felt that although DTC advertising has the primary intent of promoting a product, it also has the potential to promote awareness of undiagnosed or undertreated diseases, to promote an understanding of possible treatments, and to foster health-related discussions with physicians. In other words, it is an opportunity for two different interests to align.

But this can only happen if the promotion is done properly if, in addition to being truthful and not misleading, the promotion is clear and accessible to consumers.

Direct-to-consumer advertising has always been legal in this country, although historically it was aimed primarily at physicians, and our regulations do not distinguish between the two audiences. DTC advertising remains a small percentage of all prescription drug promotion, but it has increased sharply since the mid–1990's as broadcast DTC has become more prevalent. This increase has sparked an intense debate about the impact of DTC and about the role of regulation.

Monitoring DTC advertising is a top priority for us, but truthful advertising cannot be achieved unless it accurately communicates and balances the benefit and risk information about a prescription drug. Thus, FDA has undertaken a number of important initiatives to improve the communication of prescription drug information to consumers.

In 2004, we issued two draft guidance documents aimed at improving the quality and usefulness of DTC advertising. The first addressed alternative ways of disclosing risk information in consumer-directed print advertisements. The goal of the guidance is to encourage manufacturers to abandon the dense, tiny-type presentation of risk information and replace it with clear, comprehensible, succinct, and visually accessible paper that can serve as an edu-

cational tool and can stimulate discussion between patients and their health care providers.

The other guidance addresses and encourages what are common called help-seeking advertisements. These are ads that do not mention a particular product but are intended to raise awareness of a particular disease or condition.

In addition, FDA is finalizing a regulation that will completely overhaul the information required to be distributed with prescription drugs. Known as "the package insert," it is the long, complicated, tiny-print label that is tucked into prescription drug packages. When this regulation issues, it will require that a high-level summary of the most important information precede the detailed prescribing information contained in the package insert. This summary, which will be reviewed and approved by the FDA, will enable us and the industry we regulate to more rapidly and easily identify the risk information that should be included in advertising.

This regulation, once issued, will also support the agency's electronic health initiatives, for example, ultimately making it possible for FDA to provide concise, reliable, and up-to-date medical product information available immediately and free of charge on the Internet and in an easily searchable format.

The key issue in the DTC debate is whether it helps or harms Americans. Answering this question requires data. We must know what consumers understand, how they perceive risk information, and what helps them make informed choices, to name just a few of the questions facing us. Therefore, FDA continues to conduct research and last fall published a comprehensive report on patient and physician attitudes and behaviors associated with DTC advertising of prescription drugs.

Our data demonstrate that DTC advertising clearly provides an opportunity to inform. This number will not be a surprise: 81 percent of patients responding to our surveys have been exposed to DTC advertising, and many of them went on to seek more information, usually about the drug but sometimes about their health condition.

On the other hand, our data also show that approximately 60 percent of patients and physicians believe that DTC advertisements overstate the benefits of the product and almost as many believe that the ads understate the risks. This is a problem that must be addressed by the industry we regulate, and so we welcome PhRMA's recent announcement of voluntary guidelines to improve the quality of DTC advertising. These guidelines in particular emphasize compliance with FDA regulations and require advertising to be neither false nor misleading, to make claims only when supported by substantial evidence or substantial clinical experience, and to appropriately balance the risk and benefit information.

Another recent initiative involves the re-evaluation of our regulations. Are these regulations, implemented in the 1960's and without a consumer audience in mind, effective for DTC advertising? To help answer that question and many others surrounding DTC, we have scheduled a public hearing on November 1 and 2 of this year, and we hope to hear a broad range of opinions.

DTC advertising is advertising, but it is also an opportunity—an opportunity to help Americans become better informed about their

health and to reach Americans who may be unaware of or ignoring important health problems. This opportunity should not be missed. Therefore, the agency will continue our research to better understand the effects of DTC advertising and how best to communicate the important information about risks and benefits. We will also continue to closely monitor DTC advertising while working within industry to ensure that all promotion is fully compliant with applicable laws and regulations; and when it is not, we will take appropriate enforcement action.

Finally, we look forward to beginning a thorough evaluation of the regulations that govern promotion, and DTC promotion in particular.

Thank you, and I will be happy to answer any questions.

[The prepared statement of Dr. Behrman follows:]

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

Statement of

Rachel E. Behrman, M.D., M.P.H.

Deputy Director, Office of Medical Policy
Center for Drug Evaluation and Research

and

Director, Cross-Centers Initiatives Task Force
Office of the Commissioner

U.S. Food and Drug Administration

Department of Health and Human Services

"The Impact of Direct-To-Consumer Drug Advertising on Seniors' Health and Health Care Costs"

Before the

Special Committee on Aging

United States Senate

September 29, 2005

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INTRODUCTION

Mr. Chairman and Members of the Committee, I am Rachel Behrman, Deputy Director of the Office of Medical Policy within the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration (FDA or the Agency) and Director of the Cross-Centers Initiatives Task Force in the Office of the Commissioner.

Thank you for the opportunity to discuss the Agency's role and experience in oversight of direct-to-consumer (DTC) advertising. My testimony will review how FDA regulates consumer-directed advertising, the results of recent surveys the Agency has undertaken to ascertain attitudes of consumers and physicians toward this marketing activity, and future plans of the Agency to explore what issues may yet remain to be addressed by our regulation of DTC promotion.

Helping all Americans make better informed decisions concerning their health care is a top priority of the Agency. Opinion surveys conducted by FDA demonstrate that DTC advertising can encourage consumers to seek information about an illness or condition and more information about a drug from their physician or pharmacist. FDA research also demonstrated, however, that patients and physicians believe consumer-directed advertising frequently overstates the benefits of drugs and understates the risks.

Part of FDA's mission to protect the public health is to help ensure that prescription drug information is not false or misleading. This is accomplished through a comprehensive surveillance, enforcement and education program, and by fostering optimal communication of labeling and promotional information to both health care professionals and to consumers.

STATUTORY AND REGULATORY AUTHORITY

FDA regulates the manufacture, sale, and distribution of drugs in the United States under authority of the Federal Food, Drug, and Cosmetic (FD&C) Act, which includes approval of prescription drug labeling that provides information about the use of a drug. Section 502(n) of the FD&C Act provides the Agency with authority to regulate prescription drug advertisements, and the implementing regulations (Title 21, *Code of Federal Regulations* [CFR] section 202.1) provide specifics about the content of such advertisements. Nothing in the law or regulations prohibits DTC promotion in any advertising medium even if the drug being advertised is a controlled substance. The advertising provisions of the FD&C Act do not address the issues of pharmaceutical coverage by insurance companies or drug product price.

Consistent with the First Amendment, FDA may only regulate prescription drug advertising that is false or misleading. To that end, FDA regulations specify, among other things, that prescription drug advertisements cannot omit material facts, and must present a "fair balance"

between benefit and risk information. Further, for print advertisements, the regulations specify that every risk addressed in the product's approved labeling also must be disclosed in the brief summary. For broadcast advertisements, however, the regulations require ads to disclose the most significant risks that appear in the labeling. The regulations further require that broadcast advertisements either contain a brief summary of "all necessary information related to side effects and contraindications" or make adequate provision for dissemination of the product's FDA-approved labeling (and the risk information it contains) in connection with the ad.

With only rare exceptions, primarily for products receiving accelerated approval, FDA cannot require that prescription drug advertisements be reviewed prior to their use. In other words, FDA's review of promotional materials is intended to occur *post hoc* – once the materials have appeared in the public domain. Thus, enforcement actions for advertising violations generally are taken *post hoc* as well. Most of FDA's enforcement actions request that sponsors stop using the violative materials. In the more egregious cases, FDA asks sponsors to run corrective advertisements or issue corrective letters to correct product misimpressions created by false or misleading, materials. Perhaps related to this, frequently sponsors voluntarily seek prior comment from FDA on draft broadcast ads for their products.

Promotional Material and Types of Advertisements

FDA regulates advertisements and other promotional material, commonly referred to as "promotional labeling," disseminated by or on behalf of the advertised product's manufacturer, packer or distributor. Mostly, this means materials that the product's sponsor disseminates or places for publication, which are directed to consumers and physicians, such as ads printed in magazines, journals and newspapers; ads broadcast over television, radio and telephone; brochures, and detailing pieces. According to the October 2002 GAO report entitled, *Prescription Drugs: FDA Oversight of Direct-to-Consumer Advertising Has Limitations*, "Promotion to physicians accounted for more than 80 percent of all promotional spending by pharmaceutical companies in 2001." Therefore, the bulk of the Agency's time spent reviewing promotional material, is spent reviewing materials produced for promotion to health care professionals, such as detail aids used by manufacturer representatives, convention displays, file cards, booklets, and videotapes, which are distinct from advertising directed toward consumers.

Of the three different types of ads that product sponsors use to communicate with consumers, FDA regulates two of them; "product-claim" and "reminder" ads. The third type, "help-seeking" ads are not regulated by FDA.

"Product-claim" ads are those ads which generally include both the name of a product and its use, or make a claim or representation about a prescription drug. Claims of drug benefits, such as safety and effectiveness, must be balanced with relevant disclosures of risks and limitations

of efficacy. This balanced presentation of drug therapy is commonly referred to as "fair balance." In addition, when used in print ads, sponsors must provide a brief summary of risk information included in the product's FDA-approved labeling or, for broadcast "product-claim" ads, provide convenient access to the approved labeling. In our regulations, the phrase "adequate provision" is used to identify the convenient access option.

"Reminder" ads may disclose the name of the product and certain specific descriptive information such as dosage form (i.e., tablet, capsule, or syrup) or price information, but they are not allowed to give the product's indication (use) or to make any claims or representations about the product. Reminder ads specifically are not allowed for products with serious warnings (called "black box" warnings) in their approved labeling. The regulations specifically exempt "reminder" ads from the risk disclosure requirements because historically they were designed generally to remind health care professionals of a product's availability. These ads can be confusing and frustrating to consumers – and potentially misleading – but, increasingly, we find them to be testing the limits of what might be considered a product claim. Because we believe they serve no useful purpose in the DTC arena, and have the potential to cause harm, we welcome the recent announcement from the Pharmaceutical Research and Manufacturers Association (PhRMA) that essentially supports the elimination of this type of advertisement directed at a consumer audience.

"Help-seeking" ads discuss a disease or condition and advise the audience to "see your doctor" for possible treatments. They need not include any risk information. Because no drug product is mentioned or implied, this type of ad is not considered to be a drug ad and is

not regulated by FDA, but we enthusiastically support their use and have issued draft guidance on the subject.

HOW CONSUMER-DIRECTED ADS ARE REGULATED BY FDA

Prior to the early 1980s, prescription products were not promoted directly to consumers and patients. At that time, FDA's regulation of promotional drug material was limited to that which manufacturers prepared to present to physicians and other health care professionals. In the early 1980s, a few companies began advertising products directly to patient audiences (specifically, older people concerned about pneumonia and people taking prescription ibuprofen to treat arthritis pain). Because there was no experience with promotion directed toward consumers, concerns were expressed about its possible effect on public health. The Agency and its stakeholders needed time to assess questions and concerns posed by the newly introduced DTC promotion.

To allow time to evaluate and make this assessment, FDA issued a policy statement on September 2, 1983, requesting a voluntary moratorium on DTC ads. The industry complied with the request thus giving the Agency the time needed to study whether the current regulations developed in the 1960s for prescription drug advertising directed toward health care professionals provided sufficient safeguards to protect consumers when applied to DTC promotion. This also allowed the Agency time for a dialogue among consumers, health professionals, industry, and for interested parties to conduct research on aspects of consumer-

oriented advertising. There was much discussion about DTC advertising including a 1984 symposium sponsored jointly by the University of Illinois and the Stanford Research Institute to discuss consumer-directed prescription drug advertising from a broad research and policy perspective. The voluntary moratorium remained in effect until FDA announced in the September 9, 1985, *Federal Register* (FR) Notice (50 FR 36677) its conclusion that the "current regulations governing prescription drug advertising provide sufficient safeguards to protect consumers."

During the early 1990s, sponsors increasingly used consumer print material (magazines, etc.) to advertise their products. The ads typically included a promotional message together with the brief summary of adverse effects, similar to that used in physician-directed ads. Of note, this type of brief summary statement, which frequently appears in small print using medical jargon, is not helpful for consumers.

In the 1990s, product sponsors also started using television advertisements in a limited fashion. Television advertisements were limited because of the extensive disclosure needed to fulfill the brief summary requirement, and FDA and industry did not believe that it was feasible to disseminate the product's approved labeling in connection with the ad. There was uncertainty about how best to satisfy the risk disclosure requirements and the results typically were unsatisfactory. For example, one method would be to scroll the brief summary on the screen, which would take a minute or more at a barely readable scrolling rate. By the mid-1990s, sponsors were placing "reminder" ads on television because these ads are not required to

include a brief summary. Often these ads were confusing to consumers who were not knowledgeable about the name and use for these products.

In response to increasing consumer demand for information and clarity, FDA issued a *Federal Register* Notice on August 16, 1995, announcing a public hearing to discuss several aspects of DTC advertising and a Notice for further comment on May 14, 1996, to clarify additional issues, including the brief summary requirement. Further, in light of changes in the ability of consumers to get additional product information, FDA began to consider whether broadcast ads could be constructed to ensure access to product labeling information, the only alternative to including the brief summary requirement. FDA considered suggestions about providing access to multiple sources of product labeling as a means of satisfying the requirement that consumers have convenient access to FDA-approved labeling when manufacturers broadcast a "product-claim" ad.

In August 1997, FDA issued a draft guidance (finalized in 1999) entitled, "Guidance for Industry: Consumer-Directed Broadcast Advertisements" (see Attachment A) that clarified the Agency's interpretation of the existing regulations. The Guidance described an approach for ensuring that audiences exposed to prescription drug advertisements on television and radio have convenient access to the approved labeling of the advertised product. The proposed approach consisted of reference in the broadcast ad to four sources the consumer could use to obtain more detailed labeling information: a toll-free telephone number, a website address, a concurrently running print advertisement, and their health care professional. Following a

comment period, and detailed review and consideration of the comments, FDA issued the guidance in final form in August 1999 (64 FR 43197, also found at: *www.fda.gov/cder/guidance/1804fnl.htm*).

FDA continued to recognize that the risk information accompanying consumer advertisements was unsatisfactory and sought ways to remedy this within the existing regulatory framework. In April 2001, FDA issued draft guidance for industry entitled, "Using FDA-Approved Patient Labeling in Consumer-Directed Print Advertisements." The draft guidance described how FDA did not intend to object to the use of certain FDA-approved patient labeling to fulfill the brief summary requirement for prescription drug and biological product print advertisements directed toward consumers. FDA said it would not object to the use of FDA-approved patient labeling if such labeling were reprinted in full and discussed comprehensively in consumer-friendly language the product's most serious and most common risks. FDA believed this labeling contained the information patients likely would find helpful in deciding whether to discuss with their health care provider the possible usefulness of the product for their own health care.

Based on continuing research, including the on-going efforts to modernize the product package insert, in February 2004, FDA published a notice of availability and requested public comment on three draft guidances pertaining to consumer-directed promotion of medical products. These are entitled: "Consumer-Directed Broadcast Advertising of Restricted Devices" "Brief Summary: Disclosing Risk Information in Consumer-Directed Print Advertisements" and

"Help-Seeking and Other Disease Awareness Communications by or on Behalf of Drug and Device Firms." These draft guidances are available on the FDA website at: *www.fda.gov/cder/ddmac/lawregs.htm#Guidances* and the public comments received are available at: *www.fdagov/ohrms/dockets*. Comments on the draft guidances, and resulting research, currently are under consideration.

OVERSIGHT

FDA's Division of Drug Marketing, Advertising and Communications (DDMAC), currently with a staff of approximately 40, are responsible for the review of drug product promotional materials. Under the post-marketing submission requirement, DDMAC received approximately 31,600 pieces of all categories of promotional material in 1999; 32,100 in 2000; 34,200 in 2001, 36,700 in 2002, 40,000 in 2003, and 52,800 in 2004. Certain materials are flagged for expedited review. These include materials that introduce newly approved products or products with new indications, which we refer to as "launch" materials. Also flagged for expedited review are TV and radio advertisements. In addition to promotional materials that are submitted at the time of initial use, DDMAC reviews complaints about promotion from competitors, health care professionals, and consumers; promotional activities in the commercial exhibit halls of scientific meetings, promotional meetings, and evolving technologies.

The total number of DTC broadcast advertisements (TV and radio) submitted to DDMAC in recent years was: 1999 – 293; 2000 – 443; 2001 – 376; 2002 – 486; 2003 – 474; and 2004 - 586. This includes both those advertisements that were proposed but not aired and those that were aired. Attachment B of this testimony shows 126 different products that have been the subjects of broadcast ads since August of 1997. Many of the products have been the subjects of multiple campaigns and many of the campaigns include different length "product-claim" commercials – variations of the initial commercial submitted to the Agency.

DDMAC does not track the number of DTC print ads. Last year, however, DDMAC estimated the consumer pieces to be about one-sixth of the total, or about 8,400. It should be noted that these are not all DTC print and broadcast ads, but also consumer promotional pieces distributed by drug companies directly to consumers or through health care providers to patients.

Many companies send new proposed DTC broadcast concepts to DDMAC for comments in advance of use, although companies are under no obligation to follow DDMAC's advice. Consequently, DDMAC generally does not see the final broadcast ad before the company submits it as part of its post-marketing requirements at the time the ad is first aired on TV or radio.

Educational Programs for Industry

DDMAC aims to increase voluntary compliance by industry through educational programs. These programs include:

- Outreach Programs: FDA staff participates in many panel discussions and presentations for groups including industry, law firms, consultants to industry, and marketing and advertising agencies. These programs are intended to increase the understanding of these groups concerning regulations relating to promotion of prescription drugs so industry can better comply.

- Website Postings: CDER posts on its website all Warning Letters and untitled letters and the cited promotional materials. Industry has noted that these letters serve as useful examples of violations that FDA has acted against and helps them understand what type of promotion is unacceptable.

- Guidances: FDA publishes guidances in areas for which industry seeks clarification. An example is the guidance on broadcast advertisement published in August 1999, following on the draft guidance published in August 1997. Guidances help industry understand FDA's current thinking and how to comply with the regulations.

- Advisory Comments: Even when not required to do so, often companies request DDMAC's review and comments on proposed materials. We

provide this service so companies can ensure that their materials are in compliance with the regulations.

ENFORCEMENT RELATED TO DTC PROMOTION

As stated previously, unless sponsors submit their draft materials for comment before use, DDMAC generally sees the materials at the same time as the public. DDMAC's options to address promotional materials that are false or misleading are:

- Untitled letters –notices of violations issued to sponsors requesting that they discontinue use of the violative materials.
- Warning Letters – issued to sponsors for more serious violations, such as those possibly posing serious health risks to the public.
- Injunctions and consent decrees.
- Referrals for criminal investigation or prosecution.
- Seizures.

FDA attempts to target resources at the violations with the greatest public health impact. Since late 2001, we instituted the policy that all Warning Letters and untitled letters that originate within FDA, including DDMAC letters, must be reviewed and cleared by the Agency's Office of the Chief Counsel (OCC) before issuance. FDA's practice for clearing

DDMAC Warning and untitled letters focuses on assuring that the letters cite the appropriate statutory and regulatory violations and are legally sustainable.

Criteria Used When Issuing an Untitled or Warning Letter

Untitled letters are used for less serious violations than Warning Letters. Violations that might receive an untitled letter may include overstating the effectiveness of the advertised drug product, suggesting a broader range of conditions than the drug was approved for, or making misleading claims because of inadequate context or lack of balancing risk information. Warning Letters address more serious violations, including serious safety or health risks or repetitive violative conduct which, if not promptly and adequately corrected, could lead to enforcement actions without further notice from FDA. Warning Letters generally request that the company disseminate a remedial message to correct the violative ad.

Since August 1997, for **broadcast** advertisements, FDA has issued:

- 53 untitled (or "Notice of Violation") letters on "product-claim" broadcast ads.
- 6 Warning Letters on broadcast ads.
- 15 untitled letters on purported reminder broadcast ads.
- 3 untitled letters on purported "help-seeking" broadcast ads.

Most of the violations cited were because the ad was misleading, e.g., the ad overstated or guaranteed the product's efficacy, expanded the indication or the patient population approved

for treatment, or minimized the risks of the product, through either inadequate presentation or omission of information.

Since August 1997, for **print** advertisements, the Agency has issued:

- 63 untitled letters that addressed DTC print ads or other promotional materials, including purported "reminder" and "help-seeking" materials.
- 6 Warning Letters: four for specific DTC print ads, one that included a DTC print ad as part of an overall misleading campaign, and one for another type of promotional piece.

Generally, the violations for "product-claim" print ads were similar to those cited above. Nearly all "reminder" ad violations were the result of representations about the product that triggered the need for full disclosure of benefits and risks. "Help-seeking" ad violations were due to a particular product being suggested in the message. FDA cannot determine how many specific advertisements serve as the denominator for assessing how many have resulted in enforcement action compared with those that have not.

FDA's DTC PROMOTION RESEARCH

A number of groups, including FDA, have been conducting research on DTC promotion to learn about its effects on consumers and physicians. As part of its commitment to examine the effect of DTC promotion on public health, FDA conducted three national telephone surveys of U.S. adults to ask their views on DTC promotion of prescription drugs and its effects on the

patient-physician relationship. The consumer surveys were conducted in the spring of 1999 and again in the spring of 2002, and one physician survey was conducted in the spring of 2002. FDA held a public meeting on September 22 and 23, 2003, to present this information and give other organizations and individuals an opportunity to present their research to FDA. The transcript of this meeting is available on the Internet at http://*www.fdagov/cder/ddmac/DTCmeeting2003.html*.

In addition, FDA currently is conducting research on the best way to present information in the brief summary, the page of medical information following a print advertisement. As mentioned earlier, reprinting the physician labeling is not helpful to consumers because of small fonts, dense presentation, and highly technical language. FDA is investigating why consumers use the brief summary, what are the best types of information to include, and what are the best formats for presenting the information.

Moreover, FDA plans to begin a number of research projects in the next year, including studies on the presentation of risk information in television DTC advertisements, the use of coupons and free offers in DTC advertising, and the interpretation of common phrases in DTC advertising.

TWO FDA CONSUMER SURVEYS ON DTC PROMOTION

In the two consumer surveys, FDA gave special attention to surveying adults who had recently visited a physician or other primary health care provider (within the last three months).

Participants were asked questions measuring the influence of DTC advertising on attitudes toward prescription drugs, health-related behavior, and on aspects of the doctor-patient relationship. The full report of the surveys is available on the Internet at: *http://www.fda.gov/cder/ddmac/researchka.htm*, and the Executive Summary is contained at Attachment C of this testimony.

The results of the two consumer surveys indicate that DTC advertising is very good at increasing awareness of products and may serve as stimulus for consumers to seek more information about their health and the drug product. Patients who asked about a specific brand of drug were more likely to be prescribed the drug they asked about, compared to patients who simply asked if treatment was available for their condition. Very few patients discuss the cost of treatment with their doctors. Many patients believe the ads overstate how well the drug works and that the ads do not present a fair balance of risk and benefit information about the product.

RESULTS OF FDA's 2002 SURVEY OF PHYSICIANS

FDA's physician survey focused on 500 office-based physicians in the U.S. who were in patient care at least half-time and included 250 primary care physicians (internists, general practitioners, family practitioners, and obstetricians/gynecologists) and 250 physicians in specialty areas targeted by DTC advertising (dermatologists, endocrinologists, allergists/pulmonologists, and psychiatrists). Participants were asked questions about the role

of DTC advertising in influencing physicians' practices and relationship with their patients. The results of the physician survey indicate that:

- Physicians believe that DTC advertising had both positive and negative effects. On the one hand, physicians feel that DTC advertising can increase patient awareness of diseases that can be treated, and prompt thoughtful discussions that result in needed treatments being prescribed. On the other hand, physicians also believe DTC advertising causes patients to think that the drug works better than it really does, that patients do not understand very well the possible risks of the advertised drug, and that DTC advertising confuses patients about the relative risks and benefits of advertised drugs.

- Physicians in this survey indicate that they are comfortable in not necessarily prescribing the advertised drug for reasons including: that a different drug was more appropriate, the drug was not right for the patient, the drug had side effects of which the patient was not aware, and/or a less expensive drug was available. A small percentage of physicians felt pressured to prescribe specific branded drugs.

- In terms of the general impression of the influence of DTC advertising on their patients and practice, responses were evenly divided amongst those who felt that DTC had a positive effect on their patients and practice, those who felt it had a negative effect and those who felt it had no effect at all.

FUTURE AGENCY ACTIVITIES CONCERNING DTC ADVERTISING

FDA is committed to ensuring that its DTC advertising policies promote truthful and non-misleading advertising that helps to better inform consumers about their health and health care choices and prevents potential misconceptions about benefits and risks of the advertised treatment.

November 1 - 2, 2005, Public Hearing On DTC Promotion

On Nov 1-2, FDA will hold a public hearing to provide an opportunity for broad public participation and comment on DTC promotion of regulated medical products, including prescription drugs for humans and animals, vaccines, blood products, and medical devices. FDA is holding this hearing because it believes the Agency, the industry, and other members of the public now have enough experience with DTC promotion to understand what regulatory issues may need to be addressed in new FDA activities. FDA particularly is interested in hearing the views of individuals and groups most affected by DTC promotion, including consumers, patients, caretakers, health professionals (physicians, physicians' assistants, dentists, nurses, pharmacists, veterinarians, and veterinarian technicians), managed care organizations, and insurers, as well as the regulated industry. Although FDA is interested in any pertinent information participants in the hearing would like to share, the Agency is seeking input on a number of specific questions, including:

- Does current DTC promotion present the benefits and risks of using medical products in an accurate, non-misleading, balanced, and understandable way?

- Could changes in certain required prescription drug disclosures – the package insert for print "promotional" labeling and the brief summary for print advertisements – improve the usefulness of this information for consumers?
- Could changes in the requirements for disclosure of certain information in broadcast advertising improve the usefulness of this information for consumers?
- As new communications technologies emerge, they create opportunities for novel approaches to DTC promotion. What issues should the Agency consider with regard to the effect of these technologies on DTC promotion?
- What action should FDA take when companies disseminate violative promotional material to consumers?

Guidance Development

In addition to ongoing guidance discussed elsewhere in this document, FDA is developing draft guidance on the presentation of risk information and plans to issue guidance in this area to industry early next year. The Agency also is conducting research to determine the purpose and optimal content and format for the brief summary in DTC ads. Upon completion and evaluation of this and other research that is being conducted by others, FDA will finalize the draft guidance "Brief Summary: Disclosing Risk Information in Consumer-Directed Print Advertisements." FDA also is working on finalizing the draft guidance "Help-Seeking and Other Disease Awareness Communications by or on Behalf of Drug and Device Firms" and expects to issue the final guidance early next year.

CONCLUSION

Proponents of DTC promotion argue that it has educational value and will improve the physician-patient relationship, increase patient compliance with drug therapy and physician

visits, and generally satisfy consumer interest in obtaining desired drug information. Opponents contend that consumers do not have the expertise to evaluate accurately and comprehend prescription drug advertising, that physicians will feel pressure to prescribe drugs that are not needed, and that DTC promotion will damage the physician-patient relationship and increase drug prices. The Agency believes that, if done properly, prescription drug advertising can provide consumers with important information about new prescriptions and new indications for existing prescription drugs, as well as information about symptoms of treatable illnesses and other conditions. Done properly, prescription drug advertising can assist consumers in taking a pro-active role in improving their health. However, to be of value, these advertisements must not be false or misleading. In particular, FDA remains concerned that a majority of physicians and patients surveyed believe consumer advertisements overstate efficacy and understate risk.

As a result, FDA will continue to closely monitor DTC advertising to help ensure this promotional activity is truthful and not misleading. Through our efforts including a public meeting, guidance development, research – both ours and that of others – FDA intends to examine comprehensively the current regulatory framework to ensure that it addresses appropriately the unique issues and challenges presented by consumer-directed advertising.

This concludes my remarks, Mr. Chairman. I will be glad to answer any questions you may have.

ATTACHMENT A

Guidance for Industry

Consumer-Directed Broadcast Advertisements

U.S. Department of Health and Human ServicesFood and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Veterinary Medicine (CVM)
August 1999

DDMAC

Guidance for Industry

Consumer-Directed Broadcast Advertisements

Additional copies of this Guidance are available from:

Office of Training and Communications Division of Communications Management Drug Information Branch, HFD-210 Center for Drug Evaluation and Research Food and Drug Administration 5600 Fishers Lane, Rockville, MD 20857 (Phone 301-827-4573) Internet: http://www.fda.gov/cder/guidance/index.htm.

or

Office of Communication, Training and Manufacturers Assistance, HFM-40 Center for Biologics Evaluation and Research Food and Drug Administration 1401 Rockville Pike, Rockville, MD 20852-1448 Internet: http://www.fda.gov/cber/guidelines.htm. Fax: 1-888-CBERFAX or 301-827-3844 Mail: the Voice Information System at 800-835-4709 or 301-827-1800

or

Communications Staff (HFV-12)
Center for Veterinary Medicine (CVM)
7500 Standish Place, Rockville, MD 20855 (Tel) 301-594-1755
http://www.fda.gov/cvm

U.S. Department of Health and Human Services Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Veterinary Medicine (CVM)
August 1999

DDMAC

GUIDANCE FOR INDUSTRY[1]

Consumer-Directed Broadcast Advertisements

I. INTRODUCTION

This guidance is intended to assist sponsors who are interested in advertising their prescription human and animal drugs, including biological products for humans, directly to consumers through broadcast media, such as television, radio, or telephone communications systems.[2]

II. BACKGROUND

The Federal Food, Drug, and Cosmetic Act (the Act) requires that manufacturers, packers, and distributors (sponsors) who advertise prescription human and animal drugs, including biological products for humans, disclose in advertisements certain information about the advertised product's uses and risks. For prescription drugs and biologics, the Act requires advertisements to contain "information in brief summary relating to side effects, contraindications, and effectiveness" (21 U.S.C. 352(n)). The resulting information disclosure is commonly called the *brief summary*.

The prescription drug advertising regulations (21 CFR 202.1) distinguish between print and broadcast advertisements. Print advertisements must include the brief summary, which generally contains each of the risk concepts from the product's approved package labeling. Advertisements broadcast through media such as television, radio, or telephone communications systems must disclose the product's major risks in either the audio or audio and visual parts of the presentation; this is sometimes called the *major statement*. This guidance does not address the major statement requirement.

Sponsors of broadcast advertisements are also required to present a brief summary or, alternatively, may make "adequate provision ... for dissemination of the approved or permitted package labeling in connection with the broadcast presentation" (21 CFR 202.1(e)(1)). This is referred to as the *adequate provision* requirement. The regulations thus specify that the major

[1] This guidance has been prepared by the Intra-Agency Group on Advertising and Promotion at the Food and Drug Administration. This guidance represents the Agency's current thinking on procedures to fulfill the requirements for disclosure of product information in connection with consumer-directed broadcast advertisements for prescription human and animal drugs, and human biological products. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

[2] This guidance is not intended to cover the advertising of restricted medical devices, which are subject to the requirements of section 502(r) of the Federal Food, Drug, and Cosmetic Act.

statement, together with adequate provision for dissemination of the product's approved labeling, can provide the information disclosure required for broadcast advertisements.

The purpose of this guidance is to describe an approach that FDA believes can fulfill the requirement for *adequate provision* in connection with consumer-directed broadcast advertisements for prescription drug and biological products. The approach presumes that such advertisements:

! Are not false or misleading in any respect. For a prescription drug, this would include communicating that the advertised product is available only by prescription and that only a
prescribing healthcare professional can decide whether the product is appropriate for a patient.

! Present a fair balance between information about effectiveness and information about risk

! Include a thorough *major statement* conveying all of the product's most important risk information in consumer-friendly language.

! Communicate all information relevant to the product's indication (including limitations to use) in consumer-friendly language.

III. FULFILLING THE *ADEQUATE PROVISION* REQUIREMENT

A sponsor wishing to use consumer-directed broadcast advertisements may meet the adequate provision requirement through an approach that will allow most of a potentially diverse audience to have reasonably convenient access to the advertised product's approved labeling. This audience will include many persons with limited access to technologically sophisticated outlets (e.g., the Internet) and persons who are uncomfortable actively requesting additional product information or are concerned about being personally identified in their search for product information. One acceptable approach to disseminating the product's approved labeling is described below. This approach includes the following components.

A. Disclosure in the advertisement of an operating toll-free telephone number for consumers to call for the approved package labeling. Upon calling, consumers should be given the choice of:

! Having the labeling mailed to them in a timely manner (e.g., within 2 business days for receipt generally within 4-6 days); or

! Having the labeling read to them over the phone (e.g., by offering consumers a selection of prerecorded labeling topics).

B. Reference in the advertisement to a mechanism to provide package

consumers with restricted access to sophisticated technology, such as the Internet, and those who are uncomfortable actively requesting additional product information or are concerned about being personally identified in their search for product information. One acceptable mechanism would be to provide the additional product information in the form of print advertisements appearing concurrently in publications that reach the exposed audience. The location of at least one of these advertisements would be referenced in the broadcast advertisement. If a print advertisement is part of an adequate provision procedure, it should supply a toll-free telephone number and an address for further consumer access to full package labeling. This mechanism of providing access to product labeling has the advantage of also providing considerable information in the form of the required brief summary and in the advertising text itself.

When a broadcast advertisement is broadly disseminated, FDA believes that ensuring that passive and privacy-sensitive information seekers have adequate access to detailed product information is critical to complying with the *adequate provision* regulatory requirement. Thus, print advertisements associated with broadly disseminated broadcast advertisements should be comparably broadly disseminated in terms of the targeted audiences.

An alternative mechanism for providing private access to product information would be to ensure the availability of sufficient numbers of brochures containing package labeling in a variety of publicly accessible sites (e.g., pharmacies, doctors' offices, grocery stores, public libraries). Brochures should be available at enough sites so that most consumers exposed to the broadcast advertisement can obtain the labeling without traveling beyond their normal range of activities. This alternative mechanism is likely to be logistically feasible only when the associated broadcast advertising campaign is relatively limited in audience reach.

C. Disclosure in the advertisement of an Internet web page (URL) address that provides access to the package labeling.

D. Disclosure in the advertisement that pharmacists, physicians (or other healthcare providers), or veterinarians (in the case of animal drugs) may provide additional product information to consumers. This statement should communicate clearly that the referenced professional is a source of additional product information.

Telephone advertisements that make a product claim (not reminder advertisements) occur when there is a telephone communication between an individual and a product's sponsor where both a product name and a representation or suggestion relating to a product (e.g., its indication) are disclosed by the sponsor. Under these circumstances, such advertisements are subject to the disclosure requirements of the Act and the regulations. However, telephone advertisements are different from advertisements broadcast through television and radio. By participating in the telephone communication, the consumer has already indicated his or her willingness to discuss the topic or receive additional information. Consequently, adequate provision for disseminating product labeling in connection with telephone advertisements may be achieved with fewer of the components listed above.

For such advertisements, adequate provision could consist of the availability of the option of having product labeling mailed to the caller in a timely manner (e.g., within 2 business days for receipt generally within 4-6 days), or having the labeling read to them over the phone (e.g., by allowing consumers to select from prerecorded labeling topics), as well as disclosing that healthcare providers are a source of additional product information.

When a broadcast advertisement is presented in a foreign language, the information sources that are part of the advertisement's "adequate provision" mechanism (i.e., print advertisements or brochures, web sites, toll-free telephone number recorded messages or operators) should be in the language of the broadcast ad. Regardless of the language used for the advertisement, current broadcast advertising regulations require the dissemination of approved product labeling, which, in most cases, must be in English, and is generally written in language directed to healthcare professionals. The Agency strongly encourages sponsors to consider the benefits of ***also*** providing consumers with nonpromotional, consumer-friendly product information in the language of the broadcast ad (e.g., FDA-approved patient labeling or accurate, consumer-friendly translations of product labeling information).

The FDA encourages sponsors who use this *adequate provision* mechanism to collect relevant data on consumer use and make their findings publicly known. FDA also encourages sponsors and other interested parties to make known their research relating to the overall effects of DTC promotion on the public health.

ATTACHMENT B:

Prescription Drug Product Ads Broadcast Directly to Consumers Since 8/97
By Drug Category
Includes Product Claim Ads and Reminder Ads
As of 8/5/05

Category	Product
Cholesterol/Heart Disease	Altace Crestor Lescol Lipitor Plavix Pravachol Vytorin WelChol Zocor
Osteoporosis/Menopause	Actonel Boniva Evista Femring Fosamax Premarin Prempro
Mental-Health	Buspar (persistent anxiety) Effexor XR (radio) (depression) Paxil (social or generalized anxiety disorder) Paxil CR (depression, social anxiety disorder) Prozac (depression) (infomercial) Sarafem (PMDD) Strattera (ADHD, ADD—adults only) Wellbutrin SR (depression) Wellbutrin XL (depression) Zoloft (depression, PTSD, panic disorder, social anxiety disorder)
Smoking Cessation	Nicotrol Inhaler Zyban
Diabetes	Avandia Glucophage XR (radio) Lantus

Asthma	Accolate Advair Diskus Flovent Singulair
GERD-Related Heartburn	Nexium (EE; stomach ulcer from NSAIDs) Prevacid (EE) Prilosec Protonix (EE) Omeprazole (generic)
Obesity	Meridia Xenical
STDs	Aldara (genital warts) Valtrex (genital herpes)
Arthritis	Celebrex Enbrel (rheumatoid) Humira (rheumatoid) Mobic (radio) Remicade (rheumatoid) Vioxx
Contraception	Depo-Provera NuvaRing Ortho Evra Ortho Tri-Cyclen (and acne) Ortho Tri-Cyclen Lo Plan B (radio) Seasonale Yasmin
Allergies	Allegra Clarinex Claritin Tablets Claritin Syrup (R only) Claritin D-24 (R only) Flonase Nasacort Nasacort AQ Nasonex Patanol (ocular) Rhinocort AQ Singulair Zaditor (ocular) Zyrtec

Acute Otitis Media	Omnicef (radio) Rocephin injection Zithromax oral suspension
Respiratory Tract Infections	Avelox (radio)
Influenza	Relenza Tamiflu
Overactive Bladder	Detrol Detrol LA Ditropan XL Vesicare
Migraines	Imitrex Relpax (radio) Zomig
Insomnia	Ambien Lunesta Sonata
Skin/Hair-Related	Botox Cosmetic (brow lines--temporary) (radio-R only) Denavir (cold sores) Differin (acne) Elidel (eczema) Enbrel (mod. to severe plaque psoriasis) Lamisil (nail fungus) Luxiq (scalp psoriasis/radio) MetroGel (rosacea) Ortho Tri-Cyclen (acne/contraception) Propecia (male baldness) Protopic (eczema) Retin-A Micro (acne) Valtrex (cold sores) Vaniqa (unwanted facial hair)
Erectile Dysfunction (ED)	Cialis Levitra MUSE Viagra (R only)

Other

Androgel (hypogonadism/low testosterone)

Aricept (Alzheimer's)

Avodart (benign prostate enlargement)

Celebrex (acute pain)

Cerezyme (Gaucher disease/radio)

Combivir (HIV/radio)

Covera HS (hypertension)

Diflucan (vaginal fungal infection)

Epi-Pen (anaphylaxis)

Flexeril (muscle spasm)

Flomax (benign prostatic enlargement)

Neulasta (chemo-related neutropenia)

Periostat (periodontitis aid)

Procrit (specific anemia conditions)

Quadramet (pain from certain bone cancers)

_____ Restasis (tear production for chronic dry eye)

Serevent (COPD)

Zelnorm (irritable bowel syndrome (IBS) with constipation)

Zelnorm (chronic idiopathic constipation)

ATTACHMENT C

Patient and Physician Attitudes and Behaviors Associated With DTC Promotion of Prescription Drugs —

Summary of FDA Survey Research Results

Executive Summary
November 19, 2004

Kathryn J. Aikin, Ph.D.
Division of Drug Marketing, Advertising, and Communications
Center for Drug Evaluation and Research
Food and Drug Administration

John L. Swasy, Ph.D.
Kogod School of Business
American University

Amie C. Braman, Ph.D.
Division of Drug Marketing, Advertising, and Communications
Center for Drug Evaluation and Research
Food and Drug Administration

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research

EXECUTIVE SUMMARY

Historically, prescription drug advertising in the United States was directed primarily toward health professionals, rather than consumers. Direct-to-consumer (DTC) prescription drug advertising, however, began to appear in print as early as the 1980s and spread increasingly to broadcast formats after the publication in 1997 of the FDA guidance for industry, *Consumer-Directed Broadcast Advertisements*.[1] As the amount and visibility of DTC promotion increased, calls for research investigating the role of DTC advertising in either creating benefits or causing problems for consumers and the healthcare system intensified. To evaluate the effects of the guidance and DTC broadcast advertising, in general, on the public health and on doctor-patient interaction, FDA conducted two surveys of patients and one survey of physicians. These surveys explored patient and physician perspectives on DTC advertising as it relates to the healthcare experience. Findings indicate that DTC advertising has important positive and negative effects. The following summary provides a brief overview of the major findings from the three surveys.

PATIENT SURVEYS

Because DTC advertising for prescription drugs targets consumers, particularly those who might have a condition the drug treats, FDA surveyed samples of adults to assess their exposure to, perceptions of, and attitudes toward DTC advertising. FDA limited the sample to consumers (patients) who had visited a healthcare provider within the last 3 months because these individuals could also provide insight on how DTC advertising influenced their relationship and interactions with their health professionals. Two national telephone surveys were conducted in 1999 (response rate: 65%; sample size = 960) and 2002 (response rate: 53%; sample size = 944). The two surveys were designed to be comparable; minor modifications were made in 2002 for clarity or general improvement.

The main objective of the patient studies was to assess the variety of ways DTC advertising could influence the doctor-patient interaction. Both the 1999 and 2002 patient surveys queried respondents about:

- Their awareness of DTC advertising
- The processes used in seeking more information and asking questions about advertised drugs
- Specific behavior in raising questions and conversing with their healthcare professional
- Their general opinions of DTC advertising

[1] FDA, guidance for industry, *Consumer-Directed Broadcast Advertisements* (August 9, 1999; 64 FR 43197; see also Appendix A.

Findings

The patient studies revealed a nearly universal awareness of DTC advertising, with 81 percent reporting exposure to broadcast or print promotion in 2002, an increase from 72 percent in 1999 (all differences reported are statistically significant at the 5 percent level). Although television was the most common vehicle of exposure, with print advertisements a close second, patient awareness of advertisements on the Internet increased from 1999 to 2002. Patients also reported substantial exposure to advertisements in grocery stores and pharmacies. Regardless of whether they understood the content, most patients knew that DTC advertisements typically contain both benefit and risk information.

Seeking Information

DTC advertisements prompted a sizable percentage of patients to seek additional information about the drug, the condition it treats, or health in general. In 2002, 43 percent of respondents reported that an advertisement caused them to look for more information, either about the drug or about their health. The ***most commonly reported sources*** of this additional information were healthcare providers. Eighty-nine percent (89%) of respondents reported obtaining information from their doctors, and 51 percent obtained information from their pharmacists. A sizable proportion of respondents also gathered information from reference books (40%) and from friends, relatives, and neighbors (38%). The number of people searching the Internet for drug or health information jumped considerably—from 18 percent in 1999 to 38 percent in 2002—with information about risks being most commonly sought.

Far more people looked for information about side effects than about benefits (61% vs. 10%). Few people spontaneously reported that they search for information about cost (4%). DTC advertisements also prompted some people to seek information about new or previously untreated conditions, although the number of people who said that a DTC advertisement caused them to talk to a doctor about such conditions decreased from 27 percent in 1999 to 18 percent in 2002.

Visits to the Healthcare Provider

• Visit prompting

Our data show that people do not report DTC advertising as a primary reason for initiating a visit to the doctor. Only 4 percent of patients said they visited their doctor because of a DTC advertisement. Instead, health-related problems, such as previous conditions and check-ups, were the most common reasons given.

• Question generation

DTC advertising and other sources did appear to play a role in generating questions for the doctor. About one third of respondents indicated that a DTC advertisement had generated a question for their doctor, similar to the number that reported friends and family members as a source of questions. Approximately 20 percent reported that a reference book sparked a question.

• Expectations about receiving prescription drugs

There have been concerns that DTC advertising has the potential to create general expectations about receiving prescriptions. Our research does not provide strong support for this concern. Approximately 42 percent of patients expected a prescription at their most recent visit with their physicians. Of these patients, the greatest percentage (63%) said this was because they expected a refill for a current prescription. Another 17 percent said that they expected a prescription because they were sick and thought or knew they had a condition that required treatment. Only 6 percent said that they expected a prescription because of an advertisement they saw on television, and 5 percent said their expectations stemmed from an advertisement in a magazine. Note that these reasons are not mutually exclusive; patients may have had more than one reason for expecting a prescription (e.g., respondents could have seen an advertisement for a drug they were currently taking).

• Asking behaviors

In both 1999 and 2002, the percentage of patients asking their doctor whether a prescription was available to treat their conditions remained constant at about 32 percent. ***Of these respondents***, 39 percent asked about a specific brand. Patients described their physicians' reactions as nearly uniformly positive when they asked about a prescription drug. Over 90 percent reported that their doctor welcomed their questions, and 83 percent reported that the doctor responded as if their questions were a normal part of the visit.

• Prescribing response

About half of the patients reported that the doctor prescribed the drug they had asked *about*. Another 41 percent of patients were told to change their behavior or diet, and about a third received a recommendation for a different prescription drug. Although all patients were equally likely to receive a recommendation to make lifestyle changes or to use over the counter (OTC) or generic drugs, patients who asked specifically about a particular brand were more likely to receive a prescription for the requested drug than those who simply asked whether there was a prescription treatment available for them.

Patient Opinions about DTC Advertising

The surveys also measured patients' opinions about various positive and negative effects of DTC advertising. Because the data are most recent, the 2002 percentages are reported in this summary, but in some cases there were substantial differences between the 1999 and 2002 data. These differences are noted below. None of the differences were moderated by demographic characteristics or health conditions.

• Information

Patient perceptions of the type, quantity, and implications of the information they glean from advertisements are important considerations when assessing the effects of DTC advertising. Generally, about three out of four respondents (77%) agreed that DTC advertisements increase awareness of new drugs (a decline from 86% in 1999). Fifty-eight percent (58%) felt the ads provide enough information to make a decision about whether to discuss the drug with a doctor (a decline from 70%). In terms of specific content within the ads, 60 percent felt the ads do not provide enough information about risks, and 44 percent believed the ads lack adequate benefit information. Finally, 39 percent of respondents thought that DTC advertisements encourage patients to look for more information about potentially serious medical conditions (this question was asked only in 2002).

• Influence on relationship with healthcare provider

Seventy-three percent (73%) of patients agreed that the ads do not minimize the role of the physician in product decisions. Forty-three percent (43%) felt the ads help them have better discussions with their doctor (a decline from 62%). Moreover, 10 percent of patients were reluctant to talk to their doctors about an advertised drug for fear of implying a distrust of the doctor (an increase from 7%).

• Overstatement of benefits

Two questions in the 2002 survey addressed the issue of accuracy in DTC advertisements, particularly with regard to claims that sponsors make. A little more than half (58%) believed the ads make the products seem better than they really are. Forty-two percent (42%) felt the advertisements make it seem like the drug will work for everyone.

• Effects on own health

Finally, patients were asked about how DTC influences their own health. Thirty-two percent (32%) felt the ads help them make better health decisions (a decline from 47%). Eighteen percent (18%) of respondents agreed that DTC advertisements remind them to take their medications, whereas 17 percent reported that the advertisements cause anxiety about their health. These last two questions were not asked in 1999.

• General attitudes

About a third of respondents (32%) indicated that they "like seeing" DTC advertisements in 2002, a substantial decline from 1999, when 52 percent reported that they "liked seeing" DTC advertisements.

Other Important Findings

• Brief summary

The *brief summary*, a section of medical information that accompanies the main display portion of all print DTC advertisements, is designed to provide detailed risk information in a publicly accessible, yet anonymous, environment. Overall, patients in the 2002 survey expressed an interest in the information provided in all parts of a print advertisement when they had a reason to consider the drug. About 78 percent of respondents reported reading all or almost all of the main body of the advertisement when interested, and 45 percent of patients reported reading all or almost all of the brief summary when they were interested in the drug. Despite this desire for information, half of those who read at least some of the brief summary described it as difficult to read.

• Cost issues

Finally, respondents in our surveys reported rarely talking to their doctor about the cost of prescription drugs. Forty percent (40%) of respondents indicated that they never discuss this issue with their healthcare provider, whereas only 16 percent reported discussing it frequently. Patients who were female, in poor health, taking one or more prescription drugs, and lacking a prescription drug insurance plan were most likely to ask their doctors about the cost of treatment.

PHYSICIAN SURVEY

The third survey, conducted in 2002, questioned office-based physicians (response rate: 46%; sample size = 500) about the role of DTC in influencing physicians' practices and relationships with their patients. The 250 primary care physicians (including internists, general practitioners, family practitioners, and obstetricians/gynecologists) and 250 specialists (including dermatologists, endocrinologists, allergists/pulmonologists, and psychiatrists) in this survey were chosen randomly from the American Medical Association's Physician Masterfile, which contains a listing of all physicians who have graduated from medical school in the United States. Specialties were selected to reflect those areas of therapy in which DTC advertising was most prominent at the time of the study.

The 2002 physician questionnaire (Appendix B) asked for information regarding the frequency of questions physicians received from patients, physicians' responses to questions regarding patient questions, and prescribing behaviors involved in a recent, specific encounter in which a DTC-advertised drug was discussed. Finally, general questions were asked about physicians' opinions regarding DTC advertising.

Findings

Physicians reported an increase in the frequency of patient questions about healthcare topics during the last 5 years in all areas except OTC drugs. The most frequently asked

questions were about drug treatments, with 85 percent of physicians reporting that their patients asked about prescription drugs frequently ("often/all the time") and 62 percent reporting that their patients asked about generic drugs frequently. Primary care physicians were significantly more likely than specialists to report an increase in patient questions about prescription drugs.

Specific Patient Encounters

Physicians were asked to focus on a specific, recent patient encounter in which a patient had initiated discussion about a prescription drug the patient had seen advertised. Physicians were then asked to describe in their own words specific benefits and problems that arose because of this exposure.

• Benefits and problems of patient DTC exposure

Forty-one percent of physicians reported that DTC exposure led to benefits, whereas 18 percent reported that the exposure led to problems. Benefits included better discussions, greater awareness of treatments, and DTC as a source for informing and educating patients. Problems included the time needed to correct misconceptions, requests for unnecessary drugs, and requests for one prescription treatment when another treatment was effective. Overall, 73 percent of physicians indicated that their patient in this encounter asked thoughtful questions because of the DTC exposure. However, 41 percent of all physicians indicated that their patient was confused about the effectiveness of the drug because of the DTC advertisement.

• Patient drug requesting behavior

The physician survey distinguished between patients asking ***if*** there was a prescription drug to treat their problem and those asking ***for*** a particular prescription drug. Eighty-six percent (86%) of physicians recalled patients asking about a prescription drug, and 88 percent of these physicians reported that patients had the condition the drug treats. Although primary care physicians received more requests for a prescription treatment ***in general*** than did specialists (60% vs. 44%), the likelihood of prescribing the requested drug was similar (77% vs. 74%). When asked for a specific brand name drug, however, primary care physicians were both more likely to receive requests than specialists (65% vs. 52%) and also more likely to prescribe the drug (64% vs. 46%).

• Denial of requests

Physicians gave many reasons for not prescribing a requested drug. Among all physicians, the most frequently mentioned reasons were that the drug was not right for the patient and that another drug was more appropriate. Primary care physicians and specialists differed, however, in their primary reasons for not prescribing the requested drug. Primary care physicians reported not prescribing primarily because of the availability of a less expensive drug, the patient did not require a prescription drug, or the patient could engage in behavioral and diet changes. Specialists tended to decline the

request because a different drug was more appropriate, the drug was not right for the patient, or the drug had side effects unknown to the patient.

• Pressure to prescribe

About half of all physicians reported no pressure to prescribe, and 91 percent of physicians reported that the particular patient they recalled did not attempt to influence their treatment in a manner that would have been harmful to the patient. Primary care physicians did report more pressure to prescribe than did specialists, however, with 22 percent of primary care physicians feeling "somewhat" or "very pressured" to prescribe a drug, compared with 13 percent of specialists. Approximately 73 percent of primary care physicians reported that they thought patients came to the appointment expecting a prescription, whereas 63 percent of specialists felt the same way. Primary care physicians were more likely to say that this expectation influenced their decision to prescribe.

General Opinions about DTC Advertising

In addition to examining physicians' recall of recent, specific patient encounters, the study also investigated physicians' general opinions of the influence of DTC advertising on their patients and practices.

• Opinions about patient understanding

Doctors perceived differing levels of patient understanding about DTC advertised drugs. On one hand, more than 75 percent believed that their patients understood that these drugs are available only by prescription (92%), that only a doctor can make the decision about the appropriateness of the drugs (82%), and that patients understood the benefits of the drugs (78%). On the other hand, fewer than half believed that patients understood the risks and possible negative effects of the drugs (40%), the limitations of drug efficacy (30%), and the type of person who should avoid the drugs (25%).

• Opinions about problems

Physicians were also asked their perceptions of general problems arising from their patients' exposure to DTC advertising. A majority of all physicians felt that patients confuse the relative risks and benefits of DTC-advertised drugs (65%) and that these advertisements lead patients to overestimate the efficacy of the drugs (75%). Smaller percentages of physicians believed that DTC advertising causes patients to question their diagnoses (38%) and that the advertising led to tension in the doctor-patient relationship (28%). In general, primary care physicians were more likely than specialists to indicate that DTC advertising causes problems for their patients and practice.

• Opinions about benefits

With regard to general benefits of DTC advertising, 72 percent of physicians agreed that DTC advertising increases awareness of possible treatments, and 44 percent of physicians believed that it facilitates earlier awareness of health conditions. About a third of physicians thought that DTC advertising increases the likelihood of proper medication usage, and a third believed it helps patients maintain their treatment over time.

• Overall impressions

At the end of the interview, physicians were asked to give their general impressions of the influence of DTC advertising on their patients and practice. Responses were evenly divided, with about one-third each indicating that it had a positive effect, a negative effect, or no effect at all. Primary care physicians (38%) were more likely than specialists (27%) to rate the overall influence of DTC advertising as having a somewhat or very negative effect on their patients and practice.

CONCLUSIONS

The opinions and experiences of patients and physicians are critical to an evaluation of how DTC advertising affects public health. DTC advertising may potentially affect this interaction by motivating information seeking, healthcare visits, questions, and/or requests. Ultimately, such motivation can have both positive and negative effects.

The three surveys conducted by FDA found both positive and negative effects of DTC advertising on doctor-patient interaction. By and large, DTC advertising seems to increase awareness of conditions and treatments, motivate questions for the healthcare provider, and help patients ask better questions. Our data provided no evidence of increased visits as a result of DTC advertising, and few patients reported that DTC advertising motivated physician visits. On the contrary, most people reported that health reasons prompted their visits.

It is clear, however, that DTC advertising also has effects that can be troubling. Although few physicians report excessive pressure to prescribe requested drugs from patients who have seen DTC advertisements, nearly half report feeling at least a little pressure to prescribe. Both patients and doctors indicate that DTC advertisements overstate drug efficacy and do not present a fair balance of benefit and risk information. Patients gave only modest ratings to the understandability of the brief summary included in print advertisements, information that is meant to provide a more complete picture of the advertised product's risks. They also expressed some negative opinions about DTC advertising. Perhaps more important, fewer patients in the 2002 survey than in the survey conducted 3 years earlier indicated that DTC advertising was useful in terms of their interaction with their doctor and their healthcare decision making.

We continue to encourage research on all aspects of potential DTC influence on the interaction between patients and their physicians. The relationship between patients and physicians is essential for the proper dissemination of prescription drugs. Any influence that DTC advertising has on this special relationship may have broader implications for healthcare in general.

Senator KOHL. Thank you, Dr. Behrman.

Dr. Behrman, in the last year, I understand that FDA has issued 17 warning letters to drug companies regarding misleading advertising. While this may not seem like a lot, it is considerably more than in the past two years.

Dr. BEHRMAN. Yes.

Senator KOHL. To what do you attribute this increase? Is it a push for greater scrutiny from your agency? Is it that more drugs are on the air than ever before or more misleading drugs on the air?

Dr. BEHRMAN. There are two parts to the answer to that question. One, I believe, part of what you are asking me is are the ads getting worse, and the other is why this shift in more warning letters as compared to what we call untitled letters, which are lesser violations. In part, we have, because of resource constraints, made a very conscious and determined effort to focus on the most egregious violations and, therefore, focus more on the kinds of ads that might prompt a warning letter. That is part of the answer, and, again, part of the answer might be that it appears to us—and, again, we tend to see the worst—that there has been somewhat of a trend to ads we consider more violative.

Now, just in the last few months, we have been encouraged in that we have seen a couple of ads that really have broken a new mold and actually have done what we have all been talking about a little bit this morning, which is take more of an opportunity to inform and educate at the same time promoting the product.

Senator KOHL. Dr. Behrman, as you know, spending on DTC advertising of prescription drugs more than quadrupled between 1996 and 2003, yet there has not been a comparable increase in your staff and budget at the FDA to police all of these ads. PhRMA's new guidelines are calling for companies to submit all new TV ads to the FDA before they air. Does the FDA have the resources to do their job? What additional tools would you need?

Dr. BEHRMAN. Well, I am not here asking for resources, although asking a manager if they want more resources, I think, is very much like asking a child if they want another cookie. It is always very hard to say no.

We are very proud of our efforts. We prioritize. We target. We have not increased to the same extent, obviously, that advertising has. As you said, it is a program, if you will, the promotions are over $20 billion a year. DDMAC, the Division of Drug Marketing, Advertising, and Communications, is staffed by a staff of 40, a very dedicated and capable staff, but a staff of 40. So we prioritize, and we believe that we have a vibrant program.

Senator KOHL. As you, of course, know, Bristol-Myers Squibb recently announced a 1-year moratorium on ads for all newly approved drugs in an effort to allow physicians enough time to fully understand the appropriate use of their medicines. Would the FDA support a similar moratorium on all newly approved drugs?

Dr. BEHRMAN. Again, there are two parts to the answer. One, under our regulations and under our law and under our Constitution, DTC advertising is legal. I think what is of keen interest to the agency, which I tried to point out, are our other efforts to make sure that physicians and patients and consumers have other ave-

nues of access to information. We as an agency are extremely good at analyzing data. We have not been as good in the past about providing that data, improving our website, improving the package insert, which, when our content and format reg is finalized, will revolutionize package insert information and make it accessible in hand-held and make it accessible over the Internet. So we are focused very much on other avenues of information.

Senator KOHL. Thank you, Dr. Behrman.

Mr. Chairman.

The CHAIRMAN. Thank you, Senator Kohl.

Dr. Behrman, I am going to ask this question just for my own interest about your relationship with PhRMA and drug companies when you work out disclaimers. I always get a chuckle out of their ads, frankly, because they claim hypothetically if you take this, it will cure your hemorrhoids, but you are going to have a heart attack. What kind of dynamic is there between you? Is it contentious, or do the companies see these tag lines, these disclaimers, these warnings, as protecting them against liability? They certainly would cause me not to take the drugs.

Dr. BEHRMAN. I cannot speculate on what PhRMA thinks or what actually any individual company thinks because, remember, the ads are developed by the company, not by PhRMA.

The CHAIRMAN. Right.

Dr. BEHRMAN. It is also worth pointing out, as I am sure you know, that our enforcement process is post hoc. Companies are not, except in very rare circumstances, obligated to show us an ad before it airs. They are obligated to show us the ad at the time it airs, and then we are in this post hoc enforcement mode.

Just of note, there have been ads for certain conditions where the side effect profile is so unappealing—and this is for some of the obesity drugs—that DTC advertising was, I believe, deemed by the companies as, again, not sensible. But we are very interested in how to properly communicate risk information and to do it in such a way that it doesn't—you know, the hemorrhoid/heart attack example is an example, but what if you truly have a serious condition such as diabetes, but you find the recitation of whatever frightening? This is not what we want. We want clear, accurate communication of information and in a balanced way in the ad. That is what we believe the regulations demand, and that is what we are doing research to better understand how to accomplish.

The CHAIRMAN. Well, I think it is important that accurate appear in ads, frankly, because while there is a First Amendment right, we don't live in a snake-oil age. They need to have information regarding risks.

Dr. BEHRMAN. Exactly. One question we are bringing to this public meeting, this Part 15 hearing in November, is given that it is to a consumer audience, what is the bare minimum, if you will, of contextual information about the disease, about the condition, about other therapies that must be provided so that it is truthful and not misleading? You have the hemorrhoid and heart attack. Ours is the risk information is in Italian and the ad is in English. Is that permissible?

The CHAIRMAN. Yes. Well, I just think you are performing very important work for consumers. If the companies, are going to exer-

cise their right to advertise directly to consumers, it is important that people know whether the cure is worse than the disease.

Dr. BEHRMAN. Worse, or inappropriate for them and they should not even bring it up.

The CHAIRMAN. There really does need to be an educational component that may be at cross purposes with building brand loyalty. But that is the world we live in.

Thank you.

Senator KOHL. Thank you, Mr. Chairman.

Senator Wyden.

Senator WYDEN. Thank you, Mr. Chairman. Both of you have asked good questions. I just have a couple of quick follow-ups.

What do you do by way of defining when a company goes over the line? You said that you try to deal with the most egregious kinds of claims, which certainly is in the public interest. But how do you define that? How do you, in effect, go about the task of saying this one is over the line and we are going to send them a warning letter, we are going after them, this one is within bounds? How do you go about that?

Dr. BEHRMAN. It is a very good question. It is a very difficult decision. Anything, obviously, that requires that kind of judgment is not black and white and cannot be clearly articulated, although we try very hard to set standards that are easily understood by the industry we regulate in terms of, for example, developing more guidance because, in part, they need to produce quality ads, but in part, if we haven't made it clear to them what the standards are, it becomes harder for them to do. It also is a question sometimes of what comes to our attention. Remember, we are inundated with advertising, as we have all discussed. It is a $20 billion a year expenditure. So we don't look at every ad. It could be a complaint. It could be we see one at home. It could be a family member brings it to our attention. But then we have to make an assessment of whether indeed it is violative or not.

Senator WYDEN. You said $20 billion. I have been using this Wall Street Journal figure of direct-to-consumer advertising as $4 billion.

Dr. BEHRMAN. I am sorry, $4 billion for—yes, I am thinking of the entire mission of the division.

Senator WYDEN. OK. With respect to what is ahead, have you all given some thought to including cost-effectiveness as part of the whole debate about what goes into one of these ads? Because I think that as people look in the future—and we are certainly going to see more of this—that is one of the things they really want to know.

Dr. BEHRMAN. Cost-effectiveness of the therapy?

Senator WYDEN. Yes, and data that points to this drug that is being advertised as being more cost-effective than what is out there.

Dr. BEHRMAN. Well, our standard for putting a claim in an ad is that it be supported by substantial evidence, and if there was to be a cost claim, it would have to be supported by evidence that would be adequate.

Senator WYDEN. I am asking about whether you all are looking at requiring something like that or asking for it.

Dr. BEHRMAN. Asking for cost-effectiveness data, no, we are not.

Senator WYDEN. Do you think that would be in the public interest?

Dr. BEHRMAN. To ask FDA to evaluate cost information?

Senator WYDEN. No, no. To say that that should be included in the claim. No, you wouldn't be suddenly out there trying to make those assessments, but that that should be required as part of an ad.

Dr. BEHRMAN. Again, I am not an attorney. I think it would be very difficult for us to require certain types of speech or claims in any ad. We are required to evaluate the ads that come before us to see whether they are compliant with regulations. But other than, for example, requiring that it be consistent with labeling, we are not required to have certain types of information in the advertisement.

Senator WYDEN. So where do you look then on the label? If labeling is going to be the sort of lodestar here, you know, what do you look at in terms of labeling? Because I think that is something that the public wants to know. I mean, the public wants to know about whether it is going to be effective for them from the standpoint of their health, and the public wants to know if it is going to be cost-effective.

Dr. BEHRMAN. Well, again, whether it is going to be effective for them is a discussion they have to have with their health care provider. Whether it is going to be cost-effective for them, I am still at a loss of quite how to understand how to evaluate that. I can understand how to balance as a physician the risks and benefits for a particular patient, but I am not quite sure how I would understand how to balance how much it costs them.

Senator WYDEN. I guess what I am saying is I think this is something the Government ought to look into, because what we are seeing is enormous amounts of money spent on drugs that incrementally better than what is out there, but are much more expensive, and it just continues this spiral of cost.

I thank you, Doctor. I would only ask, Mr. Chairman, when I cited the Congressional Budget Office, I probably low-balled the number in terms of the amount of advertising, and I would just ask that that full discussion with Douglas Holtz-Eakin be put into the record, because essentially when I have said that if you take advertising out of the expenses of Medicaid, you could come close to half of the target. I used the Wall Street Journal figure, the $4 billion figure. I probably could have gone higher with Douglas Holtz-Eakin. In fairness and so that the committee has the accurate record, I would ask that Douglas Holtz-Eakin's entire set of remarks on that point be put into the record.

Senator KOHL. It will be done.

[The information referred to follows:]

Senator WYDEN. I wanted to also explore with you a topic you and I have talked about. Senator Sununu and I have been concerned about the fact that public programs, programs like Medicaid, the Public Health Service, the VA, are paying for prescription costs, you know, advertising. In effect, those programs end up getting shellacked, you know, twice. There are tax breaks for the pharmaceutical folks to advertise on TV. Nobody is quarreling with

that, trying to take it away. But after that expenditure is made with taxpayer money, then more money gets spent for in effect like Medicaid to pay for all those purple pills, you know, dancing across everybody's television set. So we are trying to address this, you know, issue and, you know, obviously advertising increases utilization of prescription drugs and, or course, the program.

Let me ask it this way: The official sources on drug advertising seems to be that the country spends between $3 billion and $5 billion a year on prescription drug advertising. According to the bipartisan experts, after the Medicare drug benefit kicks in, Medicaid is expected to be about 10 percent of the prescription drug market. That seems to be a kind of consensus recommendation.

So Senator Sununu and I are interested and working on the language of this and would very much like your counsel so as to focus on utilization and focus on market share. It is our sense that if we do that, the government could save about $300 million to $500 million a year on Medicaid, in effect over a billion dollars over a 5-year period.

Do you feel that that is essentially a reasonable kind of analysis?

Mr. HOLTZ-EAKIN. Yes. You know given that the language was tight enough that could find a way to actually recoup the costs and that we can, you know, get a sense that the numbers are on the mark. They certainly seem reasonable. Yes.

Senator WYDEN. Well, I appreciate that, and I would like to work with you on the language because I know that the way it is framed so as to focus on utilization and market share is really, really key, and if we could follow up with your technical folks. They have been very helpful to us already. This is a bipartisan bill, and I just point it out because we have Chairman Smith here, and he has done excellent work on the Medicaid program. He is trying to get $10 billion worth of savings without hurting people on Medicaid, and I would just like to, you know, make it clear, you know, for the record that Dr. Holtz-Eakin has said we could get more than a 10 percent of the savings in the target that Chairman Smith is looking at by the advertising, you know, provisions along the lines of what Senator Sununu and I have been talking about. So we will be anxious to follow up with you, and we got to figure out how to save $10 billion on Medicaid, and we all want to do it without hurting people. We just on the record a way to in the ballpark to get 10 percent of the money. That is what we ought to be trying to do is sharpen our pencils.

Senator KOHL. Thank you, Senator Wyden.

Senator Talent is here.

Senator TALENT. I want to thank the Senator from Wisconsin and the chairman for sponsoring this hearing, which I think is an important one, and it is a subject that has troubled me and I have done a lot of thinking about it, because, on the one hand—I am not going to make a long statement, I promise. But I imagine you all sort of have these conflicting feelings. On the one hand, I don't like to interrupt the flow of information or treat seniors like they can't analyze this information and make useful decisions. On the other hand, there sure are a lot more of these ads than there used to be, and I have some concerns also.

I think it is probably more appropriate to reserve most of my questions for the second panel, but, Dr. Behrman, if you would just—I will follow up on something that I think the chairman raised when I was not here. I watch these ads, and they talk about how great the drugs are, and I would expect that they would do that. There is this little voice as the end that mentioned, you know, "not for people who have had liver problems." I think you went into this a little bit, but are we doing enough to warn people about the potential negative side effects of this? Particularly I wonder if you all have done as an agency any work in an area that was raised in another hearing. Let me just give you that, and then you can answer it in light of that.

When we had the hearing on scams that are directed at seniors, one of the witnesses represented a group that had done a lot of work on how seniors get information and how they perceive it. In other words, if you remember, Mr. Chairman, they made the point that when you do bullet points to seniors, because as our memories begin to change as we get older, there are ways of communicating so that it really hits, and then ways of communicating so that they don't remember it. I wonder if, considering whether this is false and misleading, you have taken that into account, these ads that are aimed at particular parts of the population, if you guys have studied that to make certain that this information about potentially harmful side effects isn't being slipped in in a way that they know people are less likely to absorb. So if you would comment on that, I would appreciate it.

Dr. BEHRMAN. Sure. You have actually raised several different points, all of which are worth commenting on.

First, in terms of—we call it "minimization of risk information," not adequate presentation of risk information. It is one of the most common reasons we cite an ad for violation. We are very concerned. It can be buried in tiny print in a broadcast ad. It can be buried with loud music. There are many ways to bury it. That is why we have—either in print or broadcast, that is why we have started increasingly to do research on what we call the brief summary, the presentation of risk information, and issue guidance, and that is part of what we hope to hear at our public hearing.

You are referring a little bit, I believe, to chunking of information, that you can access the information better if it is chunked. It is not just seniors. It is everybody. That is why we—and it was based on those principles that we are revamping the package insert. Once the package insert is revamped, it will be much easier for industry, we hope and we believe, to better pull out the risks because, yes, we want to see ads that incorporate the risk information into the entire ad, not leave it for the end, not bury it, and not make it hard to understand.

Senator TALENT. You just may want to look at—and we can get this information to you—some interesting studies about how people absorb information in different ways as they get older. It has nothing to do with any disability or anything.

Dr. BEHRMAN. Right, sure.

Senator TALENT. It is just as your memory changes. So ads that are directed particularly at older parts of the population may be able to slip information through in that fashion.

Dr. BEHRMAN. It would be good to see that.

Senator TALENT. But I am glad to know that is a priority, and I appreciate your being here.

Thank you, Mr. Chairman.

Senator KOHL. Thank you, Senator Talent.

Mr. Chairman.

The CHAIRMAN. Doctor, both Senator Wyden and I do town halls all over Oregon, and sometimes we do them together. One of the complaints that he and I invariably hear at every stop is about direct-to-consumer advertising. Obviously you are telling us your workload has gone up. The use of advertising has increased. Have the companies ever shared with you the pluses and minuses of what they are doing? Because there is clearly a backlash among seniors to these ads as expressed. This claim is not supported by data, but it is an overwhelming complaint that we hear constantly. Can we get cheaper drugs and stop these ads? Give us the money in savings and cost; these ads are driving us crazy. These are folks who are coming out of assisted living facilities to hear a couple Senators talk, and this is what is on their minds.

Do they ever share with you the tradeoffs that they go through?

Dr. BEHRMAN. No, but—and, again, you will have the opportunity to speak with them on the next panel, but they have put out voluntary guidelines, and the guidelines do talk about appropriateness of the audience, if you will, in terms of air time. So I would—and this is a guess on my part. I would assume it is on their minds, and I would also just add that it is not just seniors, it is parents of growing children like myself who also would appreciate it if things were——

The CHAIRMAN. You don't like the Levitra ads during a football game?

Dr. BEHRMAN. At a very young age, my boys had me explain erectile dysfunction to them.

The CHAIRMAN. OK.

Senator KOHL. Thank you very much, Dr. Behrman. Your testimony has been good, and your responses to questions have been very helpful.

Dr. BEHRMAN. Thank you.

Senator KOHL. We have four panelists for our second presentation. The first witness will be Dr. Paul Antony of the Pharmaceutical Research and Manufacturers of America. Dr. Antony is PhRMA's chief medical officer. In this role, he serves as PhRMA's principal advocate on all health care and medical policy issues.

Our second witness will be Dr. Donna Sweet of the American College of Physicians. Dr. Sweet is chair of the Board of Regents of ACP, and she is director of Internal Medicine Education at Via Christi Regional Medical Center-St. Francis Campus in Wichita, KS. ACP is the Nation's largest medical specialty society, and Dr. Sweet is here to share with us ACP's position on direct-to-consumer advertising of prescription drugs.

Next we will have Dr. Peter Lurie of Public Citizen. Dr. Lurie is deputy director of Public Citizen's Health Research Group, a consumer advocacy group located here in Washington. Dr. Lurie has worked on a myriad of issues related to the cost and safety of prescription drugs.

Finally, we have Dr. Richard Kravitz. Dr. Kravitz is professor of Internal Medicine and director of the UC Davis Medical Center, Center for Health Services Research in Primary Care. His research is focused on understanding social influences on clinical practice. He is here to discuss his recent research on DTC advertising of prescription drugs.

We welcome you all here today, and, Dr. Antony, we will take your testimony.

STATEMENT OF PAUL ANTONY, MD, MPH, CHIEF MEDICAL OFFICER, PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA (PHRMA), WASHINGTON, DC

Dr. ANTONY. Mr. Chairman, Ranking Member Kohl, and members of the committee, on behalf of the Pharmaceutical Research and Manufacturers of America, I want to thank you for allowing us to participate in this hearing today on direct-to-consumer advertising. I am Dr. Paul Antony, the chief medical officer of PhRMA.

Patients are increasingly demanding more information about their health and treatment options, not less, and they are getting this information from a wide variety of sources, including newspapers, television, and the Internet. Direct-to-consumer advertising is one of the many sources patients use to obtain health information.

DTC advertising can be a powerful tool in educating millions of people and improving health. DTC advertising provides value to patients by making them aware of the risks and benefits of new drugs. It can empower patients and enhance public health. It plays a vital role in addressing a major problem in this country of under-treatment and under-diagnosis of disease. It encourages patients to discuss medical problems with their health care provider that might otherwise not be discussed due to a stigma being attached to the disease. It encourages patient compliance with physician-directed treatment regimens.

Despite the very positive role that DTC advertising can play in educating patients about health issues and options, over the years there have been concerns expressed about direct-to-consumer advertising. In order to ensure that direct-to-consumer advertising remains an important and powerful tool to educate patients, on July 29 of this year, PhRMA's Board of Directors unanimously approved a set of guiding principles on direct-to-consumer advertisements about prescription medicines.

Our principles recognize that at the heart of our companies' DTC communications efforts should be patient education. This means that DTC communications designed to market a medicine should responsibly educate patients about a medicine, including the conditions for which it may be prescribed. DTC advertising should also foster responsible communications between patients and health care professionals to help the patient achieve better health and a better appreciation of the medicine's known benefits and risks.

Our guiding principles recognize that companies should spend an appropriate amount of time educating health care professionals about a new medicine before it is advertised to patients.

Companies that sign on to these guiding principles agree to submit all DTC television ads to the FDA before releasing these ads

for broadcast, giving the agency an opportunity to review them consistent with its priorities and resources. Should new information concerning a previously unknown safety risk be discovered, companies commit to work with the FDA to responsibly alter or discontinue a DTC advertising campaign.

In addition, the principles encourage companies to include, where feasible, information about help for the uninsured and underinsured in their DTC communications. Our companies offer a host of programs that can assist needy patients with their medicines.

The principles also recognize that ads should respect the seriousness of the health condition and medicine being advertised and that ads employing humor or entertainment may not be appropriate in all instances.

As a result of concerns that certain prescription drug ads may not be suitable for all viewing audiences, the guiding principles state that, "DTC television and print advertisements should be targeted to avoid audiences that are not age appropriate for the messages involved."

PhRMA's Board also unanimously approved the creation of an Office of Accountability to ensure the public has an opportunity to comment on companies' compliance with these principles. Periodic reports will be issued by the PhRMA Office of Accountability to the public regarding the nature of the comments it receives, and each report will also be submitted to the Food and Drug Administration.

PhRMA's Board also agreed to select an independent panel of outside experts and individuals to review reports from the Office of Accountability after one year and to evaluate overall trends in the industry as they relate to these principles. These principles will go into effect in January 2006.

We believe these principles will help patients and health care professionals get the information they need to make informed health care decisions.

Given the progress that continues to be made in society's battle against disease, patients are seeking more information about medical problems and potential treatments. The purpose of DTC advertising is to foster and inform conversations about health, disease, and treatments between patients and their health care practitioners. Our guiding principles are an important step in ensuring that patients and health care professionals get the information they need to make informed health care decisions.

This concludes my oral testimony. I would be happy to answer any questions or supply any additional material requested by members or committee staff.

[The prepared statement of Dr. Antony follows:]

PAUL ANTONY, M.D.
CHIEF MEDICAL OFFICER
PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA

BEFORE THE

SENATE SPECIAL COMMITTEE ON AGING
UNITED STATES SENATE

SEPTEMBER 29, 2005

Mr. Chairman, Ranking Member Kohl and Members of the Committee, on behalf of the Pharmaceutical Research and Manufacturers of America (PhRMA), I am pleased to appear at this hearing today on direct-to-consumer (DTC) advertising. I am Paul Antony, M.D., Chief Medical Officer at PhRMA.

DTC advertising has been proven to be beneficial to American patients. And, continuing regulatory oversight by the FDA helps ensure that the content of DTC advertising informs and educates consumers about medical conditions and treatment options. PhRMA and its member companies have a responsibility to ensure that ads comply with FDA regulations. We take that job seriously. We want to continue to be a valuable contributor to improving public health.

DTC Advertising can be a powerful tool in educating millions of people and improving health. Because of DTC advertising, large numbers of Americans are prompted to discuss illnesses with their doctors for the first time. Because of DTC advertising, patients become more involved in their own health care decisions, and are proactive in their patient - doctor dialogue. Because of DTC advertising, patients are more likely to take their prescribed medicines.

PhRMA's Guiding Principles on Direct-to-Consumer Advertisements About Prescription Medicines

PhRMA and its member companies have long understood the special relationship we have with the patients that use our innovative medicines. Despite the very positive role DTC advertising plays in educating patients about health issues and options, over the years, we have heard the concerns expressed about DTC advertising – that some ads may oversell benefits and undersell risks; that some ads may lead to inappropriate prescribing; that some patients may not be able to afford the advertised medicines; and that some ads may not be appropriate for some audiences. Some doctors have also complained that drug companies launch advertising campaigns without helping to educate doctors in advance. Although actual practice and data on the effects of DTC advertising

differ from these concerns, PhRMA recognized our obligation to act. On July 29, 2005, PhRMA's Board of Directors unanimously approved *Guiding Principles on Direct-to-Consumer Advertisements About Prescription Medicines* (see Appendix A). These principles help ensure that DTC advertising remains an important and powerful tool to educate patients while at the same time addressing many of the concerns expressed about DTC advertising over the past few years.

First, PhRMA member companies take their responsibility to fully comply with FDA advertising regulations very seriously. Our advertising is already required to be accurate and not misleading; it can only make claims supported by substantial evidence; it must reflect the balance between risks and benefits; and it must be consistent with FDA-approved labeling. However, patients, health care providers and the general public expect us to do more than just meet our exacting legal obligations, and our Guiding Principles do go further.

Our principles recognize that at the heart of our companies' DTC communications efforts is patient education. This means that DTC communications designed to market a medicine should responsibly educate patients about a medicine, including the conditions for which it may be prescribed. DTC advertising should also foster responsible communications between patients and health care professionals to help the patient achieve better health and a better appreciation of a medicine's known benefits and risks. Specifically, the Principles state that risk and safety information should be designed to achieve a balanced presentation of both risks and benefits associated with the advertised medicines.

Our Guiding Principles recognize that companies should spend appropriate time educating health care professionals about a new medicine before it is advertised to patients. That way, providers will be prepared to discuss the appropriateness of a given medication with a patient.

Current law provides that companies must submit their DTC television advertisements to FDA upon first use for FDA's review at its discretion. Companies that sign onto these Guiding Principles agree to submit all new DTC television ads to the FDA before releasing these ads for broadcast, giving the Agency an opportunity to review consistent with its priorities and resources. Companies also commit to informing FDA of the earliest date the advertisement is set to air. Should new information concerning a previously unknown safety risk be discovered, companies commit to work with FDA to "responsibly alter or discontinue a DTC advertising campaign."

In addition, the Principles encourage companies to include, where feasible, information about help for the uninsured and underinsured in their DTC communications. Our member companies offer a host of programs that can assist needy patients with their medicines.

The Principles also recognize that ads should respect the seriousness of the health condition and medicine being advertised and that ads employing humor or entertainment may not be appropriate in all instances.

As a result of concerns that certain prescription drug ads may not be suitable for all viewing audiences, the Guiding Principles state that, "DTC television and print advertisements should be targeted to avoid audiences that are not age appropriate for the messages involved."

Signatory companies are committed to establishing their own internal processes to ensure compliance with the Guiding Principles and to broadly disseminate them internally and to advertisers. In addition, PhRMA's Board unanimously approved the creation of an office of accountability to ensure the public has an opportunity to comment on companies' compliance with these Principles. The office of accountability will be responsible for receiving comments from the general public and from health care professionals regarding DTC ads by any company that publicly states it will follow the principles. The PhRMA office of accountability will provide to these companies any comment that is reasonably related to compliance with the Principles. Periodic reports will be issued by the PhRMA office of accountability to the public regarding the nature of the comments. Each report will also be submitted to the FDA.

PhRMA's Board also agreed to select an independent panel of outside experts and individuals to review reports from the office of accountability after one year and evaluate overall trends in the industry as the relate to the Principles. The panel will be empowered to make recommendations in accordance with the Principles. The Principles will go into effect in January 2006.

We believe these Principles will help patients and health care professionals get the information they need to make informed health care decisions.

The Value of DTC Advertising

Informing and Empowering Consumers

Surveys indicate that DTC advertising makes consumers aware of new drugs and their benefits, as well as risks and side effects with the drugs advertised. They help consumers recognize symptoms and seek appropriate care. According to an article in the *New England Journal of Medicine,* DTC advertising is concentrated among a few therapeutic categories. These are therapeutic categories in which consumers can recognize their own symptoms, such as arthritis, seasonal allergies, and obesity; or for pharmaceuticals that treat chronic diseases with many undiagnosed sufferers, such as high cholesterol, osteoporosis, and depression.

DTC advertising gets patients talking to their doctors about conditions that may otherwise have gone undiagnosed or undertreated. For example, a study conducted by RAND Health and published in the *New England Journal of Medicine* found that nearly half of all adults in the United States fail to receive recommended health care.[1] According to researchers on the RAND study, "the deficiencies in care...pose serious threats to the health of the American public that could contribute to thousands of preventable deaths in the United States each year." The study found underuse of prescription medications in seven of the nine conditions for which prescription medicines were the recommended treatment. Conditions for which underuse was found include asthma, cerebrovascular disease, congestive heart failure, diabetes, hip fracture, hyperlipidemia and hypertension. Of those seven conditions for which RAND found underuse of recommended prescription medicines, five are DTC advertised.

The Rand Study, as well as other studies, highlight the underuse of needed medications and other healthcare services in the U.S.

- According to a nationally representative study of 9,090 people aged 18 and up, published in JAMA, about 43 percent of participants with recent major depression are getting inadequate therapy.[2]

- A 2004 study published in the *Archives of Internal Medicine*, found that, "In older patients, failures to prescribe indicated medications, monitor medications appropriately, document necessary information, educate patients, and maintain continuity are more common prescribing problems than is use of inappropriate drugs."[3]

- A May/June 2003 study published in the *Journal of Managed Care Pharmacy*, which examined claims data from 3 of the 10 largest health plans in California to determine the appropriateness of prescription medication use based upon widely accepted treatment guidelines, found that "effective medication appears to be underused." Of the four therapeutic areas of study—asthma, CHF, depression, and common cold or upper respiratory tract infections—asthma, CHF, and depression were undertreated. The researchers concluded that "the results are particularly surprising and disturbing when we take into account the fact that three of the conditions studied (asthma, CHF, and depression) are known to produce high costs to the healthcare system."[4]

- According to a study released in May 2005 by the Stanford University School of Medicine, among patients with high cholesterol in moderate and high-risk groups, researchers found fewer than half of patient visits ended with a statin recommendation. Based on the findings, the researchers say physicians should be more aggressive in investigating statin therapy for

patients with a high or moderate risk of heart disease, and that patients should ask for their cholesterol levels to be checked regularly.[5]

Increasing Communication between the Doctor and Patient

A vast majority of patients (93 percent) who asked about a drug reported that their doctor "welcomed the questions."[6] Of patients who asked about a drug, 77 percent reported that their relationship with their doctor remained unchanged as a result of the office visit, and 20 percent reported that their relationship improved.[7] In addition, both an FDA survey of physicians (from a random sample of 500 physicians from the American Medical Association's database) and a survey by the nation's oldest and largest African-American medical association, found that DTC advertisements raise disease awareness and bolster doctor-patient ties.

The doctor-patient relationship is enhanced if DTC advertising prompts a patient to talk to his doctor for the first time about a previously undiscussed condition, to comply with a prescribed treatment regimen, or to become aware of a risk or side effect that was otherwise unknown. A 2002 *Prevention Magazine* survey found that 24.8 million Americans spoke with their doctor about a medical condition for the first time as a result of seeing a DTC advertisement. Similarly, the FDA patient survey on DTC advertising found that nearly one in five patients reported speaking to a physician about a condition for the first time because of a DTC ad.[8]

PhRMA and its member companies believe it is vital that patients, in consultation with their doctors, make decisions about treatments and medicines. Prescribing decisions should be dominated by the doctor's advice. While our member companies direct a large majority of their promotional activities toward physicians,[9] such promotion in no way guarantees medicines will be prescribed.

According to a General Accounting Office report, of the 61.1 million people (33 percent of adults) who had discussions with their physician as a result of a DTC advertisement in 2001, only 8.5 million (5 percent of adults) actually received a prescription for the product, a small percentage of the total volume of prescriptions dispensed.[10] Indeed, an FDA survey of physicians revealed that the vast majority of physicians do not feel pressure to prescribe. According to the survey, 91 percent of physicians said that their patients did not try to influence treatment courses in a way that would have been harmful and 72 percent of physicians, when asked for prescription for a specific brand name drug, felt little or no pressure to prescribe a medicine.

De-Stigmatizing Disease

DTC advertising also encourages patients to discuss medical problems that otherwise may not have been discussed because it was either thought to be too personal or that there was a stigma attached to the disease. For example, a *Health Affairs* article examined the value of innovation and noted that depression medications, known as selective serotonin reuptake inhibitors (SSRIs), that have been DTC advertised, have led to significant treatment expansion. Prior to the 1990's, it was estimated that about half of those persons who met a clinical definition of depression were not appropriately diagnosed, and many of those diagnosed did not receive clinically appropriate treatment. However, in the 1990's with the advent of SSRIs, treatment has been expanded. According to the article, "Manufacturers of SSRIs 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 for depression doubled over the 1990's.[11]

Utilization and DTC Advertising

According to reports and studies, there is no direct relationship between DTC advertising and the price growth of drugs. For example, in comments to the FDA in December 2003 , the FTC stated, "[DTC advertising] can 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 their treatment options....Consumer receive these benefits from DTC advertising with little, if any, evidence that such advertising increases prescription drug prices."[12] Notably, since January 2000, the CPI component that tracks prescription medicines have been in line with overall medical inflation.

The FTC comments referenced above also note, "DTC advertising 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."[13] Likewise, a study by Harvard University and the Massachusetts Institute of Technology and published by the Kaiser Family Foundation found that DTC advertising accounts for less than 2 percent of the total U.S. spending for prescription medicines.[14]

One study in the *American Journal of Managed Care* looked at whether pharmaceutical marketing has led to an increase in the use of medications by patients with marginal indications. The study found that high-risk individuals were receiving lipid-lowering treatment "consistent with evidence-based practice guidelines" despite the fact that "a substantial portion of patients continue to remain untreated and undertreated...."[15] The study concluded that "greater overall use did not appear to be associated with a shift towards patients with less CV [cardiovascular] risk."

Pharmaceutical utilization is increasing for reasons other than DTC advertising. As the June 2003 study of DTC advertising commissioned by the

Kaiser Family Foundation found, "[O]ur estimates indicate that DTCA is important, but not the primary driver of recent growth [in prescription drug spending]."

Other reasons pharmaceutical utilization is increasing, include:

- **Improved Medicines** – Many new medicines replace higher-cost surgeries and hospital care. In 2004 alone, pharmaceutical companies added 38 new medicines and over the last decade, over 300 new medicines have become available for treating patients. These include important new medicines for some of the most devastating and costly diseases, including: AIDS, cancer, heart disease, Alzheimer's, and diabetes. According to a study prepared for the Department of Health and Human Services, "[n]ew medications are not simply more costly than older ones. They may be more effective or have fewer side effects; some may treat conditions for which no treatment was available."[16]

- **New Standards of Medical Practice Encouraging Greater Use of Pharmaceuticals** – Clinical standards are changing to emphasize earlier and tighter control of a range of conditions, such as diabetes, hypertension and cardiovascular disease. For example, new recommendations from the two provider groups suggest that early treatment, including lifestyle changes and treatment with two or more types of medications, can significantly reduce the risk of later complications and improve the quality of life for people with type 2 diabetes.[17]

- **Greater Treatment of Previously Undiagnosed and Untreated Conditions** – According to guidelines developed by the National Heart, Lung, and Blood Institute's National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP), approximately 36 million adults should be taking medicines to lower their cholesterol, a number that has grown from 13 million just 8 years ago.[18]

- **Aging of America** – The aging of American translates into greater reliance on pharmaceuticals. For example, congestive heart failure affects an estimated 2 percent of Americans age 40 to 59, more than 5 percent of those aged 60 to 69, and 10 percent of those 70 or more.[19]

While some assume that DTC advertising leads to increased use of newer medicines rather than generic medicines, generics represent just over 50 percent of all prescriptions (generics are historically not DTC advertised). In contrast, in Europe, where DTC advertising is prohibited, the percentage of prescriptions that are generic is significantly lower. Likewise, it is worth nothing that while broadcast DTC has been in place since 1997, the rate of growth in drug cost

increases has declined in each of the last 5 years and in 2004 was below the rate of growth in overall health care costs.[20]

Economic Value of DTC Advertising

Increased spending on pharmaceuticals often leads to lower spending on other forms of more costly health care. New drugs are the most heavily advertised drugs, a point critics often emphasize. However, the use of newer drugs tends to lower all types 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.[21]

The Tufts Center for the Study of Drug Development reports that disease management organizations surveyed believe that increased spending on prescription drugs reduces hospital inpatient costs. "Since prescription drugs account for less than 10 percent of total current U.S. health care spending, while inpatient care accounts for 32 percent, the increased use of appropriate pharmaceutical therapies may help moderate or reduce growth in the costliest component of the U.S. health care system," according to Tufts Center Director Kenneth I. Kaitin.[22]

Opponents also compare the amount of money spent by drug companies on marketing and advertising to the amount they spend on research and development of new drugs. However, in 2004, pharmaceutical manufacturers spent an estimated $4.15 billion[23] on DTC advertising, according to IMS Health, compared to $49.3 billion in total R&D spending by the biopharmaceutical industry, according to Burrill & Company. PhRMA members alone spent $38.8 billion on R&D in 2004.

Conclusion

DTC advertising provides value to patients by making them aware of risks and benefits of new drugs; it empowers patients and enhances the public health; it plays a vital role in addressing a major problem in this country of undertreatment and underdiagnosis of disease; encourages patients to discuss medical problems with their health care provider that may otherwise not be discussed due to a stigma being attached to the disease; and encourages patient compliance with physician-directed treatment regimens.

Given the progress that continues to be made in society's battle against disease, patients are seeking more information about medical problems and potential treatments. The purpose of DTC advertising is to foster an informed conversation about health, disease and treatments between patients and their health care practitioners. Our Guiding Principles are an important step in

ensuring patients and health care professionals get the information they need to make informed health care decisions.

This concludes my written testimony. I would be happy to answer any questions or to supply any additional material by Members or Committee Staff on this or any other issue.

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PhRMA

PhRMA Guiding Principles
Direct to Consumer Advertisements
About Prescription Medicines

Preamble

Given the progress that continues to be made in society's battle against disease, patients are seeking more information about medical problems and potential treatments so they can better understand their health care options and communicate effectively with their physicians. An important benefit of direct-to-consumer (DTC) advertising is that it fosters an informed conversation about health, disease and treatments between patients and their health care practitioners.

A strong empirical record demonstrates that DTC communications about prescription medicines serve the public health by:

- Increasing awareness about diseases;
- Educating patients about treatment options;
- Motivating patients to contact their physicians and engage in a dialogue about health concerns;
- Increasing the likelihood that patients will receive appropriate care for conditions that are frequently under-diagnosed and under-treated; and
- Encouraging compliance with prescription drug treatment regimens.

The Pharmaceutical Research and Manufacturers of America (PhRMA), represents America's leading pharmaceutical research and biotechnology companies. As the companies responsible for developing new and innovative medicines, PhRMA members want patients and consumers to talk to their physicians about the medicines that may help them and to fully understand the known risks regarding these medicines. We know that DTC communications, particularly DTC television advertising, can be a powerful tool for reaching and educating millions of people, and we are committed to ensuring that our DTC communications provide accurate, accessible and useful health information to patients and consumers. DTC advertising of such important and powerful products as prescription drugs should be responsibly designed to achieve these goals and to encourage the appropriate use of these products.

PhRMA

First and foremost, we have a responsibility to ensure that our DTC communications comply with the regulations of the Food & Drug Administration (FDA). In general, the FDA requires all DTC information:

- To be accurate and not misleading;
- To make claims only when supported by substantial evidence;
- To reflect balance between risks and benefits; and
- To be consistent with the FDA-approved labeling.

The innovative pharmaceutical industry takes its responsibilities to comply with FDA requirements seriously. Companies devote substantial time and effort, and often ask for input from FDA, to ensure that DTC communications are accurate, fairly balanced and meet all applicable legal requirements. PhRMA member companies will engage in a dialogue with FDA to maximize opportunities for FDA review of DTC advertising prior to release, consistent with these principles and the agency's priorities and resources.

Beyond meeting their legal obligations, companies strive to deliver messages that fundamentally serve to educate patients and consumers and encourage them to seek guidance from their health care professionals.

To express the commitment of PhRMA members to deliver DTC communications that serve as valuable contributors to public health, PhRMA has established the following voluntary guiding principles.

Guiding Principles

1. These Principles are premised on the recognition that DTC advertising of prescription medicines can benefit the public health by increasing awareness about diseases, educating patients about treatment options, motivating patients to contact their physicians and engage in a dialogue about health concerns, increasing the likelihood that patients will receive appropriate care for conditions that are frequently under-diagnosed and under-treated, and encouraging compliance with prescription drug treatment regimens.

2. In accordance with FDA regulations, all DTC information should be accurate and not misleading, should make claims only when supported by substantial evidence, should reflect balance between risks and benefits, and should be consistent with FDA approved labeling.

3. DTC television and print advertising which is designed to market a prescription drug should also be designed to responsibly educate the consumer about that medicine and, where appropriate, the condition for which it may be prescribed.

4. DTC television and print advertising of prescription drugs should clearly indicate that the medicine is a prescription drug to distinguish such advertising from other advertising for non-prescription products.

5. DTC television and print advertising should foster responsible communications between patients and health care professionals to help patients achieve better health and a more complete appreciation of both the health benefits and the known risks associated with the medicine being advertised.

6. In order to foster responsible communication between patients and health care professionals, companies should spend an appropriate amount of time to educate health professionals about a new medicine or a new therapeutic indication before commencing the first DTC advertising

campaign. In determining what constitutes an appropriate time, companies should take into account the relative importance of informing patients of the availability of a new medicine, the complexity of the risk-benefit profile of that new medicine and health care professionals' knowledge of the condition being treated. Companies should continue to educate health care professionals as additional valid information about a new medicine is obtained from all reliable sources.

7. Working with the FDA, companies should continue to responsibly alter or discontinue a DTC advertising campaign should new and reliable information indicate a serious previously unknown safety risk.

8. Companies should submit all new DTC television advertisements to the FDA before releasing these advertisements for broadcast.

9. DTC television and print advertising should include information about the availability of other options such as diet and lifestyle changes where appropriate for the advertised condition.

10. DTC television advertising that identifies a product by name should clearly state the health conditions for which the medicine is approved and the major risks associated with the medicine being advertised.

11. DTC television and print advertising should be designed to achieve a balanced presentation of both the benefits and the risks associated with the advertised prescription medicine. Specifically, risks and safety information in DTC television advertising should be presented in clear, understandable language, without distraction from the content, and in a manner that supports the responsible dialogue between patients and health care professionals.

12. All DTC advertising should respect the seriousness of the health conditions and the medicine being advertised.

13. In terms of content and placement, DTC television and print advertisements should be targeted to avoid audiences that are not age appropriate for the messages involved.

14. Companies are encouraged to promote health and disease awareness as part of their DTC advertising.

15. Companies are encouraged to include information in all DTC advertising, where feasible, about help for the uninsured and underinsured.

Accountability for the Guiding Principles

Companies commit to establishing internal processes to ensure compliance with these guiding principles. Companies also commit to distributing these guidelines internally and to their advertising agencies.

Each company's intentions with regard to these guiding principles will be made public.

PhRMA will establish an office of accountability that will be responsible for receiving comments from the general public and from health care professionals regarding DTC advertising conducted by any signatory company to these principles. Any company that publicly states that it will follow the principles will be considered a signatory company.

The PhRMA office of accountability will provide to the signatory company at issue any comment that is reasonably related to compliance with the principles.

The PhRMA office of accountability will issue periodic reports to the public regarding the nature of the comments and the signatory companies' responses, and will provide a copy of each report to the FDA.

One year after the effective date of the Principles, the PhRMA office of accountability will select an independent panel of credible individuals to review reports of that year, to track the overall trends in the industry as they relate to the Principles, and to make recommendations in accordance with the Principles. The panel's report will be included in the next report of the PhRMA office of accountability.

PhRMA

PhRMA Guiding Principles
Direct to Consumer Advertisements
About Prescription Medicines

Questions and Answers

Q: *What is meant by a "direct to consumer television advertisement" in the context of these principles?*

A: A direct to consumer television advertisement is a portion of television air time on broadcast or cable television that is bought by a company for the purpose of presenting information about one or more of the company's medicines. A DTC television advertisement does not include sponsorship of activities.

Q: *What is meant by "direct to consumer print advertisement" in the context of these principles?*

A: A direct to consumer print advertisement is space that is bought by a company in newspaper or magazine publications targeted to patients or consumers, or a direct mail communication paid for and disseminated by a company to patients or consumers, for the purpose of presenting information about one or more of the company's medicines. A DTC print advertisement does not include sponsorship of activities.

Q: *How long must a company wait under Principle 6 before advertising a new medicine after the medicine is approved by FDA?*

A: Principle 6 demonstrates the companies' commitment to devote sufficient resources and time to health care professional education before launching a direct to consumer advertising campaign. Principle 6 ensures that health care professionals will have a reasonable opportunity to learn about new medications before their patients ask questions about them so they will have accurate, up-to-date information to use in responding to patients' inquiries and guiding patients to the most appropriate treatment option. Establishing a single uniform waiting period for all companies and all medicines could have the unintended consequence of denying patients important information about new medicines, even after health care professionals have been well educated. Each company will decide for itself how best to implement an effective educational program, taking into account such factors as health care professionals' knowledge of the condition being treated, the severity and/or prevalence of the condition, the novelty of the new treatment, and the complexity of the medicine's risk-benefit profile and directions for use.

PhRMA

Q: *Does Principle 8 require companies to do more than what is already required under current FDA regulations?*

A: Yes. Current law provides that companies must submit their DTC television advertisements to FDA upon first use for FDA's review at its discretion. Under Principle 8, while not intending to place additional burdens on FDA, companies commit to submitting new DTC television advertisements to FDA earlier than currently required and a reasonable time in advance of first use to give FDA the opportunity to comment, consistent with its priorities and resources. Companies also commit to inform FDA when they submit an advertisement of the earliest date the advertisement is scheduled to air.

Q: *Does Principle 8 require companies to submit a new DTC television advertisement to FDA in advance, even if the advertisement reflects only minor changes to a previously submitted advertisement?*

A: No. Under Principle 8, companies are required to submit only new television advertisements or advertisements that have been changed in a way that the companies believe is significant. For instance, where a company changes an existing advertisement—possibly by changing a telephone number listed on the screen or by replacing an actor—to use for a different targeted audience, but does not substantially change the advertisement's script or theme, then the company is not required under Principle 8 to submit the changed advertisement to FDA. However, where a company changes an advertisement so that the benefit and/or risk information is presented in a different way, the company likely has made a significant change, and the advertisement should be submitted to FDA.

Q: *Does Principle 8 necessarily require a company to submit the final version of a new DTC television advertisement to FDA prior to releasing the advertisement for broadcast?*

A: No. The details of what will be submitted may be addressed in dialogue between companies and FDA.

Q: *Would additional dialogue between companies and the FDA be helpful as Principle 8 is implemented?*

A: Yes. Additional dialogue should occur to maximize opportunities for FDA review of DTC television advertising prior to release, consistent with this principle and the agency's priorities and resources.

Q: *Under Principles 3 and 9, does a company have to mention another medication that may also be appropriate for treating the advertised condition?*

A: No. These principles are intended to encourage companies to include in their advertisements information about therapeutic options and appropriate steps patients could take (which may or may not include other medicines), in consultation with health care professionals, to treat their disease or condition. This is consistent with the pharmaceutical industry's goal of helping patients achieve better overall health.

Q: *Is there only one right way to present risk information in advertisements?*

A: No. An advertisement will comply with Principle 11 if it presents information about the medicine's risks in a way that patients are reasonably likely to take in and understand this information. For television advertisements, the visual and audio presentation of risk information should be similar in terms of prominence and clarity to the visual and audio presentation of other information about the medicine. Of course, even the most informative advertisements can't provide information on all possible risks that may relate to each individual patient. Therefore, the conversation between a patient and a health care professional is critical to the patient's understanding of whether a medicine is right for that individual patient. DTC advertisements should motivate patients to ask their health care professionals for more information about a medicine's risks and benefits. These objectives can be achieved in a variety of ways, and each company will exercise its judgment consistent with FDA requirements.

Q: *What happens if a comment from the public about a company's DTC advertisement conflicts with recommendations or comments the company has received from FDA regarding the advertisement?*

A: The FDA has the authority to determine whether a particular advertisement is consistent with FDA regulations. If FDA chooses to give recommendations or comments on a particular DTC advertisement and the company follows those recommendations or comments, the company will be able to respond to any complaint regarding that aspect of the DTC advertisement that it complies with the PhRMA Principles by virtue of the fact that it followed FDA's recommendations.

Q: *Does Principle 12 suggest that all advertisements should be somber in tone and should not employ lightness, humor or entertainment?*

A: No. Principle 12 recognizes that health conditions and medical treatments are serious issues for patients. While humor or entertainment may not be appropriate in conveying all messages, they may be effective tools for attracting public attention to a particular disease or treatment, reducing any stigma associated with the condition, communicating educational messages about health conditions, and motivating patients to discuss those conditions openly with their health care providers.

Q: *What criteria should be applied to determine whether a company has complied with Principle 13 and targeted its advertising to avoid audiences that are not age appropriate for the messages in the advertisements?*

A: Advertisements containing content that may be inappropriate for children should be targeted to programs or publications that are reasonably expected to draw an audience of approximately 80 percent adults (18 years or older). Companies will be individually responsible for examining reliable, up-to-date audience composition data, to the extent that information is available, to determine whether a particular program or publication is reasonably likely to attract an audience that is age appropriate for a particular advertisement.

Senator KOHL. Thank you very much, Dr. Antony.

Dr. Sweet.

STATEMENT OF DONNA SWEET, MD, FACP, CHAIR, BOARD OF REGENTS, AMERICAN COLLEGE OF PHYSICIANS, WASHINGTON, DC

Dr. SWEET. Thank you, Senator Kohl, Senator Smith, Senator Talent, and Senator Wyden. I am, as stated, Donna Sweet, chair of the Board of Regents of the American College of Physicians, the nation's largest medical specialty society representing over 119,000 doctors of internal medicine. ACP appreciates the opportunity to testify on the subject of direct-to-consumer advertising of prescription drugs.

Internists typically provide primary and subspecialty care to large numbers of patients who are Medicare-eligible and have multiple medical problems. It is these patients who are most adversely affected by DTC advertising.

Since 1998, ACP has been opposed to the practice of DTC advertising, which often leaves our patients confused and misinformed about medications. It undermines the patient-physician relationship and impedes the practice of medicine by challenging the individual physician's medical judgment.

ACP recognizes the value of consumer education. The medical community has an obligation to empower consumers by educating them about health conditions and possible treatments. A healthy physician-patient relationship can lead to better health outcomes through appropriate use of safe and effective medications. The College also acknowledges the need for the pharmaceutical industry to market its products, but believes public education programs that do not promote a particular drug product and are financially supported by pharmaceutical companies are a better approach.

The pharmaceutical industry spends millions of dollars to support the efforts of non-profit organizations, including the ACP, to educate the public through unrestricted educational grants that do not promote a specific product. As an example, the ACP and the ACP Foundation recently received a multi-million-dollar unrestricted educational grant from Novo Nordisk to create and disseminate educational tools and information for physicians, patients, and other members of the health care team to raise awareness and teach best practices in diabetes care, not branded in any way with Novo Nordisk. That is how the industry can help both patients and physicians.

ACP also appreciates the PhRMA-issued voluntary guidelines to regulate the industry's use of DTC ads and that some companies have even gone beyond the PhRMA guidelines by voluntarily agreeing to delay advertising of new drugs to consumers until their safety and effectiveness have been tested. However, voluntary guidelines in our opinion are not a substitute for an effective regulatory approach to DTC advertising.

The power of media broadcast is huge. Pharmaceutical companies and ad agencies know that. That is why DTC advertising is done. But it does put an adversarial element into the physician-patient relationship. Even in a practice like mine, where I have the luxury of being the medical home for some of my seniors for the

last 15 to 20 years, when I have to say no to something that the healthy-looking person on television says is good for them and will make them feel better, it takes some work. Most of the major drugs seen on DTC ads target our seniors. Thick, ugly toenails, erectile dysfunction, urinary incontinence, osteoporosis—all things that need to be discussed, but not necessarily secondary to an ad that says, "This product is best."

Consider the toenail ad, my personal favorite. While I am trying to tell a senior that it is not life-threatening; that there really aren't little creatures with horns, legs, and arms under their toenails, living in sofas and chairs; that the drug is quite expensive; and that the risks of toxicity are significant and that it may not work, I lose valuable time that could have been directed at the underlying reason they have those toenails—their diabetes, their vascular disease, their cholesterol, their overall health.

Some ads, like those that tell people that there is help for embarrassing problems—urinary incontinence as an example—have opened dialog, but the ads promote the more expensive brand names when generics often work equally as well.

Last, some of the ads are just embarrassing. I was talking to a senior last week from Arkansas who was watching sports on TV with his grandkids, and he was not really paying any attention to the ads until his 7-year-old grandson pulled on his shirt sleeve and said, "Grandpa, what is a 4-hour erection?"

ACP would prefer to see Congress ban DTC advertising because it does not constitute appropriate patient education. In the absence of a prohibition, which we understand is probably not possible, the College calls on Congress, the FDA, and the industry to take actions to minimize the deleterious effects of DTC advertising, and we would recommend the following:

Federal regulations and guidelines must be expeditiously strengthened to make drug advertising as honest and useful as possible. The FDA's retrospective regulatory process should be replaced with a mandatory pre-release screening of all pharmaceutical advertising. Marketing should be directed at providing clinicians with accurate information on new drug products. Physicians and pharmaceutical companies should continue to work together to create effective advertising and educational initiatives. Finally, the Federal Government should continue to fund studies to further define and measure the impact of DTC ads.

Just as fast-food advertising to our kids is leading to an epidemic of obesity, I have to believe that DTC advertising to our seniors leads to an overconsumption of medications and sometimes outright doctor shopping if they really feel they have to have those medicines.

ACP thanks the Aging Committee for addressing this subject and for considering the views of the American College of Physicians, and I would take any questions or provide additional information as needed.

[The prepared statement of Dr. Sweet follows:]

STATEMENT OF THE AMERICAN COLLEGE OF PHYSICIANS
TO THE
SENATE SPECIAL COMMMITTEE ON AGING
For the Record of
The Hearing on the Impact of Direct-to-Consumer Advertising on
Seniors' Health and Health Care Costs
September 29, 2005

I am Donna Sweet, Chair of the Board of Regents of the American College of Physicians, the nation's largest medical specialty society representing over 119,000 doctors of internal medicine and medical students. ACP appreciates the opportunity to testify on the subject of direct-to-consumer advertising (DTC) of prescription drugs. Internists typically provide primary and subspecialty care to large numbers of patients who are Medicare-eligible and have multiple medical problems. It is these patients who are most adversely affected by direct-to-consumer advertising.

Since 1998, ACP has voiced its opposition to the practice of DTC advertising. DTC advertising of prescription drugs often leaves patients confused and misinformed about medications. It undermines the patient-physician relationship and impedes the practice of medicine by challenging the individual physician's medical judgment. According to one of our members, the current wave of DTC advertising "[puts] patients, not him, in the diagnostic driver's seat."

Adverse Consequences of DTC Advertising

Our members continue to complain that more and more patients are presenting them with a list of drugs they would like to try, based on what they see on television, magazines and the Internet, many of which may not be the best choice of therapy for individual patients. Patients arrive at the physician's office already convinced that the products advertised are the answer to their problems. Their conclusions are based on brief ads or commercials that provide insufficient information about the appropriateness of the drug for that patient, the risks and benefits, and comparable and more cost-effective options. Physicians end up spending valuable time fielding requests, clarifying misconceptions, and explaining other, sometimes more effective treatments. Time spent with the patient gets diverted from patient education to negotiation. Then, depending on the patient's insurance plan, the physician usually has to negotiate with the patient what is and is not covered. When a coveted drug is not part of a patient's health plan's formulary, patients may pressure physicians to make a case for medical necessity in hopes of getting the prescription covered—another round of hassle and effort for the physicians. And when a physician withholds something a patient wants, patients often build mistrust in the physician. The result is a subtle but chronic adversarial element in the doctor-patient relationship that takes a substantial emotional toll on physicians.

Surveys have shown that patients ask for a prescription based on an advertisement in up to seven percent of doctor visits — a rate that adds up to millions of requests a year.

According to the FDA, 65 percent of physicians believe patients misunderstand the relative risks and benefits of a drug advertised through a DTC ad and 75 percent say the ads lead patients to overestimate the medical value of the drugs. Thirty-eight percent say DTC ads cause patients to question their diagnoses and 28 percent say the ads can lead to doctor-patient tension. The FDA also has reported that although few physicians report excessive pressure to prescribe requested drugs from patients who have seen DTC ads, nearly half report feeling at least a little pressure to prescribe.

The pressure patients impose on physicians is compounded by the fact that physicians are also being ordered by health plans and administrators to hold the line on spiraling prescription costs. Spending on prescription drugs is the fastest growing component of the health care budget and DTC ads are one element – and probably an increasingly important one – in the recent sharp rise in the demand for, expanded use of, and increased spending on prescription drugs. In the four years after the FDA relaxed its guidelines on broadcast drug commercials, the amount spent on DTC ads more than doubled, from $1.1 billion to $2.7 billion. By 2003, spending on direct-to-consumer (DTC) advertising of prescription drugs totaled $3.2 billion. At least a fraction of these costs are passed on to the consumer.

In terms of increasing demand and utilization, it is estimated that between 4 percent and 6 percent of the U.S. adult population – 8.5 million to12.6 million people in 2001 – appear to have received a prescription for a drug as a *direct result* of a DTC ad. In a 2000 analysis of prescription volume and sales of advertised drugs compared to non-advertised drugs, the U.S. Federal Trade Commission (FTC) found that doctors wrote 25 percent more prescriptions for the 50 most heavily DTC-advertised drugs compared to 4.3 percent more scripts for all other drugs combined. Sales of the top 50 most heavily advertised drugs rose an aggregate 32 percent from 1999 to 2000 compared to 13.6 percent for all other drugs combined. Increases in the sales of these 50 most heavily advertised drugs accounted for almost half (47.8 percent) of the overall $20.8 billion rise in spending on drugs in the retail sector from 1999 to 2000. Although such research proves no direct cause and effect link between DTC ads and increasing drug use and spending, it is highly suggestive.

While DTC advertising may avert underuse of drugs, the practice more often promotes overuse of drugs or use of less cost-effective drugs. A study published this year in the Journal of the American Medical Association found that doctors were five times more likely to write prescriptions after patients inquired about a specific antidepressant, Paxil, as compared to patients who did not mention an ad. The study used actresses who pretended to have a mild form of depression, a condition that does not require antidepressants. Another national survey found that when a drug requested by a patient was prescribed, 46 percent of physicians said that it was the most effective drug, while 48 percent said that others were equally effective. Unnecessary spending further weighs down our health system when equally effective alternatives prove to be less expensive. Issues of therapeutic equivalence and cost-effectiveness are particularly important in light of Medicare's new drug benefit. If DTC ads continue to generate a fairly large volume of

inappropriate demand and overutilization, they could end up costing the federal government billions of dollars.

Proponents of DTC advertising claim that it promotes consumer education and stimulates dialogue between physicians and patients. They say that patients are now more willing to discuss symptoms they have seen referred to in advertisements. ACP recognizes the value of consumer education. When evidence exists on appropriateness, effective communication regarding prescription drugs can produce a social good by reducing underuse. The medical community has an obligation to empower consumers by educating them about health conditions and possible treatments. ACP supports the IOM recommendation that patients be offered the opportunity to act more like partners in their care. A healthy patient-physician relationship can lead to better health outcomes through appropriate use of safe and effective medicines that save lives, cure disease, and alleviate pain and suffering.

In addition to patient-physician communication, public media channels can be an effective way to enhance patient understanding and involvement in care. The College acknowledges the need for the pharmaceutical industry to market its products, but believes that such marketing should be directed at increasing awareness among clinicians about new medication therapies (including advertisements directed to clinicians that provide balanced and accurate information about the medication's approved uses, relative effectiveness, and risks) rather than directly marketing to a patient population that lacks the training and skills to make an informed judgment about the effectiveness of new drug products.

The College appreciates that the Pharmaceutical Research and Manufacturing Association (PhRMA) has begun to take steps to address concerns about DTC advertising by issuing voluntary guidelines to regulate the industry's use of DTC ads. We believe, however, that voluntary guidelines are not a substitute for an effective regulatory approach to DTC advertising. Further, we believe that the industry should continue to consider additional actions to limit the potential adverse consequences of DTC advertising while Congress and the FDA continue to work on creating a more effective regulatory structure. We note, for instance, that some companies have gone beyond the PhRMA guidelines by voluntarily agreeing to delay advertising of new drugs to consumers until they have been on the market long enough for their safety and effectiveness to be tested. Nevertheless, ACP continues to hold that DTC advertising *does not* constitute appropriate patient education. Instead, it results in patients attempting to influence their own treatment regimens based on what they see in the media, rather than by what may be the best medical treatment option for them.

Drug Manufacturers' Contributions to Improving Patient Care

The College's objections to DTC advertising does not imply that the pharmaceutical industry does not play an essential role in improving patient care. Quite the contrary: the College strongly believes that the pharmaceutical industry makes invaluable contributions to the field of medicine as it continues to develop new life-saving therapies

and provide financial support to public education programs that educate patients on how to manage their own health. Internists would not be able to provide patients with the benefits of life-saving therapies without the availability of the thousands of medications that are available because of the pharmaceutical industry's investment in research and development. The ability of the industry to continue to develop new therapies is essential for continuous improvements in patient care to occur.

The College also believes that there is an appropriate role for pharmaceutical companies to provide financial support for public education programs that do not promote a particular drug product. The drug industry spends millions of dollars to support the efforts of non-profit charitable organizations, including ACP, to educate the public through unrestricted educational grants that do not promote a specific product. As an example, ACP and the ACP Foundation recently received a multimillion-dollar unrestricted educational grant from Novo Nordisk to create and disseminate educational tools and information for physicians, patients, and other members of the health care team to raise awareness and teach best practices in diabetes care. This partnership illustrates that the medical and pharmaceutical professions share the goals of high quality care--including the promotion of evidence-based medicine for care of all chronic diseases, identification of the gaps between current practice and acceptable standards of care, and recognition of physicians that demonstrably improve care of their patients.

Improving Regulatory Oversight of DTC Advertising

ACP would prefer to see Congress ban DTC advertising. In the absence of a prohibition on DTC advertising, however, the College calls on Congress, the FDA, and the industry itself to take actions to minimize the deleterious effects of DTC advertising, ACP supports the following recommendations:

- Federal regulations and guidelines must be strengthened to make drug advertising as honest and useful as possible. The FDA must impose serious limits on the pharmaceutical industry to ensure that consumers receive complete and non-confusing information. While ACP appreciates recent efforts by the FDA to assure that drug ads reflect "truthful, balanced, and accurately communicated" information about drugs, including the recent creation of an independent Drug Safety Oversight Board to oversee the management of drug safety issues, the current system still lacks a sufficient process with which to review the pharmaceutical industry and the products it markets directly to the public. For example, the retrospective regulatory process used by FDA is much too lenient, allowing drug companies to transmit advertising messages directly to the public before the FDA has had a chance to check the appropriateness of the information. ACP favors mandatory pre-release screening of all pharmaceutical advertising to ensure clarity and truthfulness.
- Although DTC advertising may increase public awareness about untreated conditions, ACP feels this information could be conveyed to patients in more effective ways. For instance, marketing should be directed at providing clinicians with accurate information on new drug products, rather than overwhelming

consumers with confusing and often misinterpreted information. Physicians and pharmaceutical companies must continue to work jointly to create effective consumer advertising and educational initiatives. The pharmaceutical industry has a duty to meet with physicians to provide new information about drugs and warn physicians about the questions they will be receiving from their patients, due to an advertising campaign that is about to be launched. At the same time, ACP and other medical societies have a duty to work with the pharmaceutical industry to develop medically appropriate information that can be provided to consumers.

- Finally, the federal government must continue to fund studies to further define and measure the impact of DTC ads. While direct-to-consumer advertising has become commonplace, the practice still raises many questions. Can consumers understand advertised medical information and apply it to their own conditions? Can advertising be considered a form of education? Does the "information" presented in ads change patient expectations of the medical encounter and treatment for the better or for the worse? Does it appropriately influence the prescribing habits of physicians?

ACP is pleased that the Aging Committee has decided to address the serious problems associated with direct-to-consumer drug advertising. In addition to patient misperceptions, DTC advertising results in inefficient use of valuable physician time, challenges a physicians' professional authority, inflates the cost of drugs, and can ultimately compromise patient access to life-saving treatments. ACP asks that the Committee consider recommending that the use of direct-to-consumer ads be prohibited. At the very least, ACP calls on the federal government to expeditiously strengthen regulations governing these ads. Thank you for considering the views of ACP-- I look forward to your questions.

Senator KOHL. Thank you very much, Dr. Sweet.

Dr. Lurie.

STATEMENT OF PETER LURIE, MD, MPH, DEPUTY DIRECTOR, HEALTH RESEARCH GROUP, PUBLIC CITIZEN, WASHINGTON, DC

Dr. LURIE. Thank you. Like all interventions in health care, DTC advertising should be evaluated by comparing risks and benefits in the context of available or potentially available alternatives. On balance, we believe that the clearly demonstrated adverse effects of DTC advertising outweigh the still undemonstrated effects that might be beneficial. Where there is any hint of a beneficial effect, we find that there are better ways of accomplishing it.

Senator Kohl, you are correct that New Zealand has permitted direct-to-consumer advertising, but actually now there is a moratorium on it, and they are planning on making that moratorium final. The only country that has tried it has turned its back on it.

I will make seven points.

First, direct-to-consumer advertisements bear little relationship to public health needs. New and expensive drugs, those for diseases that are bothersome and incurable, are the ones that we see advertised. Only 14 percent of sales for the top 50 DTC-advertised drugs are for acute conditions, and only one of the top 50 DTC-advertised drugs was an antibiotic, presumably because people are quickly cured and there is no need for a refill. We see shouldered aside advertisements for generic drugs, such as those that might prevent heart attack or stroke, and, of course, any non-drug interventions, like behavioral smoking cessation, weight loss or exercise programs.

Second, many DTC advertisements are misleading or dangerous. Part, I think, of the reason we have this hearing is because of what happened with Vioxx. We should remember that Vioxx was the No. 1 DTC-advertised drug in 2000, and at $160 million was larger than the campaigns that year for either Pepsi or Budweiser. So that is one well-known example.

I have attached to my testimony a second example, which is a DTC ad which might be considered a direct-to-children ad. It is an ad for Differin, an acne medication, and if you look at my testimony, you will see that teenagers are exhorted—those at Acne High are exhorted to take a course called "Zit 101." Of course, they need to talk to their parents because children don't usually go to their doctors without their parents. If you can get your parent to help you out, you get to qualify for one of the three levels of "cool." If you sign up, you get two free music downloads. If you get and refill a Differin prescription, you get seven free music downloads. If you get your parent to help you refill it, you get ten. This is turning children into the agents of the pharmaceutical industry in a way to get around doctors. I think that is really inappropriate.

A third example, very briefly, is AstraZeneca's Crestor, a drug in which the industry actually managed to misrepresent the FDA itself by saying that the FDA had few concerns about the safety of the drug, when, in fact, they were on record saying that they did.

Point three, consumers are being misled. Sixty percent of people surveyed by the FDA thought that the advertisements provide in-

sufficient information about drug risks, and 44 percent felt similarly about the benefits. Consumer support for DTC advertisement, as all of you have hinted, is, in fact, declining. There are data from the FDA's own survey comparing the 1999 to 2002 survey that show that more and more people are getting fed up with these ads and fewer "liked seeing" the advertisements, a decline from 52 percent down to 32 percent.

Point four, doctors are being coerced. Dr. Kravitz will talk, I am sure, in great detail about his landmark study, but I will point to one part of it, which is that patients with adjustment disorder, only 10 percent of whom would otherwise have gotten a prescription for an antidepressant drug, 55 percent of those did when they went to a physician mentioning an ad for Paxil that they had seen on TV. So this is a clear increasing of prescribing when it probably is not justified.

Point five, the price of health care is being driven up. Patients are being induced to request new, more expensive medications instead of equally effective, older generic ones. The GAO concluded that, "DTC advertising appears to increase prescription drug spending and utilization." I am sure that their next study that you have requested will come to the same conclusion, and most of that is because of increased utilization, not prices.

Point six, potential benefits of DTC advertising. There is a comprehensive review study referenced in my testimony of the data on this issue. They conclude: "The onus is on those who might support [DTC advertising] to produce evidence of benefit and, in the absence of this evidence, we must assume that the likely disbenefits. . . outweigh the as yet unproven benefits."

I go on to talk about Dr Kravitz's study in which he shows that if you want people to get prescribed more antidepressants—and I shan't comment on whether that is a good idea or not. But if one did, in fact, general entreaties to physicians are more effective than direct-to-consumer advertisements.

My seventh and final point is that FDA enforcement is lackadaisical. I have attached some data for enforcement actions at the FDA dating back to 1997. These are all enforcement actions. There may be a small increase recently, but the overall trend is down and has been consistently so, in fact, going back to 1998. But there is a big drop-off after 2001, at which point all warning letters and regulatory letters needed to go through the Office of the Chief Counsel at the FDA, which resulted in a decreased number of regulatory letters being released, which the GAO said had adversely affected FDA's oversight.

So, in conclusion, then, we believe that the benefits have not been demonstrated, and to the extent that there are any they can be secured through other less dangerous routes, but the dangers are quite clear.

Our recommendations are: Firstly, the industry, the guidelines—PhRMA has been aroused to produce them only because of criticism. The guidelines are voluntary, and are they recommend, for example, if the company should wait "an appropriate amount of time"—whatever that is—after launching a new drug before initiating a DTC advertisement. Senator Frist has recommended a 2-year waiting period. Growth of DTC advertising didn't happen

magically. It is because of deregulation by the FDA. It means the genie can be put back in the bottle.

We would recommend that FDA provide proper patient information. The best way to do this is through medication guides, which the agency developed an interest in 1995. But there are only about 75 of those, and that is part of the reason the industry can get away with it—because the FDA has failed to provide this kind of information.

Federal agencies should be doing more to educate patients, and I refer to the FDA, of course. The NIH and the Agency for Health Care Research and Quality could also be doing more. The FDA has yet to publish any regulations regarding DTC advertisements. You heard Dr. Behrman talk about how they use the prescription drug advertising rules to apply to DTC. There are some guidances, but they are voluntary. They have little ability to enforce them. They are understaffed. There is no pre-review of television advertising, and we also think there should be a ban on celebrity endorsements. Most fundamentally, the agency still does not have the ability to level civil monetary penalties.

In conclusion, health care observers have long noted that health care is unlike other markets in that patients typically do not purchase services directly. Rather, because of the complexity of the decisions involved and the potentially life-threatening nature of poor choices, the physician acts as a "learned intermediary" on the patients' behalf. DTC advertising is nothing less than an end run around the doctor-patient relationship, an attempt to turn patients into the agents of the pharmaceutical industry as they pressure physicians for medications that they may not need.

Thank you.

[The prepared statement of Dr. Lurie follows:]

Peter Lurie, MD, MPH
Deputy Director
Public Citizen's Health Research Group
Testimony before the Senate Special Committee on Aging on The Impact of Direct-to-Consumer Drug Advertising on Seniors' Health and Health Care Costs
September 29, 2005

Like all interventions in health care, direct-to-consumer (DTC) advertising should be evaluated by comparing its risks to its benefits, in the context of the available or potentially available alternatives. The objective, of course, is to realize the potential benefits while minimizing the risks. On balance, we believe that the clearly demonstrated adverse effects of DTC advertising outweigh the still-undemonstrated, theoretical benefits of the advertising. Every country in the world has reached this conclusion, except the United States. Only New Zealand has ever permitted DTC advertising, but it imposed a moratorium in December 2004. The European Union considered permitting DTC advertising, but rejected the idea.

DTC Advertisements Bear Little Relationship to Public Health Needs

Predictably, DTC advertising has been concentrated on new, expensive drugs for conditions that are bothersome and incurable. Thus, according to the Government Accounting Office (GAO), the top 15 DTC-advertised drugs in 2000 accounted for 54% of all DTC advertising expenditures.[1] Only 14% of sales for the top 50 DTC-advertised drugs is for acute conditions and only one of the top 50 DTC-advertised drugs was an antibiotic, presumably because patients are generally cured and have no need for refills. Most are targeted at seniors. Strikingly, one never encounters advertisements for generic drugs, even though, for example, generic diuretics are the most cost-effective method for preventing heart attacks and stroke.[2] Because patient entreaties are unlikely to induce a physician to initiate or change a prescription for a cancer drug, these are also less likely to be advertised. Of course, DTC advertising shoulders aside non-drug interventions such as behavioral smoking cessation, weight-loss or exercise programs, which can be less costly, safer or more effective. In sum, there is little relationship between our true public health needs and the subjects of DTC advertising.

Many DTC Advertisements Are Misleading or Dangerous

In the eight years since the FDA opened the floodgates to broadcast DTC advertising, numerous inappropriate advertisements have appeared. The most widely discussed have been the massive DTC campaigns waged by the manufacturers of the Cox-2 inhibitors. Importantly, these drugs were never proved to be more effective pain relievers than many drugs available over-the-counter. For most patients the purported stomach protection offered by these drugs (a claim that the FDA permitted only for Vioxx, but through industry promotional efforts came to be associated with the other Cox-2 inhibitors as

well) was irrelevant as those patients tolerated conventional pain relievers without stomach upset. Nonetheless, an estimated two-thirds of the growth in Cox-2 use between 1999 and 2000 was among such patients.[3] In 2000, Vioxx was the number one DTC-advertised drug – at $160 million, larger than the campaigns that year for Pepsi and Budweiser – and retail sales quadrupled.[4] With as many as 140,000 serious cardiovascular events due to Vioxx alone,[5] the dangers of such promotions are now increasingly apparent. Other drugs that have been transformed from pedestrian to blockbuster in part by DTC advertising are Claritin for allergies and Singulair for asthma.

One of the more astounding DTC advertisements we have seen is attached to this testimony and is still running. Produced by Galderma Laboratories, the makers of the prescription acne medication Differin (adapalene), and broadcast both on the Internet[6] and on MTV, the advertisements direct teenage viewers to a portion of the Differin website to receive free music downloads. The advertisements are clearly directed at teenagers: the viewer is exhorted to obtain a Teen Survival Handbook and to take a self-test on acne called Zit 101, a course on offer at Acne High. The advertisement plays to teenage fears ("Remember: There are thousands of pores on your face, which means your skin has the potential to 'give birth to' thousands of microcomedones.") and notions of empowerment ("Fight Acne with Free Music. How Cool is That?"). Realizing that many teens will visit physicians only with their parents, the website has an entire section on "Talking to Parents About Acne." If you can convince your parent to help you secure a prescription for Differin, the benefits multiply: the "3 levels of cool" are Level 1: sign up (two free music downloads); Level 2: get and fill Differin prescription (seven free downloads); and Level 3: refill Differin prescription (ten free downloads). Bribing physicians to prescribe medications has long been held to be illegal. This advertisement essentially pays teenagers to convince adults to procure this drug for them, with the size of the payment in proportion to the amount of drug prescribed. Incidentally, a previous Differin DTC advertisement has already been the subject of an FDA regulatory letter.[7]

An improbable new low in inappropriate DTC advertising was reached in a November 2004 advertisement by AstraZeneca on its website and in print that actually had the audacity to mislead the public by misrepresenting the FDA. In an advertisement for the cholesterol-lowering drug Crestor, a drug associated with muscle and kidney damage, AstraZeneca claimed that "We have been assured today at senior levels in the FDA that there is no concern in relation to CRESTOR's safety." Public Citizen wrote to the FDA[8] pointing out that the agency was actually on record stating that "[the Agency] has been very concerned about Crestor since the day it was approved, and we've been watching it very carefully." The agency forced the company to terminate its campaign.[9]

Consumers Are Being Misled

Consumers have many misconceptions about DTC advertising. In one survey, 50% believed that DTC advertisements had to be pre-approved by the government and 43% thought that only "completely safe" drugs were allowed to be advertised.[10] Studies conducted by the FDA itself confirm the dangers of DTC advertising. The agency's 2002 survey[11] found that 60% of patients thought that the advertisements provide insufficient

information about drug risks and 44% felt similarly about benefits. Fifty-eight percent believed the advertisements made the drugs appear better than they are, and 42% said the advertisements made it seem as if the drug would work for everyone.

Consumer support for these advertisements is actually declining. Compared to a similar FDA survey in 1999, fewer patients responding to the FDA's 2002 survey said that the advertisements had prompted them to talk to a doctor (27% in 1999 vs. 18% in 2002), fewer said that the advertisements provide enough information even to decide whether to consult a physician (70% vs. 58%), fewer felt that the advertisements helped them make better decisions about their own health (47% vs. 32%) and fewer "liked seeing" the advertisements (52% vs. 32%).[11]

Doctors Are Being Coerced

Early defenses of DTC advertising asserted that physicians would not be manipulated by patient demands based on DTC advertisements. Unfortunately, this assertion has proved to be wrong. In an already classic study published in the Journal of the American Medical Association in April, Kravitz and colleagues sent "standardized patients" with either depression or adjustment disorder into doctors' offices.[12] The patients either 1) described their symptoms and made no specific request for medication; 2) said they had seen a program on television and wondered about drug treatment; or 3) said they had seen a DTC advertisement for Paxil. Of standardized patients with adjustment disorder, a condition not generally requiring drug treatment, 10% of those making no specific request received a prescription (none for Paxil), compared with 55% of those saying they had seen a Paxil advertisement (67% for Paxil) and 39% of those making a general request (26% for Paxil). Clearly these advertisements can spur unnecessary drug prescribing.

Of course, in principle, doctors could be grateful for patients' prompting. But other empirical research suggests otherwise. In one study, doctors were asked whether they considered drugs they had just prescribed to be only "possible" or "unlikely" choices. Fifty percent answered affirmatively for DTC-advertised drugs that were prescribed at the patient's request, compared to only 12% of new prescriptions not requested by patients.[13] Thus, physicians often accede to patients' DTC-driven requests, but are left feeling uneasy.

The Price of Health Care is Being Driven Up

Predictably, the cost of health care is being driven up, as patients are induced to request newer, more expensive medications instead of equally effective, older, generic alternatives. One report indicated that the top 25 DTC-advertised drugs accounted for 41% of the growth in retail drug spending in 1999.[14] The report did not separate the effects of DTC advertising from those of advertising to physicians, which often go hand-in-hand. The GAO agreed that "DTC advertising appears to increase prescription drug spending and utilization,"[1] primarily because of increased utilization, not increased prices. In a study that did separate out the various forms of advertising, the growth in

DTC advertisements for the 25 largest therapeutic classes accounted for 12% of drug sales growth from 1999 to 2000 and resulted in an additional $2.6 billion in pharmaceutical expenditures in 2000.[15] The GAO has estimated that a 10% increase in DTC advertising translates into a 1% increase in sales for that class of drugs, an enormous increase given that many drug classes sell in the billions of dollars.[1] One way or another – through insurance premiums, co-payments or taxes – consumers foot the bill for all this.

Potential Benefits of DTC Advertising

The principal benefit asserted by supporters of DTC advertising is that patients with undertreated conditions might receive treatment they otherwise would not have received. This claim remains unproven. The only comprehensive review of studies on DTC advertising concluded that "No empirical research has demonstrated better communication [between patients and physicians] and improved health outcomes."[16] The authors continue: "The onus is on those who might support [DTC advertising] to produce evidence of benefit and, in the absence of this evidence, we must assume that the likely disbenefits (clinical and economic) outweigh the as yet unproven benefits."

Although the review excluded the recent Kravitz study,[12] the Kravitz study hardly supports DTC advertisements. While it is true that, in the Kravitz study, DTC advertisements led to more prescribing of antidepressants for those standardized patients presenting with depression, general entreaties to physicians were actually more effective than those based on DTC advertisements (76% prescribing rate vs. 53%). (This assumes that prescribing an antidepressant to a depressed patient at his or her first visit is good medicine.) As noted, the study also showed that DTC produced massive overprescribing of antidepressants for those patients with adjustment disorder who have little need for them; the study leaves unanswered whether patients with depression or adjustment disorders are more likely to approach their doctors. Regardless, it seems clear that the purported benefits of DTC advertising can be secured more effectively through non-commercial public-service announcements, without the risk of misleading the public or driving up health-care costs unnecessarily.

FDA Enforcement is Lackadaisical

For years, Public Citizen have tracked FDA's drug advertising enforcement. The sattached figure depicts all Warning Letters and Untitled Letters dating back to 1997. Despite a small increase in enforcement activity this year (and FDA has elsewhere claimed that there has been an increase in enforcement activity for DTC advertising specifically), the broader trend is more important: an 85% decline in enforcement actions between 1998 and 2004, the last year with complete data. Much of this decrease predates the current administration, but there was an added drop in 2002. This drop was due to the policy of then-Chief Counsel Daniel Troy to require all regulatory letters to pass through his office, a departure from previous practice and a change that, according to the GAO, "adversely affected" FDA's oversight. The GAO concluded in 2002 that "Since the policy change, [the Office of the Chief Counsel's] reviews of draft regulatory letters

from FDA have taken so long that misleading advertisements may have completed their broadcast life cycle before FDA issued the letters."[1] According to a report by the Minority Staff of the Committee on Government Reform, in 2003 the average time from initial placement of a prescription drug advertisement and an enforcement action (if any) was 177 days.[17] Recidivism is common; the companies with the largest numbers of advertising-related regulatory letters between 2002 and 2005 were Pfizer (11); Roche, Boehringer Ingelheim and Novartis (five each); and Glaxo (four).[18] The drug advertising division remains greatly understaffed to cope with the continually rising levels of advertising, and DTC advertising in particular.

Conclusion

Even if one were to grant, on a strictly hypothetical basis, that DTC advertisements did, incidentally, convey some useful information to consumers, the real question remains: Are there alternative methods for conveying this information that avoid the risks of DTC advertisements? The answer, as the Kravitz study demonstrates, is an indisputable "yes": If antidepressants were indeed underprescribed, requests based on general entreaties to physicians led to more prescribing than requests based on DTC advertisements. This unproven benefit weighs poorly against the proven risks of DTC advertising.

Recommendations

In developing an approach to reducing the harms of DTC advertising, three overriding points are worth noting. First, at least under prevailing legal interpretations, DTC advertising is unlikely to be prohibited in the United States. Second, the industry has demonstrated a gross inability to police itself. It is only the public-relations disaster of the Vioxx debacle that has roused PhRMA to develop DTC advertising guidelines.[19] These guidelines are, of course, voluntary, and are designed primarily to stave off more aggressive legislation or regulation. The guidelines recommend that companies should wait "an appropriate amount of time" after launching a new drug before initiating a DTC campaign. (Senator Frist has recommended a two-year waiting period.) Third, the growth of broadcast DTC advertising did not arise magically. Rather, it was the predictable result of FDA's deregulatory efforts.* It follows that the genie can, to a large extent, be put back in the bottle.

How, then, is the public to be protected from this misleading information? First and foremost, FDA-approved patient information for all prescription drugs is necessary. In 1979, the FDA proposed just this, but opposition from organized medicine, which feared the erosion of its authority, and the pharmaceutical industry ensured that the proposal was withdrawn early in the Reagan administration. In the 1990s, the idea was revisited in the form of FDA-approved Medication Guides, but we estimate that only about 75 drugs of the thousands on the market have such Guides. Instead, the market has been left to the

* Until 1997, all DTC advertisements that sought to link a disease with a particular drug had to provide the so-called Brief Summary, an often extensive review of potential adverse effects of the drug being advertised. Since 1997, companies have been permitted to refer consumers to websites, print advertisements or toll-free telephone numbers to obtain this information.

makers of Patient Information Leaflets, which are not FDA-approved and which, as we have shown in three studies,[20,21,22] often omit important safety information. FDA-approved information for patients, rather than self-serving advertising, is the appropriate response to the dearth of patient-appropriate drug information. As Franz Ingelfinger, the editor of the New England Journal of Medicine once argued, "advertisements should be overtly recognized for what they are – an unabashed attempt to get someone to buy something, although some useful information may be provided in the process."[23]

Federal agencies could also be doing more to educate patients. The agencies most able to do this are the FDA itself, the National Institutes of Health and the Agency for Healthcare Research and Quality. The failure of these agencies to step into the information gap and fulfill their educational missions allows the industry to cloak its advertising in the mantle of education. Of course, if the industry truly wished to exhort patients to seek care for undertreated medical conditions, it would avail itself only of "help-seeking" advertisements, which inform patients of the existence of particular diseases without naming a treatment. Such advertisements are regulated by the Federal Trade Commission instead of the FDA, presumably because they have less capacity to mislead.

Even as DTC advertising has mushroomed from a $791 million industry in 1996[24] to a $4.1 billion one in 2004,[25] the FDA has yet to publish any regulations regarding DTC advertisements. Some guidances have been promulgated,[26,27,28] but these are voluntary and the agency has little ability to enforce them, in part because the advertising division is so severely understaffed and because regulatory letters have to pass through the Office of the Chief Counsel. At a minimum, regulations should provide for pre-review of television advertising and should not allow celebrity endorsements. More fundamentally, the agency still does not have the ability to levy civil monetary penalties. Instead, the FDA issues (often delayed) Warning Letters and Untitled Letters, which often arrive after the advertisement has completed its run, by which time millions of people have already been exposed to their misleading messages.

Health-care observers have long noted that health care is unlike other markets in that patients typically do not purchase services directly. Rather, due to the complexity of the decisions involved and the potentially life-threatening nature of poor choices, the physician acts as a "learned intermediary" on the patient's behalf. DTC advertising is nothing less than an end-run around the doctor-patient relationship – an attempt to turn patients into the agents of pharmaceutical companies as they pressure physicians for medications they may not need.

Differin®
(adapalene cream)

Acne Info for Teens

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Acne Basics | True or False? | Talking to Parents
Ask Your Doctor | Skin Care | The Right Routine for You

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Level	Requirement	# of Free Music Downloads
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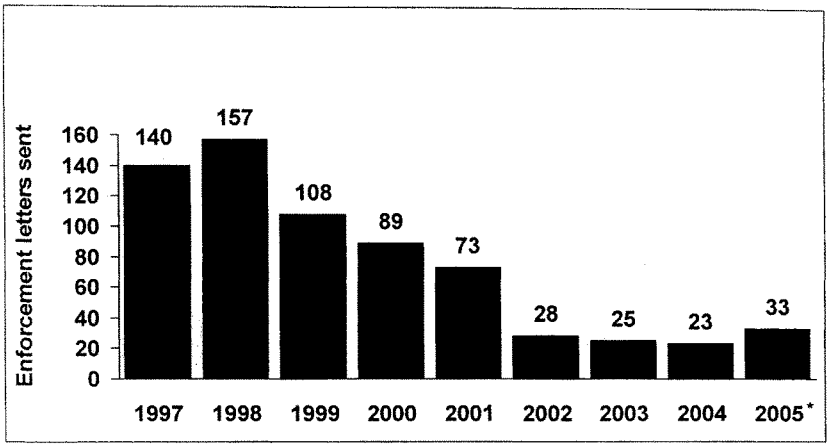
2	Get and Fill Differin® Prescription	7
3	Refill Differin® Prescription	10

sign up

FDA Warning and Untitled Letters to Drug Companies, 1997-2004



*Projected from data through August

[1] General Accounting Office. Prescription drugs: FDA oversight of direct-to-consumer advertising has limitations. GAO-03-177, October 2002.
[2] ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group, The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). Journal of the American Medical Association 2002;288:2981–97.
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[19] Pharmaceutical Research and Manufacturers Association. PhRMA guiding principles: direct to consumer advertisements about prescription medicines. August 2005. Available at: http://www.phrma.org/mediaroom/press/releases/02.08.2005.1195.cfm.

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Senator KOHL. Thank you, Dr. Lurie.
Dr. KRAVITZ.

STATEMENT OF RICHARD L. KRAVITZ, MD, MSPH, DIRECTOR, CENTER FOR HEALTH SERVICES RESEARCH IN PRIMARY CARE, UNIVERSITY OF CALIFORNIA, DAVID MEDICAL CENTER, SACRAMENTO, CA

Dr. KRAVITZ. Chairman Smith, Senator Kohl, distinguished members, thank you for inviting my testimony today.

Spending on direct-to-consumer advertising has increased every year since the early 1990's and, as we have heard, in 2003 totaled $3.2 billion, perhaps edging up to as much as $4 billion today. Much of the spending is for drugs used to treat conditions that affect the elderly, including high blood cholesterol, stomach ulcers, degenerative arthritis, strokes, and depression. As you have heard in testimony already, the debate on the proper role of DTC advertising is highly contentious.

While all the signs are that older Americans, just like their younger counterparts, are responding to DTC ads, in a telephone survey of Sacramento residents several years ago, more than half the respondents had read a DTC ad from cover to cover, and in a more recent survey conducted by Prevention magazine, 27 percent of seniors had asked their physicians about advertised medicines. The question is: Is there anything wrong with that?

Proponents of DTC advertising argue that ads educate patients and encourage appropriate care-seeking, while critics charge, as we have heard, that ads lead to overprescribing of unnecessary, expensive, and potentially harmful medications.

To shed some light on this controversy, we conducted a study that was published in the April 27th issue of the Journal of the American Medical Association. The study was designed as an experiment using standardized patients, or SPs. SPs are actors trained to portray the clinical and biographical features of a role and to do so accurately and reliably. The use of SPs allowed us to control very precisely for patient demographic characteristics and symptoms, allowing us to ascribe any differences in doctor behaviors to the kinds of requests the SPs made.

We enrolled 152 physicians in three U.S. cities. Most physicians saw two unannounced standardized patients, for a total of 298 visits. We used 18 white, middle-aged actresses who were trained to portray six roles, which we created by crossing two clinical conditions with three request types. The clinical conditions were major depression and adjustment disorder. Major depression is serious and needs to be treated promptly. Adjustment disorder represents an exaggerated reaction to life events and can usually be treated with watchful waiting.

As you will see in one of your handouts, the first one, with the little picture up in the upper right-hand corner, actresses portraying "Louise Parker," the major depression role, complained of depressed mood for a month, worse in the past two weeks. Actresses portraying "Susan Fairly," the adjustment disorder role, noted some sleep problems and low energy for a few weeks, but nothing that interfered significantly with function.

The SPs were further assigned to one of three request groups, and that is laid out in the next handout. A third of the standardized patients mentioned seeing a television ad and made a brand-specific request for Paxil. Another third told of watching a TV documentary and made a general request for medication that might help. The last third made no request at all.

We thereby created six cells, six separate conditions, with about 50 standardized patient visits in each one. The first cell, for example, contained visits in which the SP portrayed major depression and made a brand-specific request for Paxil, then major depression with a general request, no request, and so on.

The next slide shows the major results. Among SPs portraying major depression, antidepressant prescribing was highest when a general request was made, 76 percent of visits; middling when a brand-specific request was made, 53 percent; and lowest when no request was made, 31 percent. These are among SPs who, by all rights, should well have been treated at the first visit.

In adjustment disorder, prescribing occurred in 55 percent of brand-specific visits, 39 percent of general request visits, and only 10 percent of no request visits.

We went on to define——

Senator TALENT. Mr. Chairman, can I just ask a question to clarify this? It is just a factual thing.

When the drug was prescribed and when they made a brand-specific request, did the physician prescribe the brand they asked for, or was there another drug, or did you keep track of that?

Dr. KRAVITZ. We did, and, in fact, Paxil, the brand-specific drug, was prescribed about half the time when that specific drug was——

Senator TALENT. So when they made——

Dr. KRAVITZ. The other half the time another antidepressant was——

Senator TALENT. One more—was there a difference between how often the Paxil was prescribed between the control groups when they asked for it specifically or when they just said we have got a problem, maybe there is a drug that will help us?

Dr. KRAVITZ. Very interestingly, Paxil was almost never prescribed in the major depression condition unless it was asked for specifically. It was prescribed about 20 percent of the time in the adjustment disorder condition when it wasn't asked for.

Senator TALENT. OK. So half the time when asked specifically and they prescribed something——

Dr. KRAVITZ. Less than 20 percent otherwise.

Senator TALENT. OK. Thank you. I am sorry, Mr. Chairman.

Dr. KRAVITZ. We went on to define "minimally acceptable initial care" for depression as any combination of an antidepressant prescription, a referral to a mental health professional, or a follow-up appointment within two weeks. The next slide in your handout shows how minimally acceptable care was much higher for SPs making any kind of request, either brand-specific or general, than for those making no request, over 90 percent versus 56 percent.

So, in summary, patients' antidepressant requests are a powerful influence on physicians' prescribing decisions. While such requests clearly improve quality of care for patients in actual need of imme-

diate treatment, they also lower the prescribing threshold when an immediate prescription may not be in the patient's best interest.

To the extent that these results hold true for other conditions and therapies, DTC advertising is a two-edged sword, capable of reducing underuse of necessary treatment and increased overuse of unnecessary treatment both at the same time.

Thank you.

[The prepared statement of Dr. Kravitz follows:]

Written Statement

Richard L. Kravitz, MD, MSPH
Professor of Internal Medicine and Director, Center for Health Services Research in Primary Care
University of California, Davis

In Testimony Before the U.S. Senate Special Committee on Aging
September 29, 2005

Spending on direct-to-consumer (DTC) advertising of prescription drugs in the United States totaled $3.2 billion in 2003[1]. Much of this spending is for drugs used to treat conditions that affect the elderly, including high blood cholesterol; stomach ulcers and heartburn; degenerative arthritis; stroke; and depression.[2] Critics charge that DTC advertisements lead to over-prescribing of unnecessary, expensive, and potentially harmful medications, while proponents counter that they can serve a useful educational function and help avert under-use of effective treatments for conditions that may be poorly recognized, highly stigmatized, or both.

How are older Americans responding to these ads? A survey conducted by *Prevention* Magazine in late 2003 concluded that 62.4 million consumers have talked to their doctors about advertised medicines, and of these, 16.2 million have asked for an advertised medicine. Older Americans (>=65 years) are somewhat less likely to talk with their doctors about advertised medicines than "Baby Boomers," but not by much (27% vs. 36%).[3] While some physicians welcome these discussions, many find them a distraction from the myriad of clinically critical tasks already packed into a typical office visit. Furthermore in study of 1431 visits in Sacramento (CA) and Vancouver (Canada), physicians were much more likely to register "therapeutic ambivalence" after prescribing an advertised drug that a patient had requested.[4] (Ambivalence was defined as answering "possibly" or "unlikely" to the question, "If you were treating another similar patient with the same condition, would you prescribe this drug?")

There is no disputing that DTC advertisements find their audience, motivate consumers, and result in requests for medication. The question for the health of America's seniors (and younger citizens as well) is whether those requests result in better and more appropriate care. The pharmaceutical industry has long claimed that DTC ads merely educate patients about potentially beneficial treatments and that it is up to the physician to decide whether medication is warranted. After all, neither patients nor drug companies have the power to prescribe. This position assumes that physicians are reliable "learned

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[1] Prescription Drug Trends. Menlo Park, Calif: Kaiser Family Foundation; 2004. Fact sheet 3057-03.
[2] TNS Media Intelligence. In *MM&M* April 2005; p.38.
[3] Prevention Magazine's 7th Annual Survey: Consumer Reaction to DTC Advertising of Prescription Medicines, 2003-4, p. 50.
[4] Mintzes B, Barer ML, Kravitz RL et al. CMAJ. 2003 Sep 2;169(5):405-12.

intermediaries," welcoming their patients' requests for beneficial therapies but steering them away from those that are unnecessary or harmful.

To address these issues, our research group at the University of California and the University of Rochester devised an elaborate experiment focused on antidepressant medications. Antidepressant medications consistently rank among the top DTC advertising categories. Major depressive disorder carries stigma, is frequently under-diagnosed, and can be treated successfully in the majority of patients.[5] A thoughtful DTC advertising campaign could encourage patients to seek effective care. However, DTC advertising could also promote prescribing of antidepressants for patients with minor symptoms in the absence of clearly defined indications. Although some short-term studies have shown benefit from antidepressants in minor depression, there is no professional consensus about the need for immediate treatment as opposed to watchful waiting. Patients with minor symptoms of short duration who are prescribed antidepressants at initial presentation would be subject to short-term side effects (e.g., sexual dysfunction) and potential hazards (including suicidality) that would have to be weighed against marginal gains.

In an ideal world, patients presenting to primary care doctors with symptoms of major depression would almost always receive antidepressant medication (or psychotherapy), if not at the first visit then soon thereafter. Patients with adjustment disorder (transient problems in living), on the other hand, would be spared drug treatment, at least until the picture further clarified itself. With these qualifications in mind, failure to prescribe antidepressants (or to arrange for mental health consultation or follow-up) for patients with major depression constitutes "underuse" of effective care, while prescribing antidepressants at the first visit to patients with adjustment disorder is at the margins of clinical appropriateness.

Our trial used Standardized Patients (SPs) to determine how practicing physicians actually respond to patients' requests for antidepressant medicines. SPs are actors trained to portray the clinical and psychological features of a patient role. We enrolled 152 physicians in 3 US cities; each physician consented in advance to participate in 2 unannounced SP visits. (The doctors knew they would see the actor-patients but did not know when.)[6] Eighteen SPs were trained to portray 6 roles, created by crossing 2 clinical conditions (symptoms consistent with major depression or adjustment disorder) with 3 request types (brand-specific, general, or none). The overall design is depicted in the table below.

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[5] Simon GE. Gen Hops Psychiatry 2002;24:213-224.

[6] Participating physicians were told that they would see two SPs presenting with a combination of common physical and mental health symptoms but were not told specifically that some of the SPs would be making requests for medication. They also knew the visits would be audiorecorded. Project staff worked assiduously with medical office staff and insurers to arrange the visits under a veil of secrecy. Post-visit surveys suggested that 13% of physicians were "suspicious" that they had seen an SP. Practices were reimbursed for their participation in the study.

	Brand-Specific Request	General Request	No Request
Major Depression	Role A (N=51)	Role B (N=50)	Role C (N=48)
Adjustment Disorder	Role D (N=49)	Role E (N=49)	Role F (N=51)

All SPs were middle aged white women.[7] Those playing the major depression role ("Louise Parker") complained of depressed mood for a month, worse during the past two weeks, accompanied by fatigue, low energy, and early morning awakening, but no suicidality. Those playing the adjustment disorder role ("Susan Fairly") complained of much milder symptoms whose onset followed a minor upheaval at work.

To understand the effect of requests on physician behavior, actors portraying major depression were further assigned to experimental conditions A, B, or C; those portraying adjustment disorder were assigned to conditions D, E, or F (Table). Sub-roles A and D were to make a brand-specific request within the first 10 minutes of the visit or before the physical examination (whichever came first). They began: "I saw this ad on TV the other night. It was about Paxil®. Some things about the ad really struck me. I was wondering if you thought Paxil® might help." Paxil® was chosen because at the time of the study it was widely promoted, priced higher than generic fluoxetine, and available on the formularies of participating health care organizations in all three cities. Paxil® did not become available as generic paroxetine until midway through the study (September, 2003). Sub-roles B and E were to make a general request for medication. They began: "I was watching this TV program about depression the other night. It really got me thinking. I was wondering if you thought a medicine might help me." Sub-roles C and F were to make no explicit request.

Major findings from the study were as follows:

- Among SPs portraying **major depression**, antidepressant prescribing was highest when a general request was made (76% of visits), middling when a brand-specific request was made (53%), and lowest when no request was made (31%).
- Among SPs portraying **adjustment disorder**, antidepressant prescribing rates were 55% among SPs making a brand-specific request, 39% among those making a general request, and 10% among those making no request.
- The results were confirmed in statistical models that adjusted for city, specialty, physician gender, and whether the doctor was "suspicious" of seeing an SP. These same models showed that brand-specific "DTC" requests had significantly greater relative potency in adjustment disorder than in major depression. In other words, brand-specific requests promoted prescribing in both depression and adjustment disorder, but they were *particularly* effective in adjustment disorder.
- "Minimally acceptable initial care" (any combination of an antidepressant, mental health referral, or follow-up within two weeks) in the major depression role was

[7] Cost constraints precluded a more diverse sample, and in any case depression is somewhat more prevalent among women than men.

offered to 98% of SPs making a general request, 90% of those making a brand-specific request, and 56% of those making no request ($p<0.001$).

What can be learned from these results? First, patients' antidepressant requests (whether brand-specific or general) are a powerful influence on physicians' prescribing decisions. Second, such requests can improve care for patients with major depression. Third, physicians are not always be the stalwart intermediaries the pharmaceutical industry claims and the law assumes – a DTC-driven-request by "Susan Fairly" increased the probability of marginally appropriate prescribing for adjustment disorder from 10% to 55%.

The net social value of DTC advertising and the requests they engender may depend upon the specific context. The benefits of advertising will tend to dominate when the target condition is serious and the treatment is very safe, effective, and inexpensive. Harms are most likely when the target condition is trivial and the treatment is relatively perilous, ineffective, or costly. If one accepts this perspective, an outright ban on DTC advertising *could* do more harm than good. A more judicious approach would:

- Place a moratorium on DTC advertising of new drugs, allowing a reasonable period of time for important side effects to emerge;
- Raise the bar for DTC advertising in terms of public health importance, safety, and effectiveness;
- Encourage DTC advertising or joint public-private partnerships to raise public awareness of effective treatments for important public health conditions.

An ample moratorium period would allow information on potential adverse effects to accumulate. If such a moratorium had been in place during the launch of the Cox-II inhibitors, many lives would have been saved.

Raising the bar for DTC advertising means that not every FDA-approved drug could be advertised directly to the public. Under this concept, advertising would be restricted to drugs or classes of drugs that are known to treat important conditions (ie those causing significant morbidity or mortality in the population), are extremely safe and effective, or are notably under-used. The FDA would be well-positioned to make such determinations.

DTC advertising, or variations on it, should be supported and even encouraged in special cases. For example, a campaign to increase the proportion of patients with previous myocardial infarction (heart attack) who take beta-blockers and aspirin could save thousands of lives annually.

ORIGINAL CONTRIBUTION

Influence of Patients' Requests for Direct-to-Consumer Advertised Antidepressants

A Randomized Controlled Trial

Richard L. Kravitz, MD, MSPH
Ronald M. Epstein, MD
Mitchell D. Feldman, MD, MPhil
Carol E. Franz, PhD
Rahman Azari, PhD
Michael S. Wilkes, MD, PhD
Ladson Hinton, MD
Peter Franks, MD

Context Direct-to-consumer (DTC) advertising of prescription drugs in the United States is both ubiquitous and controversial. Critics charge that it leads to overprescribing, while proponents counter that it helps avert underuse of effective treatments, especially for conditions that are poorly recognized or stigmatized.

Objective To ascertain the effects of patients' DTC-related requests on physicians' initial treatment decisions in patients with depressive symptoms.

Design Randomized trial using standardized patients (SPs). Six SP roles were created by crossing 2 conditions (major depression or adjustment disorder with depressed mood) with 3 request types (brand-specific, general, or none).

Setting Offices of primary care physicians in Sacramento, Calif; San Francisco, Calif; and Rochester, NY, between May 2003 and May 2004.

Participants One hundred fifty-two family physicians and general internists recruited from solo and group practices and health maintenance organizations; cooperation rates ranged from 53% to 61%.

Interventions The SPs were randomly assigned to make 298 unannounced visits, with assignments constrained so physicians saw 1 SP with major depression and 1 with adjustment disorder. The SPs made a brand-specific drug request, a general drug request, or no request (control condition) in approximately one third of visits.

Main Outcome Measures Data on prescribing, mental health referral, and primary care follow-up obtained from SP written reports, visit audiorecordings, chart review, and analysis of written prescriptions and drug samples. The effects of request type on prescribing were evaluated using contingency tables and confirmed in generalized linear mixed models that accounted for clustering and adjusted for site, physician, and visit characteristics.

Results Standardized patient role fidelity was excellent, and the suspicion rate that physicians had seen an SP was 13%. In major depression, rates of antidepressant prescribing were 53%, 76%, and 31% for SPs making brand-specific, general, and no requests, respectively ($P<.001$). In adjustment disorder, antidepressant prescribing rates were 55%, 39%, and 10%, respectively ($P<.001$). The results were confirmed in multivariate models. Minimally acceptable initial care (any combination of an antidepressant, mental health referral, or follow-up within 2 weeks) was offered to 98% of SPs in the major depression role making a general request, 90% of those making a brand-specific request, and 56% of those making no request ($P<.001$).

Conclusions Patients' requests have a profound effect on physician prescribing in major depression and adjustment disorder. Direct-to-consumer advertising may have competing effects on quality, potentially both averting underuse and promoting overuse.

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SPENDING ON DIRECT-TO-consumer (DTC) advertising of prescription drugs in the United States totaled $3.2 billion in 2003.[1] Although expenditures may be leveling off,[2] DTC advertisements have become a stable, if controversial, feature of the media landscape.[3-6] Critics charge that DTC advertisements lead to overprescribing of unnecessary, expensive, and potentially harmful medications, while proponents counter that they can serve a useful educational function and help avert underuse of effective treatments for conditions that may be poorly recognized, highly stigmatized, or both.[7]

Antidepressant medications consistently rank among the top DTC advertising categories.[8,9] Major depressive disorder (defined in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* as ≥5 depressive symptoms lasting at least 2 weeks and accompanied by functional impairment)[10] carries stigma,[11-13] is frequently

For editorial comment see p 2030.

Author Affiliations are listed at the end of this article.
Corresponding Author: Richard L. Kravitz, MD, MSPH, University of California, Davis, Center for Health Services Research and Department of Internal Medicine, 2103 Stockton Blvd, Suite 2224, GB, Sacramento, CA 95817 (rlkravitz@ucdavis.edu).

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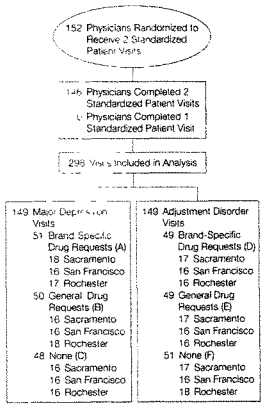
Figure. Study Flow Diagram



Standardized patient roles were created by crossing 2 clinical conditions (major depression or adjustment disorder with depressed mood) with 3 drug request types (brand-specific, general, or none). Physicians at each study site (Sacramento, Calif; San Francisco, Calif; and Rochester, NY) were randomly assigned to receive 2 standardized patient visits, 1 of each condition combined with a different type of drug request.

underdiagnosed, and can be treated successfully in a majority of patients.[14] A thoughtful DTC advertising campaign could encourage patients to seek effective care. However, DTC advertising could also promote prescribing of antidepressants for patients with minor symptoms in the absence of clearly defined indications.[15] Although some short-term studies have shown benefit from both antidepressants and brief psychological interventions in minor depression (<5 depressive symptoms),[16] long-term follow-up is lacking, and there is no professional consensus about the need for immediate treatment as opposed to watchful waiting.[17,18] Patients with minor symptoms of short duration who are prescribed antidepressants at initial presentation would be subject to short-term adverse effects (eg, sexual dysfunction) and potential hazards (including suicidality)[19] that would have to be weighed against marginal gains.

Previous studies have examined the effects of DTC advertising on consumer and clinician behavior,[4-6,20] but few have directly addressed the issue of underprescribing and overprescribing. We conducted a randomized controlled trial using standardized patients (SPs) to address 4 research questions: (1) What are the effects of patients' requests for antidepressants on physician prescribing? (2) Does it make a difference whether patients' requests are brand-specific (as might be prompted by viewing a DTC television advertisement) or general (as might arise from watching a television program about depression)? (3) Do the effects of patients' requests vary depending on the clinical indications for antidepressant therapy? (4) What are the effects of brand-specific and general requests on 2 other depression care indicators: mental health referral and primary care follow-up?

METHODS

Design Overview

The study was designed as a randomized controlled trial, with SPs making no requests (ie, presenting with symptoms only) serving as controls. Standardized patients were trained to portray 6 roles, created by crossing 2 clinical conditions (symptoms consistent with major depression or adjustment disorder) with 3 request types (brand-specific, general, or none) (FIGURE). Written informed consent for participation and audiorecording of visits was obtained from all participating physicians, and the study protocol was approved by the institutional review boards at all participating institutions.

Sampling of Practices

Primary care physicians (internists and family physicians) were recruited through 4 physician collectives: the University of California, Davis, Primary Care Network and Kaiser-Permanente in Sacramento, Calif; Brown & Toland Medical Group in San Francisco, Calif; and Excellus BlueCross BlueShield in Rochester, NY. At all sites, recruiting was conducted by mail with telephone follow-up. Physicians were told only that the study would involve seeing 2 SPs several months apart, that each SP would present with a combination of common symptoms, and that the purpose of the study was to "assess social influences on practice and the competing demands of primary care." Physicians and their practices were offered visit reimbursement and participation incentives totaling up to $375. Cooperation rates ranged from 53% to 61%. The age and sex distributions of participating physicians were similar to those of the practices as a whole.

Role Development

Detailed clinical biographies were developed for the 2 clinical presentations (major depression of moderate severity and adjustment disorder with depressed mood). Role outlines were prepared by the coinvestigators and reviewed by a scientific advisory committee consisting of national experts in psychology, psychiatry, primary care, and SP methods. Role outlines were revised iteratively until they were judged by a consensus of investigators and advisors to be clinically credible and manageable within the context of a 15- to 20-minute new-to-physician acute visit.

Role 1. The patient with major depression and wrist pain was a 48-year-old divorced white woman with 2 young adult children. She worked full time and had no chronic physical or psychological problems, and no family history of depression. She had been feeling "kind of down" for 1 month, worse over the past 2 weeks. She complained of loss of interest and involvement in usual activities, low energy and fatigue, sensitivity to criticism, poor appetite on some days only, and poor sleep with early morning awakening. She had occasional trouble concentrating at work but no excessive crying, confusion, slowing, agitation, distorted thinking, or suicidal thoughts.

Role 2. The patient with adjustment disorder with depressed mood and low back pain was a 45-year-old di-

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vorced white woman who accepted a voluntary layoff rather than relocate with her company to another region of the country. She complained of fatigue and feeling stressed and reported difficulty falling asleep 3 to 4 nights per week for the past few weeks, without early morning awakening. She recently curtailed her usual physical activity because of fatigue and fear of aggravating her back pain.

To understand the effect of requests on physician behavior, actors portraying major depression (role 1) were further assigned to experimental conditions A, B, or C; those portraying adjustment disorder (role 2) were assigned to conditions D, E, or F (Figure). Subroles A and D were to make a DTC-advertisement–driven request within the first 10 minutes of the visit or before the physical examination (whichever came first). They began: "I saw this ad on TV the other night. It was about Paxil. Some things about the ad really struck me. I was wondering if you thought Paxil might help." The selective serotonin reuptake inhibitor Paxil was chosen because at the time of the study it was widely promoted, priced higher than generic fluoxetine, and available on the formularies of participating health care organizations in all 3 cities. Paxil did not become available as generic paroxetine until halfway through the study (September 2003). Subroles B and E were to make a general request for medication. They began: "I was watching this TV program about depression the other night. It really got me thinking. I was wondering if you thought a medicine might help me." Subroles C and F were to make no explicit request.

Training and Monitoring of Standardized Patients

Standardized patients (6-7 from each city) were middle-aged, white, nonobese women, most with professional acting experience. Training focused on depicting the historical and emotional features of depression and adjustment disorder, simulating key physical findings for the 2 secondary musculoskeletal conditions, and mastering biographical details of the roles. Each SP was assigned 1 of the 6 roles for the entire study and was required to portray role details with 95% accuracy, maintain affective fidelity (agreed-on levels of depressed mood and anxiety), and demonstrate competence in completing the SP reporting form (described below).

Standardized patients were monitored throughout training and data collection. Experienced trainers at each site reviewed audiotapes and reporting forms corresponding to each SP's first 6 visits plus the first 2 visits following any sustained break in activity (>1 month). Trainers completed a checklist of behaviors and rated SPs on a 7-point scale for affect (1 = very cheerful; 7 = very depressed). Affect scores for major depression (mean, 5.56 [SD, 0.54]) and adjustment disorder (mean, 4.36 [SD, 0.51]) approached their preset target values of 5.5 and 4.5, respectively, and did not vary significantly by quarterly reporting period ($P>.20$). To ensure consistency across sites, the lead trainer at University of California, Davis, periodically monitored visits from all sites, and trainers convened weekly by conference call to discuss SP performance issues.

Within 2 weeks of an SP visit, physicians were sent a letter by facsimile asking them to indicate whether "during the past 2 weeks" they were at any time "suspicious" that a patient visiting their office was actually an SP. In 12.8% of visits, physicians responded that they had been "definitely" or "probably" suspicious before or during at least 1 patient encounter during the previous 2 weeks.

Conduct of Visits and Collection of Data

A randomized allocation scheme was designed with the following constraints: Each physician saw 1 SP with major depression and wrist pain and 1 SP with adjustment disorder and back pain; no physician saw more than 1 SP making the same type of request; and to reduce reactivity,[21] the intervals between consent and the first visit and between the first and second visit were each at least 2 months. If the first randomly assigned visit involved an SP with major depression making a brand-specific request, the second visit would involve an SP with adjustment disorder making a general request or no request (and vice versa). This prevented a physician from receiving recurrent suspicion-raising requests. To ensure realism, SPs were provided factitious insurance cards obtained from local insurance companies, false identities (including pseudonyms, local home and work addresses, and mobile telephone numbers corresponding to the cellular telephone number of the study coordinator), and cash to make any applicable co-payments.

Project staff enlisted practice managers at local clinical sites to help the SPs make medical appointments. Clinic personnel were told that the patient wished to be established as a new patient with the physician but also had an acute issue (fatigue and musculoskeletal pain) that required attention within 1 to 2 weeks.

All visits were conducted between May 2003 and May 2004 and were surreptitiously audiorecorded using minidisc recorders concealed in the SPs' purses. Immediately following the visit, SPs listened to the audiorecording and completed an SP reporting form. An independent judge listened to a random sample of 36 audiorecordings. Agreement between the SP and the independent judge concerning individual physician behaviors (ie, specific elements of history taking, physical examination, and medical decision making) averaged 92% (mean $\kappa = 0.82$). Participating physicians were debriefed in writing after the study.

Additional Measures

Information on physician specialty and sex was obtained by surveying participating physicians. A physician blinded to experimental condition reviewed SPs' medical records and classified physicians' dictated or handwritten assessments as (1) depression; (2) adjustment disorder or reactive/situational depression; or (3) other diagnosis (eg,

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Table 1. Physician Prescribing as a Function of Standardized Patient Request Behavior (Unadjusted Results)

	No. of Encounters	No. (%) [95% Confidence Interval]*	
		Received Antidepressant	Received Paroxetine/Paxil
Major depressive disorder			
Brand-specific request	51	27 (52.9) [38.4-67.1]	14 (27.4) [15.9-41.7]
General request	50	38 (76.0) [61.8-86.9]	1 (2.0) [0.05-10.6]
No request	48	15 (31.2) [18.7-46.3]	2 (4.2) [0.5-14.3]
Adjustment disorder			
Brand-specific request	49	27 (55.1) [40.2-69.3]	18 (36.7) [23.4-51.7]
General request	49	19 (38.8) [25.2-53.8]	5 (10.2) [3.4-22.2]
No request	51	5 (9.8) [3.3-21.4]	0 (0.0) [0.0-7.0]

*$P<.001$ for all comparisons among request types.

fatigue, stress, insomnia). Based on review of actual prescription forms (or, in some cases, drug samples), prescribing decisions were classified as (1) prescription for Paxil/paroxetine; (2) prescription for other antidepressant (including a newer-generation antidepressant in any dose or a heterocyclic antidepressant in a final [target] dose equivalent to at least 75 mg of amitriptyline); or (3) no antidepressant. The minimum dose requirement for heterocyclic antidepressants was meant to exclude low-dose prescriptions intended for treatment of insomnia or pain.

Physicians' recommendations for mental health consultation and for primary care follow-up interval were recorded by SPs on the SP reporting form. Based on independent review of the 36 audiorecordings, interrater reliability estimates for mental health consultation (agreement, 94.4%; $\kappa = 0.88$) and follow-up within 2 weeks (agreement, 89.3%; $\kappa = 0.61$) were acceptable. For SPs portraying major depression, we relied on national guidelines[22] to define minimally acceptable initial care as (1) receiving a prescription for an antidepressant at the index visit; (2) being referred to a mental health care professional (interval not specified); or (3) being asked to return for follow-up within 2 weeks.

Statistical Analysis

The study was powered to detect with 80% probability and $\alpha = .05$ an effect of patient requests on antidepressant prescribing equal to an odds ratio (OR) of 1.7 in adjustment disorder and 1.5 in major depression. Analyses were performed using SAS statistical software, version 9.1 (SAS Institute Inc, Cary, NC) and STATA, version 8.2 (Stata Corp, College Station, Tex). Primary analyses used the Fisher exact test to examine study hypotheses by comparing the proportions in the study groups. Small-sample adjustments were made in constructing the confidence intervals (CIs) for the proportions.[23]

We also conducted a series of supplemental analyses using generalized linear mixed models to examine the relationships between antidepressant prescribing and both clinical condition and request type, controlling for SP, physician, and other study characteristics posited to influence prescribing.[24] Analyses were conducted with each SP-physician encounter as an observation and antidepressant prescribing (vs not) as the dependent variable. Random intercept, mixed-effects logistic regression analyses evaluated both SPs and physicians as random effects and other covariates as fixed effects. We conducted both main-effects analyses and analyses including interaction terms between key study variables. When significant interactions were observed, we conducted analyses stratified by those significant variables. Covariates included physician sex and specialty, study site, whether the physician was suspicious that an SP visit had occurred, and visit order (ie, whether the visit was the first or second time the physician had seen a study SP). Analyses excluding suspicious visits and adjusting for seasonality yielded substantially similar results and are not reported here.

RESULTS

Eighteen SPs made 298 visits to 152 physicians in Sacramento (n = 101), San Francisco (n = 96), and Rochester (n = 101) (Figure). Six physicians saw only 1 SP. Two hundred visits (67%) were to general internists and 98 (33%) were to family physicians, while 201 (67%) were to male physicians and 97 (33%) were to female physicians.

Antidepressant Prescribing

Physicians prescribed antidepressants in 80 (54%) of 149 visits in which SPs portrayed major depression. In 17 (11%) of those visits, they prescribed paroxetine/Paxil (TABLE 1). Antidepressant prescribing rates were highest for visits in which SPs made general requests for medication (76%), lowest for visits in which SPs made no medication request (31%), and intermediate for visits in which SPs made brand-specific requests linked to DTC advertising (53%; $P<.001$) (Table 1). Among SPs portraying major depression, paroxetine was rarely prescribed (approximately 3%) unless the SP specifically requested Paxil; if Paxil was requested by name, 14 (27%) of 51 received Paxil/paroxetine, 13 (26%) received an alternative antidepressant, and 24 (47%) received no antidepressant (Table 1).

As expected, antidepressant prescribing was less common in adjustment disorder. Physicians prescribed antidepressants in 51 (34%) of 149 visits (Table 1). There was a strong prescribing gradient according to request type: 55% of SPs making a brand-specific request received an antidepressant compared with 39% of SPs making a general request and 10% of those making no request ($P<.001$; Table 1). Within the adjustment disorder group, prescriptions for Paxil/paroxetine accounted for two thirds of all antidepressant prescriptions given to those making brand-specific requests and for

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about one fourth of prescriptions given to those making general requests (Table 1). Among the 5 SPs in the no-request group who received an antidepressant prescription, none were offered paroxetine (Table 1).

These unadjusted results were confirmed in main-effects mixed-model regression analyses: antidepressant prescribing was more likely in major depression visits compared with adjustment disorder visits (adjusted OR [AOR], 2.92; 95% CI, 1.51-5.63) and in brand-specific (AOR, 8.50; 95% CI, 3.27-22.1) and general (AOR, 10.3; 95% CI, 3.80-27.8) request visits compared with no request visits. The effect for SP was not significant when included as a random effect (intraclass correlation coefficient, $\rho=0.04$; $P=.15$) or when each SP was included as a series of dummy fixed effects. The physician effect was significant ($\rho=0.32$; 95% CI, 0.12-0.63), indicating that individual clinicians varied in their propensity to prescribe. Examination of interactions revealed a significant interaction ($P=.04$) between brand-specific request and clinical condition: the brand-specific request had a more pronounced effect on prescribing in the adjustment disorder condition than in the major depression condition. As shown in TABLE 2, the AOR for general vs no request changed little between the depression and adjustment scenarios (7.99 vs 6.34), while the AOR for brand-specific vs no request increased markedly (2.72 vs 13.3). Adjusting for whether a mental health care referral was provided did not materially alter the estimates for the effects of brand-specific or general requests or their associated P values.

Table 2. Regression Analysis (Mixed-Effects Model) Predicting Antidepressant Prescribing Among SPs Portraying Major Depression and Adjustment Disorder

	Major Depression		Adjustment Disorder	
	Adjusted OR (95% CI)*	P Value	Adjusted OR (95% CI)*	P Value
Request type†				
Brand-specific request	2.72 (1.09-6.80)	.03	13.3 (4.20-42.10)	<.001
General request	7.99 (2.96-21.6)	<.001	6.34 (1.99-20.10)	.002
City‡				
Sacramento	0.76 (0.29-1.99)	.58	0.42 (0.15-1.18)	.10
San Francisco	0.38 (0.14-1.05)	.06	0.69 (0.25-1.91)	.47
Physician specialty: general internal medicine (vs family medicine)	1.10 (0.49-2.47)	.82	1.42 (0.57-3.57)	.45
Male physician (vs female)	1.77 (0.80-3.95)	.16	0.83 (0.35-1.94)	.66
Visit order: first (vs second)§	0.53 (0.24-1.17)	.12	0.58 (0.25-1.32)	.19
Suspicious for SP visit (vs unsuspected)	0.82 (0.28-2.39)	.71	0.33 (0.08-1.34)	.12

Abbreviations: CI, confidence interval; OR, odds ratio; SP, standardized patient.
*Values are adjusted for all other independent variables listed in the Table.
†No request is the reference category.
‡Rochester is the reference category.
§Reflects whether the visit was the physician's first or second study encounter.

Chart-Recorded Diagnoses

Physicians recorded a diagnosis of depression or possible depression in the medical record in 80% of visits by SPs portraying major depressive disorder and in 39% of visits by SPs portraying adjustment disorder with depressed mood. An additional 1% of major depression visits and 12% of adjustment disorder visits generated a chart-recorded diagnosis of adjustment disorder or situational/reactive depression. Physicians were significantly more likely to consider and record a diagnosis of depression if the SP made a request for medication compared with no request (88% vs 65%; $P=.001$ among major depression patients and 50% vs 18%; $P<.001$ among adjustment disorder patients).

Referral and Follow-up

Among SPs portraying major depression, mental health care referrals were recommended more often when SPs made brand-specific requests (45%) or general requests (54%) than when they made no request (19%; $P<.001$) (TABLE 3). Among SPs portraying adjustment disorder, mental health care referrals were recommended to about one third of SPs regardless of request category ($P=.88$; Table 3). Overall, physicians recommended primary care follow-up within 2 weeks for 33 (22%) of 149 SPs with symptoms of major depression and for 22 (15%) of 149 with adjustment disorder. Among visits by SPs portraying major depression, minimally acceptable initial care (any combination of an antidepressant, mental health referral, or follow-up visit within 2 weeks) was received by 98% of SPs making a general request, by 90% of those making a brand-specific request, and by 56% of those making no request ($P<.001$).

COMMENT

In this community-based randomized trial, antidepressants were prescribed far more often when SPs requested them. In addition, SPs portraying major depression and making either brand-specific or general requests were more likely than patients making no request to receive minimally acceptable initial depression care. These results underscore the idea that patients have substantial influence on physicians and can be active agents in the production of quality.[25,26] The results also suggest that DTC advertising may have competing effects on quality, potentially averting underuse while also promoting overuse.

A simple model of DTC advertising holds that (1) advertisement exposure raises consumer awareness of conditions and treatments; (2) increased awareness motivates patients to seek medical care and request drug therapy; and (3) patients' requests lead, ceteris paribus, to increased prescribing. Drug manufacturers endorse this model to the tune of $3.2 billion per year, but empirical evidence has been limited. Sur-

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Table 3. Mental Health Consultation and Follow-up

	No. of Encounters	No. (%) [95% Confidence Interval] Referred for Mental Health Consultation	P Value	Advised to Return for Primary Care Follow-up Within 2 wk	P Value
Major depressive disorder					
Brand-specific request	51	23 (45.1) [31.1-59.7]	<.001	12 (23.5) [12.8-37.5]	.68
General request	50	27 (54.0) [39.3-68.2]		9 (18.0) [8.6-31.4]	
No request	48	9 (18.8) [8.9-32.6]		12 (25.0) [13.6-39.6]	
Adjustment disorder					
Brand-specific request	49	17 (34.7) [21.7-49.6]	.88	6 (12.2) [4.6-24.8]	.77
General request	49	16 (32.7) [19.9-47.5]		7 (14.3) [5.9-27.2]	
No request	51	15 (29.4) [17.5-43.8]		9 (17.7) [8.4-30.9]	

vey research suggests that advertisements raise consumer awareness and motivate patients to request prescriptions in up to 7% of primary care encounters.[3,4,27-31] Although it does not address the impact of DTC advertising on consumer awareness or care seeking, our study supplies direct experimental evidence that DTC advertisement–driven requests (along with general requests) dramatically boost prescribing.

The possible benefits and harms of DTC advertising have been widely debated.[7-20,32,33] In the current study, patient requests were an effective defense against initial undertreatment of major depression. Among SPs presenting with symptoms of major depression but making no requests for medication, antidepressants were prescribed in less than one third of SP visits and minimally acceptable initial care was rendered in 56%. Although initial treatment may ultimately be less important than adequate follow-up (which affords opportunities to monitor outcomes and adjust treatment as necessary),[34] these findings are consistent with other studies conducted in primary care settings.[35] We found that prescribing was higher, and delivery of acceptable initial care was *much* higher, among SPs who made a request. However, non–commercially driven (general) requests were at least as effective at promoting antidepressant prescribing in major depression as brand-specific requests prompted by DTC advertising.

Patient requests were also associated with a sharp rise in antidepressant prescribing for adjustment disorder with depressed mood. Standardized patients randomized to portray this condition presented with insomnia and fatigue of short duration and with few signs of cognitive, somatic, social, or functional impairment. Without prompting, physicians examining these SPs were unlikely to prescribe an antidepressant, but prescription rates increased severalfold following either a brand-specific or a general request. Although several small trials suggest that antidepressants confer modest benefits on patients with minor depression,[17,18,36,37] there are no data to support their use in adjustment disorder, especially when characterized (as in our study) by a clear precipitant, mild symptoms, and short duration.[38] Thus, despite the wide therapeutic index of second-generation antidepressants[39,40] and the potential therapeutic value of acceding to patients' reasonable requests,[41] the prescription of antidepressants in this context is at the margin of clinical appropriateness.

Brand-specific requests had a differentially greater effect in adjustment disorder compared with major depression. This supports the hypothesis that DTC advertising may stimulate prescribing more for questionable than for clear indications. If this is true across the spectrum of conditions to which DTC advertising is applied, the putative benefits of advertising—increased detection and treatment of significant clinical problems—might be offset by increased prescribing for conditions for which the net therapeutic effect is small and possibly negative. Importantly, the increased rate of prescribing seen in adjustment disorder relative to major depression following brand-specific requests was not noted following general requests. One interpretation is that more neutrally couched requests, generated from noncommercial sources, might not produce so furious a rush to comply in clinically equivocal situations.

Given the likelihood that competing effects are not only possible but normative, the net social value of DTC advertising and the requests it engenders may depend on the specific clinical and epidemiological context. The benefits of advertising will tend to dominate when the target condition is serious and the treatment is very safe, effective, and inexpensive. Harms are most likely to emerge when the target condition is trivial and the treatment is relatively perilous, ineffective, or costly. From a legal perspective, these data pose a possible challenge to the "learned intermediary rule."[42] If patients can sway physicians to prescribe drugs they would otherwise not consider, physicians may not be the stalwart intermediary that the law assumes.[5]

Standardized patients have been used in medical education, quality assessment, and, increasingly, in research.[43-47] External validity of SP-based research might be threatened if SP roles are unrealistic or extreme, SP portrayals are of poor quality, or physicians "detect" the presence of an SP and act differently as a result. Roles for this project were developed by an interdisciplinary team, reviewed and edited by a national advisory panel, and field-tested with local

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physicians and clinical trainees. We trained and monitored SPs throughout the project. Our method for assessing detection was biased toward greater sensitivity than has been reported elsewhere in the literature,[45] but even so, physicians were "suspicious" in only 1 visit of 8, and 84% of physicians who reported suspicions claimed that they did not alter their usual clinical behavior (data not shown). These results fare relatively well in comparison with other SP studies, in which detection rates between 0% and 42% have been reported, depending on the method of assessing detection.[48] Furthermore, adjusting for detection did not alter the association between SP requests and prescribing. Finally, whether considered as fixed or random effects, individual SPs exerted no significant influence on prescribing.

Several other limitations deserve mention. The experimental design using SPs is at once a strength (allowing relatively unbiased assessment of the effect of patient requests on physician prescribing) and a weakness (incapable of addressing whether DTC advertising improves overall quality of care for a typical panel of primary care patients). Furthermore, we cannot determine whether DTC advertising actually produces the kinds of behaviors in real patients that were portrayed by our SPs. It is plausible that DTC advertising differentially "activates" patients with adjustment disorder compared with those with major depression; such differential activation would nudge the risk-benefit ratio of DTC advertising in a negative direction. Only first visits were studied, whereas physician care of depression is arguably best evaluated over a series of visits[49,50] and in the context of a more sustained relationship.[51] The communities in which the study was conducted are highly penetrated by managed care; underprescribing or overprescribing might be even more prevalent than observed here in less-organized settings. Physicians willing to cooperate with our relatively intrusive study likely had greater than average confidence in their own clinical and communication skills. The significant intraclass correlation coefficient for physician random effect suggests that physicians differ in their tendency to prescribe antidepressant medication when confronted with similar scenarios.

The results of this trial sound a cautionary note for DTC advertising but also highlight opportunities for improving care of depression (and perhaps other chronic conditions) by using public media channels to expand patient involvement in care. Furthermore, physicians may require additional training to respond appropriately to patients' requests in clinically ambiguous circumstances. Research in other clinical contexts is needed to confirm the results of this study and determine the relative effects of DTC advertising and noncommercial media on patient activation and outcomes.

Author Affiliations: Center for Health Services Research in Primary Care (Drs Kravitz, Franz, Azari, Wilkes, Hinton, and Franks) and Departments of Internal Medicine (Drs Kravitz and Wilkes), Statistics (Dr Azari), Psychiatry (Dr Hinton), and Family and Community Medicine (Dr Franks), University of California, Davis, Sacramento; Departments of Family Medicine and Psychiatry and Center to Improve Communication in Health Care, University of Rochester School of Medicine and Dentistry, Rochester, NY (Dr Epstein); Division of General Internal Medicine, Department of Medicine, University of California, San Francisco (Dr Feldman).

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Study concept and design: Kravitz, Epstein, Feldman, Azari, Wilkes, Franks.
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> Somewhere, something incredible is waiting to be known.
> —Blaise Pascal (1623-1662)

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Senator KOHL. Thank you very much, Dr. Kravitz.

We can stay here until about 11:20. Let's see how far we can get.

I would like to ask the whole panel, the question is: Do you think that if we either rein in or even possibly eliminate DTC advertising and also provide more comparative studies about the effectiveness of drugs, we will then be able to move toward a goal of providing the best drugs at the best prices to the American people? I will start with you, Dr. Antony.

Dr. ANTONY. Senator, let me start by saying the industry also wants to make sure we get the best drugs to the right patient at the right time, so we are committed to doing that.

On the issue of whether direct-to-consumer advertising will affect the price and cost of medicines, I am going to refer to a study that was actually done by the Federal Trade Commission where they studied that and reported back to the FDA. From their own study in 2003, they state that direct-to-consumer advertising accounts for a relatively small proportion of the total cost of drugs, which reinforces the view that advertising would have a limited, if any, effect on price. The reason that is important is everyone talks about the $4 billion that is spent on advertising, which is a large amount. But more than 10 times that amount is spent on research and development, more than $40 billion a year. So, in the overall picture, it is unclear whether reining in direct-to-consumer advertising would actually lower the price of medicines.

Senator KOHL. Dr. Sweet.

Dr. SWEET. I would agree. I think there is little evidence that it would decrease the cost of medications. But my concern is the overall health care costs that I know Senator Wyden is concerned about. Every time a physician has to see a patient back for toxicity, every time there is a drug prescribed when there might have been a lower-cost alternative drug because of DTC, you are increasing the overall health care cost. So, yes, I would agree that taking care of DTC advertising is not going to lower the overall cost of most medications. I am concerned about the overutilization, and as I stated in my testimony, we at the ACP believe that the pharmaceutical industry is a tremendous resource, and we would like to see them put those resources into the kinds of things that we know do help patients: non-branded, public relations kinds of messages that address things like depression and incontinence and even erectile dysfunction, but without specifically branding a given drug.

In answer to the first part of your question, we always need more data, and, yes, there is a real lack of data that looks at these newer, more costly agents, especially in classes where there are older, already sometimes generically available medications. It would be wonderful to have more data on truly head-to-head analyses of the overall effectiveness.

That is probably not going to happen just because of the way industry drives clinical research. But anything we could have as better data to suggest to our seniors that a generic drug for urinary incontinence works just as well as what they saw being carried behind the car and the outhouse would be helpful to us as clinicians with our patients.

Senator KOHL. Thank you.

Dr. Lurie.

Dr. LURIE. While it is true that direct-to-consumer advertising isn't the largest fraction of all advertising for drugs in this country, but it is substantial, about 20 percent, and growing. So I do think it would make a difference.

DTC ads, as I said, for the 25 largest therapeutic classes, accounted for 12 percent of drug sales growth between 1999 and 2000, and the estimate was that it would cost $2.6 billion as a result, just in those 25 therapeutic classes. So I think emphatically it would lead to an increase in the overall cost of drugs. Be careful to distinguish between drug prices and costs. I don't think that the prices would go up, but I think that the overall costs go up because people get driven away from non-drug interventions or generic drugs interventions to newly patented drug interventions which are more expensive.

The GAO estimated that a 10-percent increase in DTC advertising translated into a 1-percent increase in sales for that class of drugs, which is an enormous increase when you think about these drug classes that are selling in the billions of dollars.

So I think absolutely it makes a difference. It may or may not be the most important thing. Certainly if the committee can pay attention to the gifts and handouts that are being given to physicians and where most of the pharmaceutical company advertising does go, I have no objection to that. But in the meantime, before us we have DTC advertising and emphatically it does contribute to the overall cost of drugs.

Senator KOHL. Thank you.

Dr. Kravitz.

Dr. KRAVITZ. Well, asking a researcher whether there should be more comparative studies is kind of back to that cookie situation that Dr. Behrman mentioned. But, yes, I think there should be more comparative studies of two types. First, there is a desperate lack of head-to-head comparisons between individual drugs within a class, so that not only consumers but physicians have little basis to distinguish between drugs within a category. Second, the moratorium on DTC advertising for a period of time that has been proposed in several quarters should be extended to place a greater emphasis on more rigorous post-marketing surveillance so that we can use that period of time to actually collect some systematic, useful information.

As far as reining in DTC, I think indeed much more could be done to raise the rigor of the education that is provided to patients, but my own view is that DTC should not, in fact, be banned, and that, in fact, in some situations we need not less DTC but more. For example, patients who are discharged from the hospital having suffered a heart attack should be on medicines called beta blockers as well as aspirin. I would be highly supportive of a DTC campaign to encourage patients who have had a heart attack to go on these two medications, which have been associated with a 30-percent reduction in mortality. We see study after study showing that somewhere between 60 and 90 percent of patients receive these drugs, where the figure should really be closer to 100.

Senator KOHL. Thank you.

Mr. Chairman.

The CHAIRMAN. Senator Kohl, I am tempted to ask Dr. Sweet, How did Grandpa answer his grandson about the 4-hour issue? When my son asked me that, I told him if he ever has that problem, we need to talk. [Laughter.]

Dr. SWEET. He similarly dodged the issue.

The CHAIRMAN. OK. On a more serious issue—and in fairness, I probably should have asked this to Dr. Behrman. But if I am not mistaken, wasn't Vioxx an arthritis drug broadly advertised? If it was broadly advertised, wasn't it later pulled from the market or had substantial warnings placed on it because in fact, it did highly elevate the risk of heart attack.

What does that say about all of this? Am I right in my recollection, and what does it say about all of this?

Dr. SWEET. I will start. You are very right in your recollection, and as testimony has said, in 2000 Vioxx was the most advertised directly-to-consumer drug in our nation. I think that is what has led all of us to believe that some sort of a moratorium on these new drugs prior to direct-to-consumer advertising so that the drug can be looked at in a larger group of people would be useful. When you do clinical studies, you have a very limited group of people that you look at, and generally, they are well selected. The pharmaceutical industry wants to make sure that their drug gets approved. It is only when you then put a drug into a much larger population at all ends of the spectrum of disease states and clinical conditions, liver and kidney problems, that you really see what goes on. I think that is exactly what happened to Vioxx.

In my opinion, Vioxx is not a bad drug. Vioxx is a drug that was overused in many people who it had not been studied in and for which we had no data. As a result, we now have this real—what many people would consider a debacle in the industry. It is too bad because there were many people who were helped by Vioxx. But there were too many people that got it, often as a result of bringing that ad in, and it happened to me more than one time where somebody brings the ad in or writes it down from the television, and they are hurting and they want something to help, and, "Doctor, this one will work this time. I have got to have it." So, yes, I do believe that actually some of the—and perhaps Dr. Antony wants to comment, but I do think some of the decrease in direct-to-consumer advertising that we are seeing now is a result of the industry seeing what happened. It is one of the reasons that the ACP certainly would like to see very much more data on efficacy and safety prior to broad-range direct-to-consumer advertising so that we know more about what our seniors and others are asking about.

Dr. ANTONY. Chairman, I would like to respond. Dr. Sweet raises this very important issue of what do we do with information about medicines and health care as it develops and as we learn more information, because we never have all of the information when we originally release a product.

Dr. Kravitz just mentioned the issue of beta blockers and their use after heart attacks, and he actually recommends that we do more direct-to-consumer advertising in that area. That is a good real-time example of what should we do with more information, because just this week JAMA, the Journal of the American Medical Association published a study that said those beta blockers, which

we have been really pushing, encouraging physicians to prescribe, it looks like that in many patients it doesn't help them, and in certain patients it may actually harm them.

So now what do we do? There was no conspiracy to hide this information, and what I will tell you that is interesting about it is I am a member of the AMA, I subscribe to that journal. But the way I learned about this information was a Bloomberg report that summarized that report. I got it on my BlackBerry, and it was even before the journal was published.

So I as a clinician now—and I was telling people to take these medicines because that was the best information that was available. Now I have just learned via Bloomberg that apparently there is at least one study that says we have to be cautious.

So in this new information age this issue that you are discussing now as a committee is a critical one, and all I would say as an individual clinician and as an industry is that until we sort this out, this answer that we can't share any information, that somehow we are not going to disclose information, that that is potentially dangerous, and that a better view is how can we make information more reliable, more fair and balanced, not how do we try to hide information from people.

Dr. LURIE. If I may, on Vioxx, I disagree with Dr. Sweet in the sense that there was never a study that showed that Vioxx was a more effective medication than any nonsteroidal anti-inflammatory drug on the market—aspirin, ibuprofen, naproxen, et cetera. There was a claim, ultimately allowed by the FDA, that it was less toxic to the gastrointestinal tract. So the patients for whom the drug made sense were those who had not tolerated the previous drugs well.

However, two-thirds of the increase in drug sales between 1999 and 2000 was precisely among those who did not have GI toxicity. The reason for that in part was DTC advertising, but also because of other advertising that the pharmaceutical companies undertake.

As far as the notion of there being more direct-to-consumer advertising, of course, I don't agree, but we should be careful about what we mean when we talk about that. This conversation has been about those DTC ads that have linked drugs and diseases. But there is, in fact, a capacity for the pharmaceutical industry to engage in disease-only advertising, and those are called help-seeking advertisements. If the industry was that interested in those, we would be seeing a massive growth in that kind of advertising rather than the growth in product-related advertising that we do so.

So as to the beta blocker example, we are never going to see a DTC advertisement for those because they have been off patent for many years, anyway.

Senator KOHL. Senator Wyden.

Senator WYDEN. Thank you, Mr. Chairman.

Dr. Antony, the heart of the case for PhRMA is that direct-to-consumer advertising is for consumer education. You say that. In fact, I guess you use those words, "The heart of our company's direct-to-consumer efforts is patient education." But I never see on television any drug advertised for which there is a small market, which it seems to me undermines the argument this is about patient education.

Could you give me an example of a drug that is advertised on television for which there really is a need for patient education for which there is a small market?

Dr. ANTONY. Let me respond, again, and I am going to cite a study that was conducted by RAND, and I am going to use examples of conditions where there is a need for patient education. This RAND study talked about.

Senator WYDEN. But if I could, because time is short.

Dr. ANTONY. Sure.

Senator WYDEN. We see all these ads on TV. Could you give me an example of a drug advertised on TV where there is a small market?

Dr. ANTONY. Senator, I can only address the ones that I am aware of, which tend to be diseases that affect a lot of people and they may be undertreated. So I don't—I can't answer that in terms of one that is for a small market because I think that what the companies want to go after in a mass marketing or a television ad is diseases that affect a lot of people. They may be underused—I mean, as opposed to this idea of they are going after things that there is already adequate treatment, and I will use asthma as an example of something where a lot of people suffer it, it is a chronic problem. I would argue it is more than bothersome. It is a real issue for people. So, yes, you are going to see advertising in those categories. Where with a condition that may only affect a few dozen people, I think it is unlikely that you would see television advertising.

Senator WYDEN. How would you reconcile the idea of voluntary guidelines with the fact that people who work for pharmaceutical companies get bonuses for increasing sales for drugs that are advertised? I don't see how you reconcile those two.

Dr. ANTONY. Senator, I will answer your question, again, both as a clinician that was treating patients full-time before joining industry and the industry position. This discussion is on direct-to-consumer advertising. A number of years ago, there was significant concern about the direct markets that companies were doing to physicians in terms of what the sales reps were doing in the physician offices. The industry came together working with the American Medical Association to develop a code of conduct for how sales reps, pharmaceutical sales reps should interact with physicians, and it was a voluntary code. But there is no question that physicians saw a dramatic change in the behavior of those sales reps, so much so that many of them actually now complain to me and say, "Why can't I take my wife to these continuing education dinners because I don't have very much time and I am losing family"——

Senator WYDEN. That is not what I am asking, Doctor. I am asking how the voluntary guidelines restricting direct-to-consumer advertising can be reconciled with the fact that people who work for the companies get bonuses for increasing sales in direct-to-consumer products?

Dr. ANTONY. Senator, I can't answer the specific question about the bonus.

Senator WYDEN. OK. Let me ask you one last question, because I know Senator Talent wants to get some questions in before the

break. Why should Medicaid pay for all of these advertisements on television? Your companies already get a tax break for advertising on TV. Why should Medicaid pay this double subsidy at a time when the program is being cut so dramatically? That is, of course, what Senator Sununu and I would stop in our bipartisan bill, but I would like to have you tell me why Medicaid should pay for those advertising expenses.

Dr. ANTONY. Senator, I don't know the details of how much, what percentage of the costs are paid by Medicaid or any other payer. My understanding is that Medicaid gets—the pricing to different groups is very different, and so I don't know what percentage of any cost is actually being picked up by Medicaid.

Senator WYDEN. But should Medicaid pay for advertising expenses, just as a concept? Is it the position of PhRMA that Medicaid should pay for advertising expenses?

Dr. ANTONY. Senator, it is my understanding that PhRMA does not have a position on that specific question.

Senator WYDEN. OK. Thank you very much, Mr. Chairman.

Senator KOHL. Senator Talent.

Senator TALENT. Thank you, Mr. Chairman, and thanks again for this hearing. It has been very useful to me. It has established some parameters. When we talk about DTC, we are talking about prescription drugs, not over the counter. Is that fair?

We have referred to—the ranking member referred to the Constitution, and I think you did also, Dr. Lurie. It is your understanding that—I thought you did, that there are restrictions, and we really don't, I guess, have a witness on that question. But I think it is everybody's understanding that there are at least some limits on what we can constitutionally do. Is that one of the reasons you guys are not proposing—or some of you are saying a ban is something we cannot do? Is it because of your understanding of the Constitution?

Dr. SWEET. Well, I think Dr. Behrman addressed that, and with the right to speech and capitalism and all of those things—that is why the College's position is that if we had our druthers, banning would be nice. But we realize that in our constitutional arena, it is probably not ever going to happen, which is why we then go to a greater degree of regulation.

Senator TALENT. I am not, by the way, trying to make a point here. I don't know that I would agree with that ruling, if that is indeed the ruling.

Is there any evidence or do you all have a good feel, at least anecdotally, for how many of the drugs that are advertised in this fashion are generally covered by insurance where people have insurance and how many of the people more generally have to pay for out-of-pocket? With that affect your opinion on this issue?

Dr. SWEET. I will answer that as somebody that does this every day. The drugs that Senator Wyden had on his list of Medicaid and Medicare drugs are absolutely the most popularly prescribed and generally needed drugs.

Again, when you look into—as an example, the number of drugs on his list for gastroesophageal reflux disease, the so-called proton pump inhibitors, three or four of them were up there.

You get into the issue that somebody comes in and they want the purple pill, and yet if they have insurance, their formulary says they can only get the pink pill. Then you have to either convince them that the pink pill works as well, or they want you to pre-authorize the drug which is another layer of paperwork for clinicians. But some seniors are very adamant that they want the purple one, they don't want the pink one, the pink one is not going to work as well.

Then you compound that with the fact that one of the drugs that was more heavily advertised in 2000 that Senator Wyden had up there, Prilosec, is now omeprazole over the counter, which is 68 cents a day compared to well over $3 a day for the other drug.

So, again, there is this whole layer of, yes, proton pump inhibitors are wonderful for people who have reflux disease, but if you look at the clinical data—Dr. Kravitz and Dr. Lurie look at this all the time—in my opinion and in the opinion of most Medicaid programs that have looked at this, there is no clinically significant difference between those drugs in outcomes. Yes, each company's package insert is a little different and some of the reps will argue with me. But overall, clinically, they work well.

So my job as a clinician and a Medicaid advocate and a Medicare advocate is to make sure that I use the best drug at the lowest cost—where you get into this cost-effectiveness. But that is a difficult debate—when you have somebody in front of you with the ad that says this one is going to work better. The general concept in our population is that generics are somehow not as good. Where that came from I am not sure, but I do think DTC advertising perhaps contributed to that feeling that a branded drug is better than a non-branded drug at this point.

So there are so many layers, and I agree—I think Dr. Lurie said exactly what I said about the overall cost. Whether the cost of the purple pill goes down by 20 cents if you don't have as much advertising is not nearly as important as the fact that there are a lot of purple pill prescriptions written at roughly $100 to $110 a month when you could get by with Prilosec, over-the-counter omeprazole.

Senator TALENT. Well, I am wondering—and maybe you would like to comment, Doctor—whether this does not cut both ways. On the one hand, a drug, unless it is the whole generic brand name distinction, a drug that is not likely to be covered because it is maybe a cosmetic or something like that, on the one hand, if the person is responsible for paying for it, if the patient is, that is sort of a countervailing influence that is introduced as against the advertising. On the other hand, those are also perhaps more likely to be the kinds of drugs for which there is less of a need under your criterion, Dr. Kravitz.

So do you think that that cuts both ways? Should that be a factor in trying to figure out how to regulate this, Dr. Lurie, or just don't worry about that? What do you think?

Dr. LURIE. Well, to me the consumer foots the bill no matter what happens, whether it is in the form of insurance premiums, whether it is in the form of copayments, whether it is in the form of taxes, whether it is in the form of what Senator Wyden refers to as the double subsidy. Either way the patient pays.

To answer your initial question, my position would not be changed according to who the payer is, because ultimately the payer is the patient.

Senator TALENT. Yes, and I am not arguing for it. I am exploring it. If a person going in and asking for something knows they are going to have to pick up more of the cost, that is an incentive for them not to ask for it, notwithstanding. Then we have more like a typical market where you are advertising anything else that a person has to pay for.

Dr. LURIE. Certainly there are data to that effect. The problem always has been that those kinds of copayments are very blunt instruments in that they can dissuade patients from taking both unneeded drugs or marginally needed drugs and those truly needed ones.

Senator TALENT. It would be very awkward to make a regulatory arrangement turn on that, because how do you—some things are covered by some policies and not by others and in different degrees. But it makes it look a little bit more like an over-the-counter drug where you are not proposing restrictions on that, in part because people are paying for that themselves, and so I think we have faith in the consumer to balance the claims against the price under those circumstances.

Dr. LURIE. Well, the underlying assumption about the over-the-counter drug is that the gravity of the decision in deciding whether or not to take the drug is one that the patient can make for themselves, or that the drug is needed on an emergency basis and you don't want to wait for the doctor. So I think that there is an appropriate distinction between OTC, and that is precisely why the concern about direct-to-consumer advertising has not focused on them. It has focused on the prescription drugs and the notion that the physician, who has always been the arbiter of that decision, hopefully in collaboration with the patient, is having an end run made around him.

Senator TALENT. I suspect also the courts would view our interest in regulating advertisement of those more serious drugs more favorably than the other.

Dr. Kravitz, let me ask you a couple things about your study to make sure I understand the conclusions. As I read it, in the cases where the person presented, the actor or actress, I guess, presented evidence of a major problem, where they made a brand-specific request, it seems to me like they were measurably less likely to get medicine prescribed than when they just made a general request. Is that true, and how do you explain that?

Dr. KRAVITZ. It is true. The percentage who received prescriptions with a general request was about three-quarters and with brand-specific a little over half.

Senator TALENT. That is, obviously, statistically significant.

Dr. KRAVITZ. That is statistically significant and clinically important. We did not measure the thought process of the clinician, and so we don't—you know, all we have is theories. But one theory is that clinicians may rebel a little bit against requests that are branded, and they may be more likely to retain an open mind when the requests are not branded, when they are more general and when they focus on a condition. This has been a longstanding con-

cern about the so-called poisoning of the physician-patient relationship with respect to DTC ads.

Senator TALENT. Yes, I am wondering whether—but that did not present—I mean, that is not the same situation when they had presented minor symptoms.

Dr. KRAVITZ. In fact, that is right.

Senator TALENT. Isn't that interesting. So you think that maybe the physician involved, if they mentioned a specific drug, perhaps suspected some of the underlying statements, thinking they are just trying to get this drug, and so they maybe were less likely to prescribe it?

Dr. KRAVITZ. Possibly, or I think they may be—in a major depression condition, at least, we believe that they are hearing the general request as, "Do you think I might have this serious medical condition?" They are hearing a brand-specific request as, "I am the consumer, I watch a lot of TV, and I want this specific drug, and your judgment to the wind." So there is a little bit of a backlash there, we think.

Senator TALENT. One more question for you then. If we go to the next page in your handouts, patients receiving minimally acceptable initial care, does that show that people were more likely to get minimally acceptable care in general if they made a request of some kind for prescription drugs?

Dr. KRAVITZ. Yes, that is right, and this is a key finding. We found that in the absence of a request, 56 percent of patients, actors, with major depression received minimally acceptable initial care, which sounds low, but it pretty much precisely corresponds to what some large national studies of quality of care for depression and lots of other chronic conditions have found. That percentage went up dramatically with any kind of request, even a little higher with——

Senator TALENT. Dr. Sweet and Dr. Lurie, does that give you some pause in your desire for regulation? I mean, if it is true that people are more likely to get—even though we do not understand why, more likely to get minimally acceptable initial care if they have made a request for some kind of prescription drug, would that change at all your attitude toward regulation of the DTC?

Dr. SWEET. From my perspective, no, because one of our "asks" at the ACP is that there be more non-branded, disease-specific, public information, true consumer education, and I think Dr. Kravitz's study supports that, especially in that 75 versus 50 percent. Those who asked, "in general do you think there is something that might help me," probably got better care in the long run.

Senator TALENT. OK.

Dr. LURIE. No. In fact, that is what I referred to in my testimony. The point is that if you believe that a patient ought to get the antidepressant, the best way to do it is not through a DTC brand name advertisement. It is by a more generic request. So if that was the concern, this is actually not the most effective way. Of course, a more general public service announcement, for example, from the Public Health Service, would not have all the risks that we have otherwise talked about here.

On the other hand, the brand name advertisements have distinctly negative effects when it comes to adjustment disorders. So, no, I think it shows risk without benefit, as far as I am concerned.

Senator TALENT. I have got to go. My staff tells me we are voting on confirming the next Chief Justice, and I probably ought to cast a vote in that. [Laughter.]

So I am going to go ahead and go. Thank you all. This has been very interesting, I am sure, to all of us. I appreciate it, and I guess the hearing is now adjourned.

[Whereupon, at 11:35 a.m., the committee was adjourned.]