April 1998

NATIONAL HEALTH POLICY FORUM

Direct-to-Consumer Advertising of Prescription Drugs

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Summary—*Since 1985, direct-to-consumer (DTC) advertising of prescription drugs has become a critical part of pharmaceutical marketing strategy. While the object of such advertising is to stimulate consumer demand, it may also provide information that promotes public health, for example, by increasing diagnosis of disease and improving compliance with prescribed drug regimes. However, the regulatory requirements that DTC ads must satisfy were originally developed for professional audiences. In light of the increased prevalence of DTC advertising, policymakers may want to reconsider these requirements to ensure that consumers can understand the benefit and risk information such ads contain.*

DTC advertising has proved highly successful in stimulating consumer demand for prescription drugs. Today, patients often initiate conversations with their doctors about the advertised medications and even ask for them. It is unclear how well-equipped physicians are to respond to such requests, especially as the universe of approved drugs continues to expand. Most medical school curricula place little emphasis on therapeutics. Once doctors have received their training, they often depend heavily on commercial sources of information about drugs. Improving medical school training in therapeutics and ensuring a flow of unbiased, high-caliber research on drugs would give physicians information critical to providing good care. A demonstration program that would establish one or more centers for education on research and therapeutics, authorized by the Food and Drug Administration Modernization Act of 1997, addresses the clinical community's need for such research and may also help satisfy consumers' desire for reliable and objective information.

In addition, the potential contribution of pharmacists to improved prescribing practices deserves attention. There is a growing body of evidence that pharmacist intervention can reduce the risk of adverse drug events in hospitalized patients, especially older ones with polypharmacy. Some evidence is also emerging that pharmacist counseling of ambulatory patients, especially those who are prescribed high-risk medications for serious diseases, can reduce the incidence of adverse events and, consequently, decrease health system utilization and costs.

Finally, DTC advertising is likely to contribute to the already high inflation in prescription drug spending. While its impact on total health system costs is unknown, some are concerned that it may stimulate demand for products whose benefits are not commensurate with their costs. This is particularly true for new products addressing diseases or conditions that are primarily cosmetic or that may affect quality of life but do not lead to increased morbidity and mortality. It is likely that the clinical community and payers will need more comparative and cost-effectiveness information as a basis for rational drug selection. Further, policymakers and payers may be faced with considering equitable ways to ration access to the most expensive therapies.

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Since 1985, direct-to-consumer advertising of prescription drugs has grown from nothing into a significant market force. By 1997, the pharmaceutical industry was spending nearly a billion dollars a year on this form of promotion, placing it on a par with consumer product industries that rely on direct advertising to promote national brands. Regulation may have impeded the early growth of consumer advertising of prescription drugs. By the 1990s, however, companies that used it had achieved so high a return on their investment that it became, seemingly overnight, a major engine of sales and earnings growth. Today, regulatory requirements are moderating and industry observers expect DTC advertising to continue to expand.

This explosion in consumer-oriented promotion is a sign that pharmaceutical companies have shifted their strategy in response to structural changes in the health care market. In the current managed care environment, drug manufacturers increasingly face purchasers, such as health maintenance organizations (HMOs) and pharmacy benefits managers (PBMs), that put restrictions on consumer access to some prescription drugs. As a result, they have often found it more difficult to introduce new products, especially those that cannot demonstrate significant therapeutic advances or cost savings over existing therapies. In response, they have gone directly to the consumer. Evidence is growing that this strategy has been successful in motivating patients to approach their doctors with requests for specific prescription drugs. Physicians, so far, have tended to accommodate these requests. In effect, the pharmaceutical industry has been able to circumvent managed care barriers to the consumer retail market. It may also have challenged professional control over prescription decisions.

For the moment, DTC advertising appears to be helping pharmaceutical companies regain ground in the struggle to control the retail prescription drug market. However, the rapid expansion of consumer promotion raises questions about the appropriateness of the existing regulatory framework, the health care system's ability to deal with a surge in patients' requests for

drugs, and the impact that increasing demand will have on health system costs.

EARLY REGULATION

Traditionally, the advertising of prescription drugs was limited to medical journals or health care trade publications aimed at physicians. In 1981, the pharmaceutical industry raised the question of a new kind of advertising that would recommend such drugs directly to consumers. Two years later, FDA Commissioner Arthur Hull Hayes, Jr., M.D., asked for a voluntary moratorium on such advertising to enable the agency and other interested parties to pursue research on its likely effects. During this moratorium, several studies of varying rigor were conducted. Most of these investigated public attitudes toward DTC advertising and, more generally, consumer demand for health care information. With some exceptions, they suggested that consumers wanted more information about prescription drugs and would tend to view DTC advertising favorably.[1] Further, an FDA-commissioned study showed that both print and television advertisements were capable of communicating information about risk as well as about benefit to consumers, even though test subjects tended to retain more information regarding benefit than risk. The study also revealed that the format in which risk information is conveyed—that is, whether it is through print or through broadcast media—affects the level of understanding in the reader or viewer.[2]

In September 1985 the FDA lifted its moratorium on DTC advertising by publishing a *Federal Register* notice. The notice stated that current regulations governing prescription drug advertising provided "sufficient safeguards to protect consumers."[3] While not expressly forbidding DTC advertisements, the agency thus indicated that existing standards, which had been developed to regulate advertisements directed to physicians, must be followed for DTC advertising as well. This action both cleared the way for DTC advertising of prescription drugs and set in place a regulatory structure for consumer advertising whose effectiveness has been questioned.

By lifting the moratorium in 1985, the FDA asserted its authority to regulate prescription drug advertising to consumers, even though the enabling legislation had been enacted long before DTC advertising of such drugs was envisioned. In 1938 Congress had granted the FDA jurisdiction over the labeling of all drugs,[4] both prescription and over-the-counter, by passing the Food, Drug, and Cosmetic Act (the act). Jurisdiction over drug advertising, however, remained with the Federal Trade Commission (FTC) until 1962, when the Kefauver Harris Drug Amendments (the amendments) transferred jurisdiction over prescription drug advertising to the FDA, while leaving the FTC with jurisdiction over the advertising of over-the-counter products.[5] Some analysts have argued that when Congress enacted the amendments, its sole concern was to ensure that drug advertisements to physicians would not mislead them or negatively influence their prescribing practices. In 1962, direct-to-consumer advertising of prescription drugs was unthinkable for policymakers and regulators.[6]

In the two decades following passage of the amendments, the FDA developed an extensive set of regulatory requirements for prescription drug ads that appeared in medical journals and health-related trade publications. These requirements derived authority from Section 502(n) of the act, which requires that all prescription drug advertising include "such . . . information in brief summary relating to side effects, contraindications, and effectiveness as shall be required in the regulations."[7] Some of these requirements address the principal features that a prescription drug advertisement must have (for example, warnings and contraindications). Others specify what such an ad must not do. In particular, an advertisement is deemed to violate Section 502(n) if it is false, misleading, or lacking in "fair balance."

Thus, from Section 502(n) of the act flowed a set of standards that were well-established by the time the FDA withdrew its moratorium on consumer advertising:

- Regulation required that "product-claim" advertisements, that is, those that recommend a drug for a particular disease or condition, present a fair balance of benefit and risk information. For example, claims of safety and efficacy had to be balanced with relevant disclosures of risks and limitations of efficacy. These were to be reasonably prominent and readable in the main body copy of the advertisement.
- Regulation required all product-claim advertisements to contain the "brief summary" of comprehensive risk information, including, among other things, the drug's uses or indications, contraindications, warnings, adverse reactions, and overdoses.[8] In practice, manufacturers usually met this requirement by printing or, in the case of broadcast ads, scrolling the product labeling information.

When the FDA lifted the moratorium in 1985, it did not develop new regulations to adapt statutory requirements to the needs of a consumer audience. Rather, it applied the

existing regulations *in toto* to DTC advertising. Soon after, the FDA began to request that drug companies voluntarily submit proposed direct-to-consumer promotional copy prior to use, with a view to giving the agency an opportunity to review and comment on the materials before they reached the public.[9] Drug manufacturers, with some exceptions, have complied with this request.

The FDA's advertising regulations, developed for physician-directed marketing, created some difficulties in DTC contexts. A case in point is the so-called brief summary. Not at all brief, in a print advertisement it usually fills a separate page with fine print; in rare cases it may require two or three separate pages. The FDA study mentioned earlier, which examined how consumer understanding of risk information varied when it was conveyed in different formats, found that inclusion of the brief summary in print advertisements did not enhance readers' understanding of risk.[10] To the contrary, test subjects exposed to the brief summary in print ads actually scored lower in their understanding of risk than those who were exposed to risk information in other formats. From the manufacturer's perspective, the brief summary requirement raised the cost of print advertising. Thus, it may have delayed the adoption of print as a medium to reach consumers. Over time, however, the return on investment for print advertising proved so attractive to manufacturers that their initial resistance was overcome. The 1990s have seen an explosion of DTC advertising of prescription drugs in print media.

The brief summary requirement has also created challenges for television advertising. The FDA study cited above found that in the case of TV ads, consumer understanding of risk is enhanced by providing more rather than less information.[11] This finding suggests that the brief summary might add value to broadcast ads. However, full disclosure of the risk information contained in the product labeling normally would take far longer than the time available within the framework of a 30-second commercial. As a result, drug companies have avoided televised product-claim ads and chosen instead between (*a*) describing the symptoms of the disease or condition without mentioning the brand or (*b*) mentioning the brand without identifying the disease or condition that it treats. Within these limitations, some companies have used "institutional" or "see your doctor" ads. These typically inform the viewer about a disease and its symptoms and recommend that those who recognize such symptoms in themselves consult their doctors about available therapies. Others have used "reminder ads," which may include the name of the drug and other limited information but no representations or suggestions about the product's intended use or benefits.

Truncated, institutional advertisements may provide useful information to consumers and enhance the public image of their sponsors, but they hold only modest appeal for manufacturers. Drug companies face a "free rider problem" in disease-oriented advertisements, which are just as likely to stimulate demand for their competitors' products as their own. On the other hand, using ads that mention a product but not the condition that it treats may confuse viewers or fail to attract those with the relevant health problem.[12] Creative strategies used to suggest the condition that the drug is meant for, without actually mentioning it, have sometimes backfired and brought the company into conflict with the FDA. For example, in 1996 Hoechst Marion Roussel began broadcasting a consumer ad to promote its antihistamine Allegra. The ad, which showed the image of a woman windsurfing through a field of wheat, violated regulatory requirements because consumers were usually able to figure out that Allegra was meant to treat allergies. The ad was removed.[13] Because of this strict regulatory environment, broadcast media have hitherto played a limited role in DTC advertising of prescription drugs.

The FDA, in recognition of issues raised by DTC advertising, held a public hearing in October 1995. The purpose of the hearing was to "solicit information from, and the views of, interested persons, including health care professionals, scientists, professional groups, and consumers."[14] Nearly two years later (August 1997) the agency issued, in draft form, proposed new guidance for broadcast advertising.[15] In general, this guidance defines compliance with the statutory brief summary requirement in a way that allows DTC television commercials to mention both the brand name of the drug and the condition it treats without simultaneously disclosing all of the product's risk information. Instead, the broadcast ads can fulfill the requirement by making a "major statement" about the most important risks of the advertised drug in the audio or the visual parts of the presentation. In addition, they must make "adequate provision" for the dissemination of the approved product labeling. In practice, the commercial can make adequate provision by including each of the following: (*a*) a statement that professionals may provide additional information; (*b*) a toll-free number for obtaining the product labeling information by mail, fax, or phone; (*c)* reference to print advertisements or brochures; and (*d*) a Web site address. The FDA requires that the manufacturer make the labeling information available through multiple channels to ensure that consumers with different levels of literacy, access to technology, and propensity to seek information will be able to get it.

In the same *Federal Register* notice, the FDA requested public comments on the draft guidance, including data from sponsors and other interested parties on the impact of DTC promotional messages. The agency said that, within two years of publication of the final guidance, it would evaluate its effects and decide whether to continue, withdraw, or modify the guidance to reflect its current thinking. Some have suggested that the new guidance is an interim step on the way to new regulation designed specifically for consumer-directed advertising.

GROWTH OF DTC ADVERTISING

After its somewhat slow start in the 1980s, DTC advertising grew rapidly in the 1990s, when it attracted the interest of pharmaceutical manufacturers facing price pressures, increased generic competition to branded products, and more difficult market entry conditions. According to a Competitive Media Reporting (CMR) study cited in *Advertising Age*, total drug company spending on DTC advertising of prescription drugs rose from $55.3 million in 1991 to $164.3 million in 1993 and $340.0 million in 1995.[16] Total spending on DTC advertising nearly doubled again in 1996, to $595.5 million.[17] Scott-Levin Associates, a market research firm based in Newtown, Pennsylvania, estimates that spending reached $915.7 million in 1997.[18] *Advertising Age* expects this to rise to more than $1.5 billion by the year 2000. Such a level would place consumer-oriented prescription drug advertising ahead of traditional heavy spenders, such as fast food and soft drink marketers.[19]

Much of this spending growth will probably occur in broadcast media. Until recently, pharmaceutical companies spent only a fraction of their total DTC prescription advertising budgets on TV commercials: just $67.1 million, or about 11 percent of the total, in 1996.[20] However, industry observers believed that the FDA's proposed new guidance for broadcast advertising will greatly enhance the attractiveness of TV commercials to drug manufacturers.

DRIVING FORCES

The forces driving growth in DTC advertising of prescription drugs are strong and are being reinforced by structural changes in the health care market. A decade ago, when fee-for-service medicine dominated U.S. health care, FDA approval of a new drug often ensured market acceptance. Since then, managed care organizations (MCOs) and pharmacy benefits managers have established new criteria for drug selection. In general, these purchasers have demanded that new products demonstrate either cost advantages or therapeutic advances proportional to any increase in cost over existing therapies. They have limited consumer access to expensive and ineffective prescription drugs through a number of mechanisms, such as restricted formularies, generic substitution, and drug utilization review. These policies have placed pressure on drug companies' revenues and made it more difficult for them to launch new products, especially those that provide only marginal therapeutic advantages or address conditions viewed as primarily cosmetic, such as nail fungus or baldness.

Advertising directly to consumers provides a way to stimulate demand for new products, especially those that are differentiated only to a limited degree by greater effectiveness, milder side effects, or easier dosing forms. For example, after Merck invested $28.4 million in DTC advertising for its osteoporosis treatment Fosamax in 1996, the product gained 40 share points, moving from a 31 percent to a 71 percent share of the total market.[21] It is unclear whether Fosamax, which some clinicians view with skepticism, would have enjoyed such success without advertising-induced consumer demand.

Despite the resistance of managed care purchasers and physicians, consumer advertising has been so successful in stimulating demand that industry analysts are now citing it as a major engine of drug company sales and profits. A recent *Wall Street Journal* article attributed much of the third-quarter 1997 earnings growth of three major drug companies to aggressive consumer advertising.[22] For example, sales of Bristol-Myers Squibb's anticholesterol drug Pravachol increased 34 percent in the third quarter to $350 million, despite the recent introduction of Lipitor, a more potent anticholesterol drug by Warner Lambert. Bristol-Myers had invested heavily in both print and broadcast advertising of Pravachol. Similarly, Schering-Plough's TV advertisements of its Claritin antihistamine helped to increase its quarterly sales by 39 percent, to $448 million. These drugs may have benefitted from other factors; for example, Claritin increased its market share just as its competitor Seldane fell from favor because of its risk of serious interactions with other drugs. Even so, most observers have attributed much of the success of these brands to consumer advertising.

U.S. consumers have long reported an interest in information about prescription drugs. Since the 1990s, however, concern over access to prescription drugs has

intensified their desire for information. Public awareness of health maintenance organization (HMO) cost control mechanisms, such as restricted formularies and financial risk sharing by physicians, has grown over the past few years. This awareness has tended to undermine consumers' faith in their physicians and to increase skepticism about whether the therapeutic alternatives presented are always in the best interest of the patient. HMO resistance to public disclosure of coverage policies has exacerbated public mistrust. For example, a recent *Wall Street Journal* article reported that when Stephanie Yoder, a consumer activist with Citizens for the Right to Know, approached 48 HMOs last year and asked them to provide lists of the medicines they covered, nearly 25 percent said that they would not provide such information, even to their own members.[23] Against this background, consumers are demanding to know more about diseases and the therapies, including prescription drugs, that are available to them.

Finally, DTC advertising is taking hold under a political and regulatory climate favorable to giving consumers access to health care information. Over the past few years, the increased penetration of managed care and public furor over the restrictions it has imposed on patients have raised concern in the administration and Congress. As a result, consumer protection has become a prime issue. It is important to note, however, that the definition of "consumer protection" in today's environment has shifted from what was meant a decade ago. Traditionally, the term usually meant shielding consumers from harm that might be done to them, for example, by false or misleading advertising claims. Today, "consumer protection" increasingly balances this with concern about the value of the information that would be lost if advertising were eliminated or restricted. The FDA's recent decision to publish less restrictive guidance for broadcast advertising may reflect a wish to ensure that consumers have greater access to information about prescription drugs and the conditions they treat.

In sum, this combination of forces—financial incentives for drug companies to invest in DTC advertising, intensifying consumer demand for information about drug therapies, and a regulatory climate that favors consumer access to information—seem likely to drive growth for some time to come.

PUBLIC POLICY ISSUES

No sooner had the question of DTC advertising been raised in the early 1980s than it became the subject of intense debate. Despite a lack of evidence to support views either pro or con, positions were staked out and defended, sometimes vehemently. Most of the arguments advanced addressed the question of whether DTC advertising would be helpful or harmful to consumers. This question was raised against the background of a health care delivery system in which fee-for-service medicine dominated and many patients paid for their drugs out of pocket. As a result, some of these arguments now need to be revisited in the light of changes that have occurred in the organization of health care delivery over the past decade.

From the 1980s to the present, proponents have argued that DTC advertising (*a*) fulfills consumers' need for health information, especially in the area of disease, symptom, and treatment awareness; (*b*) encourages consumers to seek medical advice for conditions that might otherwise go untreated; (*c*) promotes compliance with medically recommended drug therapies by helping the consumer to choose from a range of appropriate therapies the one with the least objectionable side effects; and (*d*) speeds the adoption of important new medical advances. Opponents of DTC advertising, on the other hand, have emphasized its potential dangers to the consumer and inflationary effect on health care costs. In general, they have claimed that such advertising may (*a*) lead patients to put pressure on physicians to prescribe unnecessary and unindicated drugs, (*b*) confuse consumers by leading them to believe that minor differences among competing products represent major therapeutic advances, (*c*) foster consumer loyalty to branded products rather than generic equivalents, and (*d*) lead to higher prices for prescription drugs.[24]

Since consumer-directed advertising has met no serious challenge in the courts or from Congress, it is probably here to stay. If this is the case, the questions facing public policymakers have to do with how it should be regulated and what public and private initiatives might ensure that consumers are protected from any problems that may arise.

Issue 1—*What kinds of prescription drug information are more helpful to consumers? How can this best be conveyed to them?*

As noted earlier, consumer advertising expanded so rapidly in the 1990s that it now appears well on the way to being established as a channel, albeit an imperfect one, of prescription drug information. Several studies conducted over the past 15 years have found that consumers have a keen interest in knowing more about prescription drugs. Furthermore, they believe that DTC

advertising can provide them with information that they have a right to know.[25] Yet a recent national telephone survey of over 1,200 consumers suggests that DTC ads are not generally perceived as very clear or useful. This survey, which was jointly sponsored by the American Pharmaceutical Association (APhA) and *PREVENTION Magazine*, asked consumers who had seen or heard DTC prescription drug ads to rate them on a four-point scale of clarity and usefulness. It found that only one in four (25 percent) consumers who have seen DTC ads thinks that they are "very clear." Slightly more (27 percent) think that they are either "not too clear" (17 percent) or "not at all clear" (10 percent), while 46 percent think they are "somewhat clear."[26] Clarity appeared to be the most important determinant of usefulness to consumers. It is therefore not surprising that only 25 percent of the consumers who had seen or heard DTC ads found them "very useful."

This relative lack of clarity and usefulness may result, in part, from the FDA's history of using regulatory standards unsuited for lay audiences. At their worst, these standards prevented consumer ads from conveying their most basic message: what condition the product is supposed to treat, as in the ill-fated Allegra commercial. According to some, broadcasted reminder ads that complied with the older FDA guidance were particularly apt to confuse consumers. Although these ads were appropriate for physicians who knew what the drug was intended to treat, they left the laity in the position of having to guess. As a result, some physicians have been approached by patients with requests for unsuitable medications—for example, a man who had seen a Claritin ad and believed that the drug could help his heart condition.[27]

While the FDA now appears to be trying to develop more consumer-friendly regulations, it will have to address several questions before it can develop a framework that will foster a flow of clear and useful information. In broadest terms, one set of these questions is concerned with the content of consumer-directed ads, the other with the forms or mechanisms of communication. In practice, however, these questions cannot be addressed in isolation from each other, or from others having to do with public health goals, consumers' responses to direct advertising, and the effects that demographic factors such as age and education may have on the way commercial messages are received and interpreted.

What kinds of information do consumers need to see in ads?—While the FDA requires that DTC ads not be false, deceptive, or lacking in fair balance, these standards do not ensure that the major statement in the main body of the ad includes information that might be important to consumers. There is some evidence that a significant proportion of consumer ads lack information that, in the opinion of professionals, it would be helpful for them to know.

In 1996, Martin S. Roth of Boston College's Carroll School of Management published a study on patterns in DTC prescription drug print advertisements.[28] Roth analyzed approximately 90 percent of all such print ads placed into media in the period from 1993 through mid-1995. His purpose was to test a series of hypotheses about the types of drugs advertised, their information content, and their demographic targeting. These ads had been cleared by the FDA before publication and so presumably had met the agency's standards for fair balance, truthfulness, and lack of deception. Roth used a panel of pharmacists to judge the information content of the ads based on whether they presented a fair balance of benefit and risk information.

The judges used a paraphrased description of what constitutes fair balance, not the agency's formal definition. The statutory requirement 21 C.F.R. 202.1(e)(5) states that both risk and benefit information must be presented in comparable depth and detail. Hence, as Roth points out, a manufacturer who prefers to limit risk information may satisfy the fair balance requirement by limiting benefit claims commensurately. In such cases, the advertisement could be fairly balanced but not contain information that consumers might find useful.[29] Thus, the fair balance standard ensures proportionality but not adequacy in the content of the information presented in the main body of the ad.

Roth's expert panel judged that only 65 percent of the ads presented a fair balance of information. Roth noted that the pharmacist panel may have been sensitive to the completeness of pharmacological information presented in the ad, not simply to balance per se. When the judges were asked for their reasons for finding some of the ads unbalanced, they most frequently cited the absence of risk and/or side effect information (15 percent of the ads) or the shortage of such information (10 percent). The expert panel also found that 88 percent of the ads did not contain information on the potential for misuse of the drug and that over half (58 percent) did not provide directions for use.

These findings raise questions about the type and amount of information that should appear in the main body copy of the ad. However, it is difficult to answer these questions until more is known, in turn, about how

material in the ad might contribute to a dialogue between patients and their physicians, how it might affect public health goals, and how well-equipped consumer audiences are to understand and interpret it.

What information would be most likely to foster public health goals?—In 1985, Alison Masson and Paul H. Rubin published an essay in the *New England Journal of Medicine* that argued that direct advertising of prescription drugs would benefit consumers.[30] They maintained that the information provided by such ads would facilitate patient-physician communication and result in a more precise matching of drugs with patient needs and preferences. Consumer-oriented ads may alert patients to the existence of a disease, to the availability of treatment, and to therapeutic alternatives with more tolerable side effects or acceptable risks. Such information enables the patient to approach his or her physician with information about health status or preferences that might otherwise be lost or overlooked. For example, a consumer who has seen an ad containing information on a disease may recognize its symptoms in himself or herself and report these to a doctor, who would diagnose and treat the patient for a condition that otherwise might go unrecognized. Similarly, a patient with an intolerance for certain side effects, such as nausea, might learn from an ad about a brand of medicine that does not cause the objectionable side effect. The patient's mentioning this intolerance and the advertised medicine to his or her doctor might result in a prescription that encouraged better compliance.

The argument advanced by Masson and Rubin suggests that information conveyed through direct advertising may contribute to better clinical outcomes. Further, they suggest, in areas of disease that are believed to be prevalent but often undiagnosed (for example, depression and diabetes) or in those where noncompliance with drug therapy is an established problem (for example, hypertension), consumer advertising could make a substantial contribution to public health. The essay, though theoretical in its approach, thus opened a fruitful line of empirical inquiry: which kinds of information, when communicated directly to consumers through advertising, would be likely to have the greatest impact on public health? To date, little research has been undertaken to assess the impact of different kinds of advertising content (for example, disease identification, side effects, contraindications, risks, directions for use, potential for misuse, and advice on obtaining professional guidance) on physicians' prescribing behavior and patients' actual drug use behavior (not just their attitudes or intentions). A better understanding of these relationships might help the FDA develop DTC advertising guidelines that foster important public health goals, such as early diagnosis of disease, improved compliance with prescribed regimes, and reduced adverse drug events.

How do consumers respond to prescription drug ads? What demographic variables affect their response patterns?—The *PREVENTION*/APhA study found that consumers are highly responsive to direct-to-consumer advertisements. By March-April 1997, when this survey was conducted, 63 percent of all consumers could recall seeing a DTC prescription drug ad. Of this group, almost a third (31 percent) reported that they had asked their doctors about a medication they had seen advertised. Of these, nearly one-third (29 percent) had asked the doctor for a prescription, which he fulfilled almost three-fourths (73 percent) of the time.[31]

The *PREVENTION*/APhA study also found that three demographic factors—age, previous use of prescription drugs, and education—affected responsiveness to DTC advertising. First, consumers over the age of 50 were more likely to have spoken to their physicians about an advertised medication than younger adults (36 percent versus 28 percent). Second, those who were already taking a prescription drug were also more likely to talk to their doctors than those who were not (38 percent versus 24 percent). Neither interaction is surprising, since older people and those whose health has already been compromised tend to use more prescription drugs and to see their physicians more often. Finally, 36 percent of consumers who were college graduates had talked with their doctors about an advertised medication, while only 26 percent of those without any college education had done so.[32] While the reason for this disparity is unclear, it is possible that better-educated consumers are more likely to have health insurance and access to physicians. Hence, they would be more likely to consult their doctors about advertised drugs that interest them.

What formats and mechanisms should DTC advertisements use to convey information to consumers?—Since 1985, the FDA has relied on the brief summary to ensure full disclosure of risks in print ads. It has done so despite the evidence from its own study that had demonstrated by 1984 that test subjects learn little about risks when these are presented in the brief summary format. For lay audiences functioning in "real life" circumstances, several characteristics of the brief summary may prevent it from conveying information effectively. Normally, it is published in fine print that is difficult to read, perhaps impossible for seniors with

fading vision. It tends to be off-putting in length and is not structured in a way that makes finding information easy. Finally, it is couched in technical and scientific language originally intended for physicians, which may be beyond the comprehension of many consumers.

There are similar problems with the adequate provision requirement of the new guidance for broadcast commercials. In general, this requirement can be satisfied by the use of alternative mechanisms for distributing the same product labeling material that is typically used in print ads to satisfy the brief summary requirement. Critics maintain that consumers who learn little from reading the product labeling in print ads will probably not learn more from brochures containing the same material. And, they say, it is unlikely that a consumer without the skill to read and comprehend the product labeling will benefit from having someone else read it to him over the telephone, in response to a call to an 800 number. The language, the structure, and the "packaging" of risk material may need to be reconsidered, both for print and broadcast ads.

No matter how the flow of information to consumers is encouraged and regulated, physicians and pharmacists are likely to face increasing demands for guidance and education. Even today, doctors are being called on to provide more counseling and to make more prescription decisions within the context of patient-initiated conversations. The *PREVENTION*/APhA study estimated that, by the spring of 1997, 35.5 million adults had already seen a prescription drug advertisement and, as a direct consequence, talked with their doctors about an advertised medication. Of this group, an estimated 10.2 million had asked their doctors for a prescription. As a result of the very high prescription fulfillment rate (73 percent), an estimated 7.5 million patients had had their requests honored.[33] Thus, DTC advertising raises a second major issue for policymakers.

Issue 2—*How well-equipped are physicians to respond to consumer demand for prescription drugs? What kinds of support might pharmacists provide?*

Physicians' knowledge of drugs and their authority to give or withhold prescriptions for more potent and risky medications are critical elements of patient care (or, in this context, consumer protection). However, some have questioned whether physicians are adequately trained in the use of drugs and whether their actual prescribing practices reflect a scientific understanding of diseases and appropriate drug therapies. While these issues have been raised for nearly a century, consumer response to DTC advertising is likely to increase the stress on a system that may already be weak. As a result, policymakers may need to consider whether the present system is adequate to protect consumers and, if it is not, what measures might be taken to strengthen it. In particular, the following policy questions are raised:

What kind of training in clinical therapeutics do physicians need?—Medical education in therapeutics has been recognized as deficient for some time. In 1988, the Health and Public Policy Committee of the American College of Physicians published a statement calling for increased emphasis on therapeutics in medical school curricula and in-house officer training.[34] The paper pointed to the post-World War II revolution in drug therapy that has resulted in a vast array of available prescription drugs and combinations of drugs and an increasing number of prescriptions per person written in the United States (6.2 per person by 1981). Medical education, the committee argued, had not kept pace with this explosion in drugs. Virtually all formal pharmacological education occurs in the second year of medical school, before significant exposure to clinical medicine. House officers also lack adequate training in the basic elements of prescription writing. Finally, after completion of formal medical school and house officer training, physicians receive no systematic exposure to intelligent, informative, and unbiased assessments of drug therapy. According to the committee,

> Continuing education in pharmacology occurs as the result of random encounters with a variety of information sources, including medical journals, the lay press, interactions with colleagues, and pharmaceutical sales representatives. The entire process can be characterized as largely random, incomplete, and subject to distortion.[35]

Little has changed in the broad base of U.S. medical education in the decade since this statement was published. However, for physicians with little pharmacological training, the knowledge gap in therapeutics has grown and may continue to grow worse. Since 1992, when Congress passed the Prescription Drug User Fee Act (PDUFA), the FDA has increased the rate at which it completes premarket reviews for drugs and biologics products. As a result, today's medical school graduates face a larger and faster-expanding universe of drugs and vaccines than ever before. Further, many young doctors will practice in managed care settings, where their prescription choices may be governed by multiple formularies assigned by different payers. As a result, these physicians may have little opportunity to prescribe within a limited "comfort zone" of well-known drugs.

With respect to their prescribing decisions, how vulnerable are physicians to commercial influences and patient and market pressures?—Even before the advent of DTC prescription drug advertising, some argued that this lack of training and continuing education had left physicians susceptible to commercial influences.[36] In 1982, Jerry Avorn, M.D., of Harvard Medical School published evidence that physicians tend to be more influenced than they realize by commercial channels of information and patient preferences. In a study of 85 randomly chosen primary care doctors, Avorn found that they were likely to rate their training and experience, along with scientific papers, as the most important influences over their prescribing practices. Conversely, they tended to downplay the role of patient preferences and commercial sources of drug information such as advertisements and manufacturers' representatives. However, their behavior in respect to two specially chosen "index drugs" belied their claims. These drugs were chosen as indices because their pharmacological effects had been shown by controlled studies to be minimal or not different from those of nonprescription medications, even though they were heavily advertised as being effective.[37] Avorn found that physicians' beliefs about the index drugs were heavily influenced by nonscientific channels of information and that they tended to be unaware of this influence. Moreover, while doctors usually dismissed the importance of patient preferences, their actual prescribing behavior tended to be accommodating.[38]

Avorn concluded that "in the absence of mandatory postgraduate education or recertification, pharmaceutical advertising becomes . . . the major source of continuing education for American physicians."[39] This predominance of commercial over scientific sources of drug information is consistent with communications theory and marketing research data.

> Drug advertisements are simply more visually arresting and conceptually accessible than are papers in the medical literature, and physicians appear to respond to this difference. When the use of a product promoted in this way is also encouraged by patient demands and the desire of the physician to "do something medical," counter-arguments from empirical evidence may prove relatively weak and ultimately powerless.[40]

Vulnerability created by gaps in medical training will likely be tested by several forces over the next few years. One of these is the rising volume of patient demand for prescription drugs. Evidence from several sources suggests that consumers have clout. Advertising executives familiar with prescription drug campaigns claim that their research shows that doctors tend to fulfill patients' requests about 85 percent of the time, unless there is a clear counterindication—a claim similar to the *PREVENTION*/APhA survey findings.[41] Finally, Rebecca K. Schwartz and colleagues of Harvard Medical School analyzed the motivations reported by 110 physicians who were part of a large, multistate randomized control trial on academic detailing. When these doctors were asked why they had made inappropriate prescribing decisions, nearly half (46 percent) cited "patient demand." Some expressed fears that, in the competitive world of medicine, refusal to accommodate patients might result in a loss of business and reputation.[42]

In addition to triggering these "patient pressures," drug companies expect to coordinate consumer advertising campaigns with parallel promotion to physicians. Doctors who are prepared for patient-initiated conversations are believed to be more receptive to prescription requests.[43] This dynamic will likely reinforce physicians' dependence on commercial sources of information. In addition, manufacturers will be rushing to fill an information need that will continue to expand as more new products reach the market. As mentioned earlier, the FDA's efforts to increase the efficiency of its premarket review programs have worked so well that the agency is now approving an unprecedented number of new molecular entities each year. Industry observers, noting the full pipelines of many drug companies, expect the flow to continue.

Finally, managed care appears to exert diverse and sometimes conflicting pressures on physician prescribing behavior. Managed care organizations often attempt to influence doctors' use of therapeutics through mechanisms such as drug utilization review, formularies, generic substitution, step care protocols, and research-based guidelines. At the same time, however, they may increase the vulnerability of physicians in indirect ways. For example, some MCOs rely on primary care doctors to provide part of the care that would be given by specialists in a fee-for-service environment. This increases the primary care physician's scope of clinical responsibility and, along with it, the number of drug therapies that he or she must understand and deploy. Moreover, physicians practicing in a managed care environment often carry heavy case loads and have little time to spend with individual patients. According to some, writing a prescription is a way to signal that the interview is over and to satisfy the patient that therapy is being offered. Without appropriate support, for example, from continuing education in the use of drugs, research-based guidelines, or consulting pharmacists,

primary care physicians could become easy targets for commercial promotion and importunate patients.

Several suggestions for improving physicians' prescribing practices have been put forward over the past decade. The one mentioned earlier, strengthening the therapeutics component of medical education, could not be expected to make a difference in the short term, for it would not affect practicing physicians. And the speed with which new drugs and biologics products are being released into the market suggests that medical school training needs to be complemented by continuing education of all practicing physicians.

For this reason, policymakers may want to consider ways to increase the flow of noncommercial, research-based information to physicians throughout their careers. To address such a need, Section 409 of the Food and Drug Modernization Act of 1997 (P.L. 105–115) authorizes $14 million in grants over a five-year period to establish one or more centers for education and research on therapeutics (CERTs) under a demonstration program.[44] These centers would be charged with conducting drug research that is unlikely to be undertaken by the private sector, with a view to providing a flow of unbiased information to physicians, consumers, managed care organizations, and insurers. This law was passed late in 1997; the authorized funds have not yet been appropriated.

What roles might pharmacists play to reduce prescribing errors and educate patients?—Another option is to increase communication between physicians and pharmacists. Research performed over the past two decades has shown that such communication improves prescribing practices. For example, in the early 1980s a randomized controlled trial of 435 physicians demonstrated that a combination of pharmacist counseling and printed educational materials could significantly reduce poor prescribing practices.[45] More recently, a randomized controlled trial of 208 elderly patients who were receiving five or more medications found that the intervention of a clinical pharmacist to evaluate their drug regimes and make recommendations to their physicians significantly reduced inappropriate prescribing and adverse drug events (ADEs).[46] Polypharmacy (the concurrent use of several drugs) is common among the elderly[47] and tends to increase the risk of ADEs. It is likely to become more prevalent as the U.S. population ages and as consumer-directed advertising increases the demand for prescription drugs. Since pharmacist intervention has been shown effective in reducing the risks to patients on several drugs at a time, it may be prudent to consider strategies that would promote greater cooperation between physicians and clinical pharmacists.[48]

Pharmacist counseling of patients may also help to reduce adverse events and ensure compliance. While the effect of such counseling on clinical outcomes is unknown, emerging evidence shows that it can reduce health system utilization and costs. Jeffrey S. McCombs and his colleagues have just completed a large study, the Kaiser Permanente/USC Consultation Study,[49] to assess the impact of different models of pharmacist counseling on the use and cost of health care services consumed by patients. McCombs has found that pharmacist counseling of patients is generally associated with lower utilization and costs. For patients who are prescribed high-risk drugs, appropriate intervention can reduce hospitalization by over half (53 percent), presumably through prevention of catastrophic adverse events. These findings suggest that greater communication between pharmacists and ambulatory patients could promote public health. As more becomes known about the impact of pharmacist counseling on clinical outcomes, policymakers may wish to consider ways to ensure that such intervention occurs when appropriate.

Issue 3—*How will DTC advertising affect total health care costs? What tradeoffs will need to be made among the cost, effectiveness, and safety of prescription drugs?*

Today, few would question that consumer advertising will help to drive demand for prescription drugs over the next few years. There is no consensus, however, on the impact it will have on health system costs. Some have argued that consumer advertising will inflate drug expenditures in several ways. According to these critics, such advertising will result in higher prescription drug prices, promote the use of branded products over generic equivalents, and lead to overuse of prescription medications. Moreover, consumer-directed promotion will tend to undermine the strategies—such as restricted formularies, generic substitution, and drug utilization review—that MCOs have developed over the past decade to control drug cost inflation. Countering these claims, others have argued that increased diagnosis and better compliance might improve outcomes and reduce total health care costs.[50]

While most of these arguments seem plausible in the abstract, there is little empirical evidence to decide among them. DTC advertising has not been used long enough for its effects on health care delivery costs to be measured. However, it seems reasonable to expect that

consumer advertising will increase the use of prescription drugs within several distinct clinical contexts over the next few years. Most of these areas present cost containment challenges that are familiar to policymakers and payers. Thus, while consumer advertising may aggravate existing problems, the policy approaches to dealing with them are the same or similar to those that have already been proposed or are now in use.

The rest of this section will examine (*a*) the kinds of contexts in which consumer advertising is likely to increase prescription drug costs and (*b*) policy options for achieving efficiencies in each one. These options do not assume that cheaper is better or that increased spending is always bad. Several studies have shown that a singular focus on reducing drug costs is likely to result in higher total health care costs by increasing disability, morbidity, and mortality. Rather, a rational approach looks for ways to allocate limited resources in such a way that incremental dollars are spent only in situations that warrant it, for example, whenever desirable patient outcomes cannot be achieved by more economic means.

In what contexts can increased drug usage be expected?—Over the next few years, consumer advertising may contribute to increased drug usage in five clinical situations:

- *Category A*—New therapies intended to treat conditions that were formerly untreatable or only marginally treatable, such as Alzheimer's disease or migraine headaches.
- *Category B*—Drugs for conditions, such as depression and hypertension, that have a history of being underdiagnosed and undertreated, even though drug therapies were available.
- *Category C*—Drugs whose lower risks or milder side effects expand the number of patients who can tolerate them.
- *Category D*—Branded products that have cheaper, generic or over-the-counter (OTC) equivalents.
- *Category E*—Products that provide little benefit but that physicians may prescribe anyway, either out of ignorance or in order to accommodate patients.

While the impact of DTC advertising on usage in each of these five categories is unknown, the Roth study suggests that some areas may become the focus of intense consumer promotion. Roth tested several hypotheses about the characteristics of drugs that manufacturers are more likely to advertise. In general, he found that the majority of ads were used to promote drugs intended for the maintenance of patients with chronic conditions rather than for short-term, periodic use; drugs whose side effects were neither prevalent nor severe; drugs that were early in their product life cycle, that is, with four or more years of patent protection remaining; and drugs intended for conditions with less disease, symptom, and treatment complexity.[51] However, he also found several cases in which manufacturers spent heavily late in a drug's product life cycle, perhaps with a view to building market position and brand loyalty before the drug lost patent protection.

While Roth's findings do not rule out consumer promotion directed toward any of the five categories, they suggest that manufacturers might especially target advertising toward new drugs (category A). These would normally have several years of patent protection left, during which they might command premium prices—unless competing therapies entered the market. Manufacturers would also be likely to advertise drugs directed toward chronic conditions that are relatively easy to diagnose and treat (category B) and drugs that are differentiated by the low prevalence and mildness of their side effects (category C). While it seems unlikely that drug companies would advertise prescription drugs that have already gone off patent, DTC advertising of products late in the life of patent protection might have carry-over effects that would reduce the rate of price and market share decline once they have become subject to generic competition. Hence, DTC advertising may contribute to the use of branded products in category D as well. Roth's findings are not revealing about category E. Thus, the extent to which consumer promotion might contribute to the use of such products remains an open question. The policy issues raised by these five categories range from straightforward and easy to address, in the case of D and E, to relatively complex and difficult, in the case of A, with B and C occupying a middle ground.

Which kinds of increased drug use are medically unwarranted? What strategies might be used to reduce them?—Of the five areas in which DTC advertising may affect usage, categories D, branded drugs with cheaper, generic or OTC equivalents, and E, those that provide little benefit, have the most straightforward implications for policymakers. Both are medically unwarranted, inflationary, and therefore to be discouraged. At the practical level, the issues they raise may also be relatively simple to address. In the case of D, there is some evidence that consumers are concerned with drug prices and may be elastic in their demand for

drugs.[52] Thus, if they are made aware that a cheaper, generic equivalent to the branded drug exists, for example, by required disclosure at the point of sale, and if they are required to pay the difference between the generic and branded price, it is likely that many consumers will chose the generic equivalent. Education of consumers who are likely to be susceptible to brand loyalty might foster more rational choices. However, policymakers and payers also have recourse to tougher mechanisms, such as restricted formularies, or mandatory generic substitution to control unwarranted costs.

In the case of category E, education of physicians through so-called academic detailing programs has been proven effective in reducing unnecessary prescribing. In 1983, in the *New England Journal of Medicine*, Avorn and colleagues reported the results of a randomized controlled trial of medical-school–based, face-to-face detailing by specially trained clinical pharmacists. Four hundred thirty-five physicians in four states were randomly allocated to a control group and to two experimental groups. The authors compared the effects of using printed educational materials (called "unadvertisements") alone with an intervention combining this material with educational visits to doctors' offices by clinical pharmacists who were trained in principles and techniques of persuasion. The objective was to reduce the utilization of three drug classes that are either marginally effective or known to be overused.

Avorn and colleagues found that the group receiving the print materials plus two 15-minute face-to-face visits by a clinical pharmacist reduced their prescribing by 14 percent, an effect that was sustained for the full nine months of follow-up, with no increases in undesirable substitute drugs. At the time, the savings from drugs alone more than paid for the cost of the program.[53] Since the trial was conducted, opportunities to lever academic detailing efforts through the use of information technology, including the Internet, have increased dramatically. Such programs might be developed either by institutions, such as MCOs and health systems, or at the national level, for example, in connection with the CERTs authorized under P.L. 105-115. Other industrialized countries, such as Australia, are already in the process of developing these programs.

Which kinds of drug use are medically warranted but allow providers to chose among a range of therapeutic alternatives?—Drugs in category B, which treat underdiagnosed and undertreated diseases, and in category C, which have lower risks and milder side effects, are alike in that they often have therapeutic alternatives with the same or similar effectiveness but different levels of safety and cost. Efficient use of these drugs requires the physician to make tradeoffs between safety and cost that are appropriate to the patient. Cheaper drugs might be used as front-line treatment of patients who are able to tolerate their side effects, while more expensive drugs, with less prevalent and severe side effects, might be reserved for higher-risk patients.

To make rational decisions about the use of alternative therapies, physicians and payers need comparative information about the effectiveness, safety, and costs of such drugs.[54] Moreover, they often need information about the relative performance of drugs in specific classes of patients, for example, the elderly, children, or pregnant women, in order to limit the use of drugs that are toxic for certain populations even though they are safe and effective for others. The major obstacle to implementing such a cost containment strategy is, of course, the paucity of comparative information. In the private sector, payers (especially MCOs) began to demand comparative studies several years ago, while the public sector has been slower to discipline the market, despite its tremendous negotiating power with drug companies.

DTC advertising is likely to increase the pressure on payers to demand comparative studies from manufacturers. In the case of category B, consumer advertising has the potential to stimulate significant demand in diseases, such as hypertension and diabetes, that may be expensive to treat and whose prevalence will increase as the population ages. Being prepared to prescribe efficiently for such patients as soon as they are diagnosed is likely to result in substantial savings. In the case of category C, the development of research-based guidelines for qualifying patients to receive more expensive medications may be critical not only to controlling costs but also to settling conflicts of interest between payers and patients who have learned about new products with milder side effects and have begun to demand them.

What kind of drugs are medically warranted and lack therapeutic alternatives?—Drugs in category A, new therapies for conditions that were formerly untreatable, pose the most difficult challenges for policymakers, as they do for public and private payers. These are "breakthrough" products which lack robust therapeutic alternatives, that is, they are differentiated in effectiveness. Manufacturers are more likely to be able to extract premiums for these drugs than from any other kind; consumers are likely to demand them once they know about them. As a result, these treatments have the potential for raising drug expenditures substantially and

for provoking conflicts of interest between payers and patients. The recent debate over who should have access to a very expensive but effective combination of HIV drugs is a case in point.

The cost of some breakthrough drugs may be justified, in the sense that reductions in disability, morbidity, and mortality compensate for the increased expenditures over the long term. Even so, significant demand for a breakthrough drug has the potential to overwhelm resources available at the time it is introduced. As a result, policymakers and payers may face what are ultimately rationing decisions for these products: who will have early access to the new therapy and who will not. Such decisions, while repugnant to many, have already been made in situations of limited supply, such as for AZT. Moreover, some industrialized countries with nationalized medicine (for example, the United Kingdom) have traditionally used guidelines to determine access to very expensive therapies, such as dialysis, for publicly insured patients.

Policymakers and payers must also grapple with decisions over coverage of drugs that treat conditions viewed as primarily cosmetic, such as toenail fungus, or that affect quality of life but not do not cause morbidity or mortality, such as impotence. Pharmaceutical companies have spent heavily and successfully on consumer advertising to launch such products. For example, Johnson & Johnson spent $38 million in 1996 to promote Sporanox, its treatment for toenail fungus. As a result, doctor visits for toenail fungus more than doubled from 1993 to an estimated 1.6 million in 1996. Of those visits, 39 percent resulted in a prescription for Sporanox and 18 percent for its rival Lamasil, which was also heavily promoted to consumers in 1996.[55] Yet the market for toenail fungus remedies is probably tiny in comparison with the one for impotence, for which Pfizer has a drug (Viagra) recently approved by the FDA. This drug, unlike some earlier medications for impotence, appears to be effective and have few side effects.[56] As a result, analysts expect that Viagra will become a blockbuster. DTC advertising will likely be a major component of the campaign.

While drugs such as Sporanax and Viagra may contribute to the quality of life for some patients, they may also contribute to drug spending inflation. It is unclear whether, or under what circumstances, public and private payers have the same responsibility to underwrite the costs of such drugs as they have for drugs used to treat life-threatening conditions, such as asthma, diabetes, or cancer.

It is beyond the scope of this paper to suggest the principles and procedures that should be followed in developing guidelines for rationing access to expensive new therapies. It is clear, however, that the lack of such standards may ultimately confuse consumers and pave the way for litigious settlement of conflicting claims.

CONCLUSION

Direct-to-consumer advertising has already become established as an important component of prescription drug marketing in the United States, despite the need to satisfy regulatory requirements that were originally designed for professional audiences. Over the next few years, these requirements may need to be reconsidered in light of lay audience needs. Moreover, the surge in consumer demand for advertised products will probably exert pressure on physicians and insurers to prescribe and to underwrite the cost of new medications. As a result, policymakers may want to identify strategies that will enhance the clinical community's ability to make sound and cost-effective prescribing decisions.

ENDNOTES

1. Louis A. Morris, David Brinberg, Ron Klimberg, Carole Rivera, and Lloyd G. Millstein, "The Attitudes of Consumers toward Direct Advertising of Prescription Drugs," *Public Health Reports*, 101, no. 1 (January-February 1986):82-89.

2. Louis A Morris and Lloyd G. Millstein, "Drug Advertising to Consumers: Effects of Formats for Magazine and Television Advertisements," *Food Drug Cosmetic Law Journal*, 39 (1984):497-503.

3. Federal Register, 56 (September 9, 1985):36677.

4. The Food, Drug, and Cosmetic Act defines labeling as any written, printed, or graphic matter upon or accompanying the drug (21USC 321[k]); however, the material need not physically accompany the product, only "supplement or explain it." Hence brochures, calendars, mailing pieces, sound and film recordings, letters to formularies, detailing pieces, and so forth are all considered labeling, so long as they are sponsored or supported by the drug's manufacturer, packer, or distributor. By contrast, the act does not define what constitutes advertising. The FDA generally regards as advertising anything other than labeling that promotes a drug and that is sponsored by its manufacturer. For more discussion on labeling and advertising, see David A. Kessler and Wayne L. Pines, "The Federal Regulation of Prescription Drug Advertising and Promotion," *Journal of the American Medical Association*, 264, no. 18 (November 14, 1990):2409-2410.

5. Kessler and Pines, "Federal Regulation," 2409.

6. Lance S. Gilgore, "A Consideration of Direct-to-Consumer Advertising of Prescription Drugs and Potential Legal Problems with the Brief Summary Requirement: Is the FDA's Regulatory Authority Illusory?" *Food Drug Cosmetic Law Journal*, 46 (1991):849-859.

7. 21 C.F.R. 202.1(e)(5). Also see discussion in Geoffrey M. Levitt, "Advertising Prescription Drugs Directly to the Consumer: Can FDA Stop Worrying and Learn to Love Direct-to-Consumer Advertising?" *Food Drug, Cosmetic and Medical Device Law Digest*, 12, no. 2 (September 1995). Available: http://www.venable.com.govern.dirtocon.htm. Accessed on December 20, 1997.

8. The September 9, 1985, *Federal Register* notice ending the moratorium stated, "Although consumer-oriented advertising via electronic and print media is permitted, law and regulations governing prescription drug advertising require, with certain exceptions, a brief summary of all necessary information related to side effects and contraindications in any advertisement that promotes a drug for a particular use."

9. "Direct-to-Consumer Promotion: Public Hearing," *Federal Register*, 60., no. 158 (August 16, 1995):42582.

10. Morris and Millstein, "Drug Advertising to Consumers," 501.

11. Morris and Millstein, "Drug Advertising to Consumers," 501.

12. Alison Masson and Paul H. Rubin, "Warning: Brief Summaries May Be Hazardous to Your Health (and Wealth) or The Real Issues in Prescription Drug Advertising to Consumers," *Journal of Pharmaceutical Marketing and Management*, 1, no. 2 (Winter 1986):29-43. Originally published in 1986 by *Regulation*.

13. Michael Wilke, "Drug Category Feasts on Direct-to-Consumer," *Advertising Age*, September 29, 1997, 24.

14. "Direct-to-Consumer Promotion: Public Hearing," *Federal Register*, no. 158 (August 16, 1995):42581.

15. "Draft Guidance for Industry; Consumer-Directed Broadcast Advertisements; Availability," *Federal Register*, 62, no. 155 (August 12, 1997):43171.

16. Michael Wilke, "Ad Fever Sweeps Healthcare Industry," *Advertising Age*, January 13, 1997, 1.

17. Michael Wilke, "FDA Close to Easing Limits on TV Ads," *Advertising Age*, June 30, 1997, 1. Estimate provided by Competitive Media Reporting (CMR).

18. Elyse Tanouye, "Health Journal," *Wall Street Journal*, December 22, 1997, B1. The 1997 spending level was privately communicated to the author by Scott-Levin Associates.

19. Beth Miller, "Why Consumer RX Drug Ads Fail Creativity Test," *Advertising Age*, September 1, 1997, 18.

20. Wilke, "FDA Close to Easing Limits," 1.

21. Wilke, "Drug Category," 24. Market share estimates reported in this article were developed by IMS America and based on all channels, including hospitals, HMOs, and drug/food/retail stores where prescription drugs are sold. Advertising expenditures were developed by Competitive Media Reporting.

22. Robert Langreth, "Three Drug Makers, Helped by Ads, Post Higher Profits," *Wall Street Journal*, October 22, 1997.

23. Rhonda L. Rundle, "HMOs Brace Themselves for 'Avalanche' of New Laws," *Wall Street Journal*, February 20, 1998, B4.

24. Morris et al., "Attitudes of Consumers," 83.

25. See Matthew Perri and W. Michael Dickson, "Direct to Consumer Drug Advertising and Physician Reaction," *Journal of Pharmaceutical Marketing and Management*, 2, no. 1 (Fall 1987):2-23; Matthew Perri and Arthur A. Nelson, Jr., "An Exploratory Analysis of Consumer Recognition of Direct-to-Consumer Advertising of Prescription Medications," *Journal of Health Care Marketing*, 7, no. 1 (March 1987):9-17. Morris et al., "Attitudes of Consumers," contains a useful summary of the consumer attitude surveys that were performed through the mid-1980s.

26. *PREVENTION* and American Pharmaceutical Association (APhA), "Navigating the Medical Marketplace: How Consumers Choose," a joint survey, Washington, D.C., 1997, 27-28.

27. Personal communication from a physician to the author, February 1998.

28. Martin S. Roth, "Patterns in Direct-to-Consumer Prescription Drug Print Advertising and Their Public Policy Implications," *Journal of Public Policy & Marketing*, 15, no. 1 (Spring 1996):63-75.

29. Roth, "Patterns," 66.

30. Alison Masson and Paul H. Rubin, "Matching Prescription Drugs and Consumers: The Benefits of Direct Advertising," *New England Journal of Medicine*, 313, no. 8 (August 22, 1985):512-515.

31. PREVENTION and APhA, "Navigating the Medical Marketplace," 25-29.

32. PREVENTION and APhA, "Navigating the Medical Marketplace," 29.

33. PREVENTION and APhA, "Navigating the Medical Marketplace," 28-29.

34. Health and Public Policy Committee, American College of Physicians, "Improving Medical Education in Therapeutics," *Annals of Internal Medicine*, 108, no. 1 (January 1988):145-147.

35. Health and Public Policy Committee, "Improving Medical Education," 146.

36. The *Journal of the American Medical Association* published a circular to physicians in 1892 that condemned commercial promotion of drugs to physicians in the strongest

terms, noting that those engaged in drug manufacturing "do not hesitate to manufacture explanations of pathological conditions which will apparently favor the use of their remedies." *Journal of the American Medical Association,* 18 (1892):563. Reprinted as "Drug Manufacturers as Medical Teachers" in *Journal of the American Medical Association,* 267 (1992), no. 16. Since that time, physician directed advertising has become regulated to ensure that it is not false, misleading, or lacking in fair balance. However, physicians' reliance on commercial sources of information, which the circular finds objectionable, remains an issue.

37. In 1992, the *Annals of Internal Medicine* published a study of the information conveyed by prescription drug advertisements that appeared in leading medical journals. This study, often referred to as "the Wilkes paper" after its lead investigator, found deficiencies in areas in which the FDA had established explicit standards of quality. However, the study has been widely criticized on methodological grounds and may have limited value in assessing the quality of physician directed prescription drug advertising. See Michael S. Wilkes, Bruce H. Doblin, and Martin F. Shapiro, "Pharmaceutical Advertisements in Leading Medical Journals: Experts' Assessments," *Annals of Internal Medicine,* 116, no. 11 (June 1, 1992):912-919. See also William G. Castagnoli, "Critics Dissect, Authors Defend Wilkes Paper on Advertising," *Medical Marketing & Media,* December 1992, 14-22; Jacob Jacoby, "Misleading Research on the Subject of Misleading Advertising," and Paul H. Rubin, "Are Pharmaceutical Ads Deceptive?" *Food and Drug Law Journal,* 49 (1994), no. 1:7-36.

38. Jerry Avorn, Milton Chen, and Robert Hartley, "Scientific versus Commercial Sources of Influence on the Prescribing Behavior of Physicians," *American Journal of Medicine,* 73 (July 1992):4-8.

39. Avorn et al., "Scientific versus Commercial Sources," 7.

40. Avorn et al., "Scientific versus Commercial Sources," 8.

41. Based on the author's interviews of advertising agency executives, October 1997.

42. Rebecca K. Schwartz, Stephen B. Soumerai, and Jerry Avorn, "Physician Motivations for Nonscientific Drug Prescribing," *Social Sciences and Medicine,* 28 (1989), no. 6:577-582.

43. Based on the author's interviews of advertising agency executives and pharmaceutical industry observers in the fall of 1997.

44. Available: http:\\www.thomas.loc.gov. Accessed on February 20, 1998.

45. Jerry Avorn and Stephen B. Soumerai, "Improving Drug-therapy Decisions through Educational Outreach. A Randomized Controlled Trial of Academically Based 'Detailing,'" *New England Journal of Medicine,* 308, no. 24 (June 16, 1983):1457-1463.

46. Joseph T. Hanlon, Morris Weinberger, Gregory P. Samsa, Kenneth E. Schmader, Kay M. Uttech, Ingrid K. Lewis, Patricia A. Cowper, Pamela B. Landsman, Harvey Jay Cohen, and John R. Feussner, "A Randomized, Controlled Trial of a Clinical Pharmacist Intervention to Improve Inappropriate Prescribing in Elderly Outpatients With Polypharmacy," *American Journal of Medicine,* 100 (April 1996):428-437.

47. See F. Ascione, J. James , S. Austin, and L. Shimp, "Seniors & Pharmacists: Improving the Dialogue," *American Pharmacy,* 5 (1980):30-32; C.R. Smith, "Use of Drugs in the Aged," *Johns Hopkins Medical Journal,* 145 (1979), no. 2:61-64; Lawrence W. Green, Patricia D. Mullen, and Gene L. Stainbrook, "Programs to Reduce Drug Errors in the Elderly: Direct and Indirect Evidence from Patient Education," *Journal of Geriatric Drug Therapy,* 1 (Fall 1986):3-18.

48. Adverse drug events are common among the elderly and have been cited by a panel of geriatrics experts as one of the five most important quality-of-care problems in older people. For example, a recently published cohort study of 167 high-risk older outpatients (taking five or more scheduled medications) found that there were 80 self-reported adverse drug events (ADEs) involving 72 medications taken by 58 (35 percent) of the patients. Seventy-six of the 80 ADEs (95 percent) were classified as Type A (predictable) reactions. Sixty-three percent of patients with ADEs required physician contacts, 10 percent emergency room visits, and 11 percent hospitalization. Twenty percent of medications implicated with ADEs required dosage adjustments, and 48 percent of ADE-related medications were discontinued. This study is reported in Joseph T. Hanlon, Kenneth E. Schmader, Michael J. Koronkowski, Morris Weinberger, Pamela B. Landsman, Gregory P. Samsa, and Ingrid K. Lewis, "Adverse Drug Events in High Risk Older Outpatients," *Journal of the American Geriatrics Society,* 45, no. 8 (August 1997):945-948. The Health and Public Policy Committee of the American College of Physicians, in its statement on medical education, cited various studies which have estimated that between 10 percent and 15 percent of all hospitalized patients have an adverse reaction to a drug during a hospital stay. Moreover, estimates of the frequency with which adverse drug events result in hospitalization range from 0.5 percent to as high as 7.9 percent. One study of 2,499 hospital admissions found that 4.1 percent were due to adverse reactions and estimated that 27 percent of these could have been prevented with more prudent drug therapy.

49. Jeffrey S. McCombs, Weiwei Feng, Gordon Liu, Marisue Cody, Jinhai Shi, and Joseph P. Parker, "The Kaiser Permanente/USC Patient Consultation Study: The Use and Costs of Health Services." This study, which was shared in a personal communication with the author, has been accepted for publication by the *American Journal of Health Systems Pharmacy*.

50. Some have argued that consumer advertising will tend to lower prescription drug prices. However, the evidence for this argument is inconclusive. For example, there is only one published study which examines the impact of DTC advertising on prescription drug prices: Steven W. Kopp, "Direct-to-Consumer Advertising and Consumer Prescription Prices," *Drug Information Journal,* 30 (1996):59-65. This study found that DTC advertising tends to lower the prices of the advertised drugs *relative to other medications.* According to Kopp, this effect is predictable and in line with dual-stage economic

theory. According to this theory, consumer-directed advertising forces all drug retailers to carry the advertised drugs and to price them competitively with other retailers. They typically do so by reducing their profit margins on the advertised products, so that these become less expensive relative to others in their mix. However, Kopp noted that retailers may use the advertised prescription drugs as "loss leaders," just as grocery stores do with popular brands, and offset their reduced margins on these products by raising prices on other, less visible items. Thus, the jury must still be out on whether consumer advertising leads to *overall* drug price inflation.

51. Roth, "Patterns," 68-71.

52. Kopp, "Direct-to-Consumer Advertising," 61.

53. Avorn and Soumerai, "Improving Drug-therapy." See also discussion in Stephen B. Soumerai, "Factors Influencing Prescribing," *Australian Journal of Hospital Pharmacy*, 18, no. 3 (1988 supplement):11.

54. Jerry Avorn,"Balancing Costs, Efficacy, and Side Effects," *PharmacoEconomics*, 6 (1994), supplement1:63-66.

55. Tanouye, "Health Journal." DTC spending levels were provided by Scott-Levin Associates.

56. David Stipp and Robert Whitaker, "The Selling of Impotence," *Fortune*, March 16, 1998, 114-124.