ECONOMIC ANALYSIS AND THE REGULATION OF PHARMACEUTICAL ADVERTISING†

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Perhaps more than in any other industry, information is a central aspect of the pharmaceutical business. Indeed, the difference between a deadly poison and a useful medicine is the knowledge of how it should be used to treat a particular condition.

Production of knowledge about pharmaceutical products is the central objective of pharmaceutical research and development, supplemented by substantial public sector expenditures for medical research and the activities of a wide array of clinicians and academicians. Before that knowledge constitutes useful information, however, it must be disseminated to the practitioners who can use it. Dissemination of pharmaceutical information is an industry unto itself, involving medical journals, textbooks, consensus conferences under governmental auspices, and substantial manufacturer expenditures on promotion. Thus, pharmaceutical research and development and pharmaceutical promotion are complementary activities.

Dissemination of medical knowledge is an important issue, and an important part of the work of such agencies as the National Institutes of Health. During the time lag between the discovery of a new treatment and its application by physicians, patients with serious medical conditions are not treated with the best available therapy. Moreover, the recommendations of expert reviewers and medical textbooks have been found to lag behind the emerging results of randomized clinical trials.[1]

Decisions about which drug to use are made by physicians as expert agents of the consumer, rather than the ultimate consumer of the product.[2] Appropriate choices are critical, as inappropriate

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[1] Elliot M. Antman et al., *Comparison of Results of Meta-analyses of Randomized Control Trials and the Recommendations of Clinical Experts: Treatments for Myocardial Infarction*, 268 JAMA 240 (1992).

[2] Moreover, as with other medical expenses, an increasing fraction of prescription drug costs are actually paid by third party providers. Third party reimbursements covered 44% of prescription drug outlays in 1987, up from 28% ten years earlier. F.

decisions may result in severe side effects or the failure to treat an underlying medical condition. The range of options available, along with the introduction of new products, makes the choice problem a difficult one.[3]

Section I of this Article considers the economics of information and its implications for the regulation of seller-provided information. Section II applies the analysis more specifically to pharmaceutical advertising regulation, with special attention to the issue of off-label (or unapproved) uses of drugs that are marketed for a different condition. Section III offers some brief conclusions.

I. ADVERTISING AND THE ECONOMICS OF INFORMATION

Consumer choices guide a market economy. The products consumers choose and the prices they are willing to pay, signal producers to produce more or less of a particular product and signal the kinds of product changes that consumers would find desirable. Thus, market outcomes guide producers to better satisfy consumer preferences.

Consumer choices, however, depend on the available information. Absent certain facts, or misinformed about particular product features, consumers are likely to make different choices than they would otherwise make if better information were available. Thus, when information is imperfect, consumer choices may misdirect market activity, rather than guide market outcomes to maximize consumer satisfaction.

A. Imperfect Information

Two different types of imperfect information are important. First, facts may be misrepresented. Consumers may have been told, either directly or by implication, that a particular product possesses some feature or characteristic that it does not in fact possess. As a result, consumers will purchase too much of the product. Consumers who purchase the product because they desire the misrepresented feature are damaged, in that they do not receive the benefit for which they bargained. Moreover, there may be direct consumer injury from reliance on deceptive claims.

M. Scherer, *Pricing, Profits, and Technological Progress in the Pharmaceutical Industry*, 7 J. ECON. PERSP. 97, 98 (1993).

[3] It has been estimated that as many as 37,000 prescription drug products are available in the United States. Patricia Winters, *Prescription Drug Ads Up*, ADVERTISING AGE, Jan. 18, 1993, at 10. Since 1940, some 1200 new chemical entities have been introduced into American therapeutic practice. Scherer, *supra* note 2.

Markets also provide incentives for advertisers to tell the truth. When consumers can readily evaluate the truth of a claim, either before or after purchase, there is little payoff for deceptive claims because consumers will simply not purchase the product again.[4] When consumers cannot evaluate the truth of a claim even after using the product or service, the potential for deceptive claims is greater.[5] Although sellers can invest in reputations, developed in part through advertising expenditures, to offer assurance that claims are accurate,[6] the possibility of deceptive claims remains. Government intervention in such instances can enhance market performance.

Second, information may be incomplete if consumers are unaware that a product possesses a particular characteristic. The effects of incomplete information depend on the nature of the unknown fact. If consumers are unaware of a positive attribute of the product, they will purchase too little. If, for example, consumers are unaware that diets high in fiber may reduce the risk of cancer, they will purchase fewer high fiber products and consume less fiber than they would otherwise prefer. When the missing information is negative, however, consumers will purchase too much of the product. Consumers seeking the health benefits of a low fat diet, for example, but unaware that a particular product is high in fat, will consume too much of the product. Because of over- or underproduction of certain goods, lack of information may lead to adverse health consequences for consumers, whether the missing information is positive or negative.

Like everything else, information is costly. In some instances, the costs of information are monetary, as when a consumer consults a physician for medical information or purchases a subscription to *Consumer Reports*. Even when information is available free of charge, through the media or discussions with friends, acquiring information takes time and effort. Moreover, consumers must expend time and effort to process the data, once acquired, and understand its implications for their behavior.

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[4] When evaluation is only possible after purchase, the incentives for accuracy are greatest when the product is inexpensive and frequently purchased. *See* Phillip Nelson, *Advertising as Information*, 82 J. POL. ECON. 729 (1974); Phillip Nelson, *Information and Consumer Behavior*, 78 J. POL. ECON. 311 (1970).

[5] Such products are called "credence goods." *See* Michael R. Darby & Edi Karni, *Free Competition and the Optimal Amount of Fraud*, 16 J.L. & ECON. 67 (1973).

[6] Pauline M. Ippolito, *Bonding and Nonbonding Signals of Product Quality*, 63 J. BUS. 41 (1990); Benjamin Klein & Keith B. Leffler, *The Role of Market Forces in Assuring Contractual Performance*, 89 J. POL. ECON. 615 (1981).

The costs of obtaining and using information mean, for nearly any decision, that it will not pay for consumers to seek out and acquire all available information that may be relevant. Instead, consumers will balance the benefits of better information (in the form of improved decisions) against the costs involved in obtaining this information. The greater the costs of obtaining information, the less information consumers will generally acquire. Thus, changes that reduce the cost of acquiring information will lead consumers to obtain and use more of it. Even when information costs are relatively low, however, most consumers are likely to find that complete information is not worth its cost. Consumers will therefore make the best decisions possible on the basis of incomplete information.

Sellers have powerful incentives to assure that consumers have adequate information about the benefits of their products and the drawbacks of competing alternatives. Through advertising, labeling, and other marketing techniques, sellers attempt to ease the difficult task of information acquisition whenever providing information will increase sales of the product. Information about product benefits is likely to do just that. The incentive to provide information also includes negative characteristics as long as a product has less of a particular drawback than competing products. For example, many food manufacturers have chosen to advertise that their products have less fat than others.[7]

In effect, seller-provided information reduces the cost of obtaining information, and therefore leads consumers to obtain and use more of it. As George Stigler noted, "advertising is an immensely powerful instrument for the elimination of ignorance."[8] Marketing information is presented in small doses, designed to attract the reader's attention. It is easy to understand, easy to use, and easy to remember. Because advertising messages interrupt edi-

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[7] As one commentator noted, consumers will rationally assume that critical information is not provided because the product is among the worst with respect to the omitted attribute. Paul H. Rubin, *The Economics of Regulating Deception*, 10 CATO J. 667 (1991). Products with quality levels above the minimum thus have incentives to advertise that fact. Empirically, studies have found high levels of disclosure of negative nutritional characteristics for all but the worst products in cereals, bread, butter, and margarine. Similarly, they found that lower tar cigarettes are more likely to disclose tar content on the package. Pauline Ippolito & Alan D. Mathios, *The Regulation of Science-Based Claims in Advertising*, 13 J. CONSUMER POL'Y 413 (1990). The Nutrition Labeling and Education Act of 1990 now requires disclosure of nutritional information on product labels. Nutritional Labeling and Education Act of 1990, Pub. L. No. 101-535, 104 Stat. 2353 (1990).

[8] George J. Stigler, *The Economics of Information*, 69 J. POL. ECON. 213 (1961).

torial or program material, paying attention to them requires relatively little additional time or effort. Techniques such as attractive graphics, attention getting headlines, and colorful illustrations, all widely used in pharmaceutical advertisements, facilitate this communication process.[9]

Because it fosters competition, the information provided through advertising enhances market performance. Consumer choices can more effectively guide producer decisions in the directions that consumers most prefer. The beneficial effects of the ability to provide information through advertising are revealed in the price consumers pay for the product and in the nature of the product itself.

B. Advertising and Price

One of the earliest studies of the effects of advertising on product prices examined the differences in the price of eyeglasses between states that prohibited advertising by opticians and states that allowed advertising. It found that where advertising was prohibited the average price of eyeglasses was approximately twenty-five percent higher than in states without restrictions. Prices were higher whether the restrictions involved price or non-price advertising.[10] Moreover, the reduction in price when advertising was permitted seemed to be greatest for the least educated consumers.[11]

The price reducing effects of advertising are not confined to the market for eyeglasses. Studies of legal services,[12] advertising of prescription drugs by pharmacists,[13] and retail gasoline price post-

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9 For example, a study of special techniques such as die cuts and textured paper in pharmaceutical inserts found that recall was 125% higher for such special treatment ads than the average ad. Special treatments that were related to the advertisement's message (e.g., a sandpaper texture in an ad for an arthritis product) were particularly effective. Glenn Mohrman & Jeffrey E. Scott, *Ad Performance Insights: Special Treatment Inserts*, MED. MARKETING & MEDIA, Feb. 1988, at 32.

10 Lee Benham, *The Effect of Advertising on the Price of Eyeglasses*, 15 J.L. & ECON. 337 (1972). An FTC study of a variety of other restrictions in the optometric market found similar results. *See* Ronald S. Bond et al., *Effects of Restrictions on Advertising and Commercial Practice in the Professions: The Case of Optometry* (FTC Bureau of Economics Staff Report 1980).

11 Lee Benham & Alexandra Benham, *Regulating Through the Professions: A Perspective on Information Control*, 18 J.L. & ECON. 421 (1985).

12 John R. Schroeter et al., *Advertising and Competition in Routine Legal Service Markets: An Empirical Investigation*, 36 J. INDUS. ECON. 49 (1987); William W. Jacobs et al., *Improving Consumer Access to Legal Services: The Case for Removing Restrictions on Truthful Advertising* (FTC Staff Report, 1984).

13 John F. Cady, *Restricted Advertising and Competition: The Case of Retail Drugs* (American Enterprise Institute, 1976).

ing[14] have all found that restrictions on the flow of information increase the price that consumers pay. Similarly, the introduction of toy advertising directed to children reduced toy prices.[15]

Most of the available evidence concerns situations in which advertising has been entirely prohibited. Even where restrictions are less drastic, however, fewer restrictions on advertising are associated with lower prices. In the legal services market, for example, states with more restrictions on advertising have higher prices than states with fewer restrictions.[16] Although the evidence is more tentative, it suggests that the ban on broadcast advertising of cigarettes also increased product prices.[17]

The same competitive effects of advertising on price also occur in prescription drug markets. When already-marketed products are approved for a new use, additional advertising by the entrant reduces the average price paid for drugs used to treat that indication (relative to the prices of all drugs). This effect occurs primarily because additional advertising by the entrant reduces the price of competitive products.[18] Previous studies have also found that entry, assisted by pharmaceutical promotion, tends to reduce the price of competitive products.[19]

C. Advertising and Product Changes

The ability of producers to provide information also influences the nature of the products available in the market. Advertising is an important means of informing consumers about the availability of new products or of new information about existing products. In turn, the ability to tell consumers about product im-

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14 Alex Maurizi & Thom Kelley, *Prices and Consumer Information: The Benefits from Posting Retail Gasoline Prices* (American Enterprise Institute 1978).

15 Robert L. Steiner, *Does Advertising Lower Consumer Prices?* 37 J. MARKETING 19 (1973) (toy advertising directed to children).

16 Jacobs et al., *supra* note 12.

17 Robert H. Porter, *The Impact of Government Policy on the U.S. Cigarette Industry, in* EMPIRICAL APPROACHES TO CONSUMER PROTECTION 447-81 (Pauline Ippolito & David Scheffman eds., FTC 1986).

18 Because approval is for a new use, the product is already available on the market and is used for the new indication to some extent. With approval of the new use, the essential change is that the drug's manufacturer can now inform physicians that the product is effective for the new use. *See* J. Howard Beales III, *Marketing Information and Pharmaceuticals: New Uses for Old Drugs*, presented at American Enterprise Institute Conference on Competitive Strategies in the Pharmaceutical Industry (Oct. 1993) (forthcoming in conference volume).

19 Keith B. Leffler, *Persuasion or Information? The Economics of Prescription Drug Advertising*, 24 J.L. & ECON. 45, 73 (1981).

provements provides an incentive for manufacturers to make desirable product changes.

One of the clearest demonstrations of the significance of advertising comes from the introduction of health claims for fiber cereals. In October 1984, Kellogg initiated an advertising campaign, with the support of the National Cancer Institute, stating that diets high in fiber may reduce the risk of some kinds of cancer. The advertising, and accompanying label claims, were in violation of long-standing Food and Drug Administration (FDA) policy that prohibited any labeling discussion of the link between diet and disease.[20] Although the government had recommended for several years that Americans should increase the fiber content of their diets, prior to 1985 there was no significant trend toward increased fiber consumption. After 1985, however, there was a significant increase in the weighted average fiber content of cereals. Moreover, the average fiber content of new cereal products increased significantly.[21]

Changes in the tar and nicotine content of cigarettes also demonstrate the effects of advertising on product characteristics. As health concerns about cigarettes increased in the late 1950s, tar content became an important dimension of competition. In 1960, however, the Federal Trade Commission (FTC) reached an agreement with the cigarette companies prohibiting any mention of tar content.[22] In the four years preceding the agreement, the sales weighted average tar content of cigarettes fell twenty-nine percent; in the four years after the ban it declined only sixteen percent.[23] As one observer concluded, the policy "hindered the growth and development of cigarettes which might have been 'safer' due to advanced filters and lower tar and nicotine content."[24] In 1967, the FTC reversed its position and adopted a standardized methodology for measuring tar content. By 1981, the sales weighted aver-

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[20] The Kellogg campaign led eventually to the Nutrition Labeling and Education Act of 1990, which authorized certain health claims subject to prior FDA approval. The statute and the FDA's approach to implementation are discussed at length in chapter 5 of J. HOWARD BEALES & TIMOTHY J. MURIS, STATE AND FEDERAL REGULATION OF NATIONAL ADVERTISING (1993).

[21] Pauline M. Ippolito & Alan D. Mathios, *Information, Advertising and Health Choices: A Study of the Cereal Market*, 21 RAND J. ECON. 459 (1990); Pauline M. Ippolito & Alan D. Mathios, *Health Claims in Advertising and Labeling: A Study of the Cereal Market* 35, 45 (FTC Bureau of Economics Staff Report, Aug. 1989).

[22] Robert McAuliffe, *The FTC and the Effectiveness of Cigarette Advertising Regulations*, 7 J. PUB. POL'Y & MARKETING 49 (1988).

[23] Data obtained from the Tobacco Institute. *See also* John E. Calfee, *The Ghost of Cigarette Advertising Past*, 10 REG., Nov.-Dec. 1986, at 35.

[24] McAuliffe, *supra* note 22, at 50.

age tar content of cigarettes had fallen thirty-nine percent from its 1968 level.[25]

The importance of advertising in conveying information has also been demonstrated in pharmaceutical markets. When already-marketed products are approved for new uses, the drug's manufacturer can begin to promote that use. Before approval, use of the product for the new indication is unrelated to promotional expenditures. After approval, however, the product's share of the market for the new use increases significantly. Moreover, that increase is directly linked to the manufacturer's promotional expenditures.[26]

D. Implications for Regulatory Policy

The inevitable fact that consumer information is imperfect provides the central rationale for a regulatory presence to govern the flow of information. Policies seeking to assure that consumers have accurate information and that the flow of information is adequate for informed choices can offer important consumer benefits.

Concern about misrepresentation has been the central focus of regulatory activities regarding information. The vast majority of FTC cases involving advertising concern a seller's claim that is either alleged to be untrue, or which the seller cannot support with sufficient evidence to convince the Commission of its likely truth.[27]

Information regulators have also addressed problems that arise from the lack of information about possible drawbacks of a product. Failure to provide information has been found deceptive when disclosing only part of the truth leads consumers to conclusions that an undisclosed fact would contradict, and this failure may also be unfair in other circumstances.[28] Numerous FTC orders require disclosure of particular facts that are likely to reduce demand for the product.[29] Similarly, concerns about missing nega-

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[25] Federal Trade Commission, Report to Congress, Pursuant to the Federal Cigarette Labeling and Advertising Act for the Year 1981, at 31, Table 12 (July 1984).

[26] *See* Beales, *supra* note 18.

[27] FTC law requires that a seller have a "reasonable basis" to substantiate the truth of its claims. The amount of evidence required depends on the benefits that will result if the claim is true, the costs that will result if it is false, the nature of the product, the costs of testing, and the amount of evidence that experts in the field would consider reasonable. *See* Thompson Medical Co., 104 F.T.C. 648 (1984), *aff'd sub nom.* Thompson Medical Co. v. F.T.C., 791 F.2d 189 (D.C. Cir. 1986), *cert. denied*, 479 U.S. 1086 (1987); FTC Policy Statement Regarding Advertising Substantiation Program, 49 Fed. Reg. 30,999 (1984).

[28] *In re* International Harvester Co., 104 F.T.C. 949, 1060 (1984).

[29] A study of FTC orders issued between 1970 and 1977 found 226 orders requir-

tive information provide the rationale for food labeling requirements and for the requirement that prescription drug advertising include a "brief summary" of side effects and contraindications.

The FTC, which regulates advertising of most consumer products, has also recognized the need for regulatory attention to the other half of the incomplete information problem: impediments to the provision of information about product benefits. Since the early 1970s, the Commission has sought to remove various private and governmental restraints on the flow of information. For example, the FTC urged the television networks to end their restrictions on comparative advertising[30] and has urged other federal agencies to adopt the same standards for comparative and noncomparative advertising.[31] It has challenged private restraints on advertising in professional codes of ethics[32] as well as state prohibitions on advertising.[33] Moreover, in amicus briefs addressing First Amendment issues, the Commission has consistently urged the Supreme Court to preserve the free flow of commercial information.[34]

The importance of the free flow of seller-provided information to market performance has three implications for regulatory standards.[35] First, regulatory policy should avoid prohibiting truthful information. Second, it should avoid acting against strained interpretations of seller communications that are unlikely to mislead ordinary readers. Third, it should recognize that seller-provided information cannot be literally complete.

1. Avoid Prohibiting Truthful Information

The lessons of various prohibitions on advertising discussed

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ing affirmative disclosures of various information, excluding cases arising from disclosures required by specific statutes. *See* William L. Wilkie, Affirmative Disclosure: A Survey and Evaluation of FTC Orders Issued from 1970-1977, Report submitted to the FTC (June 1980).

30 16 C.F.R. § 14.15 (1993).

31 For example, the Commission's efforts to encourage the Bureau of Alcohol Tobacco and Firearms to permit comparative claims for alcoholic beverages are described in F.T.C. Policy Review Session, Consumer Information Remedies 218-20 (June 1, 1979).

32 *In re* American Dental Ass'n, 94 F.T.C. 403 (1979); *In re* American Medical Ass'n, 94 F.T.C. 701 (1979).

33 F.T.C. Ophthalmic Practices Rules, 16 C.F.R. § 456, 54 Fed. Reg. 10,285 (1989), *rule vacated by* California State Bd. of Optometry v. F.T.C., 910 F.2d 976 (D.C. Cir. 1990).

34 Brief for the Federal Trade Commission as Amicus Curiae at 8, Peel v. Attorney Registration & Disciplinary Comm'n of Ill., 496 U.S 91 (1989) (No. 88-1775).

35 These implications, along with their reflection in regulatory policies of the FTC, are discussed at greater length in chapters 2-4 of BEALES & MURIS, *supra* note 20.

above make clear the value of truthful information to market performance. Competitive flows of information drive down product price, in pharmaceuticals and in other industries. The information provided through advertising can have important influences on consumer choices, as in the case of claims about the health benefits of high fiber diets. Clearly, advertising induced changes in consumer fiber consumption that are considered desirable by both consumers and regulators. Product changes that resulted from competition on fiber content led to further consumer benefits. Similarly, marketing expenditures on pharmaceutical products that have been approved for a new use significantly increase use of the product. Policies that prohibit truthful information deny consumers these important benefits.

The value of truthful information has led the United States Supreme Court to extend constitutional protection to truthful commercial speech.

In the landmark decision of *Virginia State Board of Pharmacy v. Virginia Citizens Consumer Council, Inc.*,[36] the Court overturned a state ban on price advertising for prescription drugs. The Court focused on the "strong interest in the free flow of commercial information" because a market economy depends on informed consumer decisions to achieve efficient resource allocation.[37] Communications that are true and not deceptive can be regulated only if there is a substantial governmental interest, the regulation directly advances that interest, and the regulation is no more extensive than necessary to achieve the objective.[38] Although commercial speech restrictions need not satisfy the "least restrictive alternative" test applied in other First Amendment contexts, the Court has emphasized that restrictions must be "narrowly tailored to achieve the desired objective."[39]

2. Avoid Strained Interpretations

Virtually any communication is subject to misinterpretation. Moreover, the interpretation an individual recipient assigns to the message will depend on his or her background and experience with the product and the issue. When numerous recipients with different backgrounds and educations interpret a single message, it

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[36] 425 U.S. 748 (1976).

[37] *Id.* at 764.

[38] Central Hudson Gas & Elec. Corp. v. Public Serv. Comm'n, 447 U.S. 557, 563-66 (1980).

[39] Board of Trustees of the State Univ. of N.Y. v. Fox, 492 U.S. 469, 480 (1989).

is almost inevitable that some of the interpretations will not accord with the facts about the product.[40]

Marketing communications that mislead ordinary viewers about product attributes impair the efficient operation of competitive markets and should be stopped. When a communication is correctly understood by the vast majority of recipients, however, prohibiting the message because a small fraction may misunderstand the message denies valuable information to the majority.

The regulatory problem is one of striking a balance between the interests of the majority and protection of the minority who may misunderstand. In FTC cases, the issue is whether a challenged interpretation of a seller's message is "reasonable."[41] In Lanham Act cases, the plaintiff must show "that there is actual deception or at least a tendency to deceive a substantial portion of the intended audience."[42] Either approach protects the interest of the majority in the flow of truthful information.

3. Information Is Necessarily Incomplete

No single communication can possibly provide literally complete information about a product. That is particularly true for prescription drugs where a single product may be the subject of hundreds if not thousands of journal articles.[43] Equally obvious, it is not possible to highlight everything in a given communication. Some facts are selected over others, and some of the included facts are more prominent than others.

Of course, selective presentation of truthful information can lead even a careful and skeptical reader to incorrect conclusions. As the Fourth Circuit noted, "[t]o tell less than the whole truth is a well known method of deception."[44] Regulatory requirements to

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40 Richard Craswell, *Interpreting Deceptive Advertising*, 65 B.U. L. REV. 657 (1985). Studies of brief communications in television and in print indicate that miscomprehension of the intended message is relatively common, generally between one-quarter and one-third of the audience. *See* JACOB JACOBY ET AL., MISCOMPREHENSION OF TELEVISED COMMUNICATIONS (1980); Jacob Jacoby & Wayne D. Hoyer, *The Comprehension/Miscomprehension of Print Communication: Selected Findings*, 15 J. CONSUMER RES. 434 (1989).

41 *FTC Policy Statement on Deception, reprinted in* 45 Antitrust & Trade Reg. Rep. (BNA) 689 (Oct. 14, 1983).

42 United States Healthcare, Inc. v. Blue Cross of Greater Philadelphia, 898 F.2d 914, 922-23 (3d Cir.), *cert. denied sub nom.* Independence Blue Cross v. United States Healthcare, Inc., 498 U.S. 816 (1990).

43 Products approved for a new indication for use between 1984 and 1987 appeared in an average of 5641 articles in the MEDLINE database by 1992. In 1992 alone, each drug appeared in an average of 387 articles in MEDLINE.

44 P. Lorillard Co. v. F.T.C., 186 F.2d 52, 58 (4th Cir. 1950).

include the missing data are an appropriate response to such instances.

There is, however, a tension between policies designed to assure that consumers have complete information and the need to facilitate the flow of information through advertising. Requiring additional information to qualify a claim or identify possible drawbacks of a product increases the costs of advertising and other forms of marketing communication. If a significant fraction of each communication must be devoted to required disclosures, sellers may disseminate information about product advantages less widely. Faced with an all or nothing choice between "complete" information and no information at all, sellers may choose silence even when consumers would prefer partial information.[45] Because the FTC required detailed disclosures of all possible limitations in advertising for product warranties, for example, there was very little such advertising.[46] Disclosure requirements were relaxed in 1985, and as a result advertising of warranties and competition over warranty terms has increased.

II. REGULATION OF PHARMACEUTICAL ADVERTISING

A. Jurisdiction and Enforcement

The FTC regulates most advertising pursuant to § 5 of the Federal Trade Commission Act, which prohibits "unfair or deceptive acts or practices."[47] Although trade regulation rules[48] or guides[49] govern certain advertisements, most advertising is regulated through individual cases against advertisements that are allegedly deceptive or unsubstantiated. The result has been the development of a substantial body of law concerning the meaning of deception. The FTC has declared that an ad is deceptive if it is likely to mislead consumers, acting reasonably in the circumstances, about a material issue.[50]

Jurisdiction over prescription drug advertising was transferred

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[45] The impact of disclosure requirements on seller behavior is discussed at length in J. Howard Beales et al., *The Efficient Regulation of Consumer Information*, 24 J.L. & ECON. 491 (1981).

[46] Federal Trade Commission, Guides Against Deceptive Advertising of Guarantees, 16 C.F.R. § 239, 50 Fed. Reg. 18,462, 18,467 (1985).

[47] 15 U.S.C. § 45 (1988).

[48] *E.g.*, Rule Pursuant to the Telephone Disclosure and Dispute Resolution Act of 1992, 16 C.F.R. § 308, 58 Fed. Reg. 42,364 (1993).

[49] *E.g.*, Guides Against Deceptive Pricing, 16 C.F.R. § 233 (1993); Guides Concerning Use of Endorsements and Testimonials in Advertising, 16 C.F.R. § 255 (1993).

[50] *In re* Cliffdale Assocs. Inc., 103 F.T.C. 110 (1984).

to the FDA in 1962.[51] Although a detailed set of regulations is in place, there are no cases interpreting the rules or the statute itself. As one commentator noted, "[n]o federal court has yet been put in a position to issue an opinion construing the meaning or application of the provisions of section 502(n) of the Food, Drug, and Cosmetic Act [which governs prescription drug advertising] in an advertising case."[52] Instead, cases are resolved informally, through telephone calls, meetings, and letters. Between 1971 and 1983, the FDA sent 1069 letters requesting corrective action, resulting in 858 cancelled advertisements, 968 cancelled pieces of promotional labeling, and only seventeen regulatory letters.[53]

The agency's remarkable success in obtaining agreement to its wishes stems in part from the fact that it also exercises jurisdiction over the products themselves.[54] Manufacturers are therefore dependent on the FDA for approval of new products, an interest likely to loom far larger than any individual promotional campaign. As the current FDA Commissioner noted before assuming his position, "[c]ompanies interested in maintaining positive relationships with the FDA usually agree to the FDA's remedy."[55] The sanctions available to the FDA also contribute to its success. A drug advertised in violation of the rules can be considered misbranded, giving the agency the option of criminal prosecution against individual employees.[56] Moreover, the FDA can seize a manufacturer's inventory of the product without prior judicial proceedings[57] and has reportedly threatened to do so to compel agreement to its

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51 W. Benjamin Fisherow, *The Shape of Prescription Drug Advertising: A Survey of Promotional Techniques and Regulatory Trends*, 42 FOOD DRUG COSM. L.J. 213 (1987).

52 *Id.* at 230.

53 *Id.* at 230-31.

54 *See id.* (noting the significance of the FDA's dual role as regulator of the product and its advertising); Richard T. Kaplar, *The FDA and the First Amendment*, *in* BAD PRESCRIPTION FOR THE FIRST AMENDMENT: FDA CENSORSHIP OF DRUG ADVERTISING AND PROMOTION (Richard T. Kaplar ed., 1993) [hereinafter BAD PRESCRIPTION]; John E. Calfee, *The Leverage Principle in FDA Regulation of Information*, presented at American Enterprise Institute Conference on Competitive Strategies in the Pharmaceutical Industry (Oct. 1993).

55 David A. Kessler & Wayne L. Pines, *The Federal Regulation of Prescription Drug Advertising and Promotion*, 264 JAMA 2409 (1990). Good relations are also important for issues that may arise regarding other advertising. One FDA employee who reviews promotional materials has stated that "we may become sensitized to the products of a given pharmaceutical firm," and that "frequent correspondence on any one subject is also likely to draw continued attention after the instant matter is resolved." Arthur K. Yellin, *FDA Prescription Drug Enforcement Policies and Techniques*, 42 FOOD DRUG COSM. L.J. 552, 554 (1987).

56 21 U.S.C. § 333 (1988 & Supp. III 1992).

57 21 U.S.C. § 344 (1988).

terms.[58] Rarely, if ever, would the value of a challenged advertising claim be worth the risk to the manufacturer, however great its value to consumers.

B. The Regulatory Requirements

FDA regulations and the statute itself distinguish between "labeling" and "advertising." The FDA construes both terms quite broadly, and together they cover, at least in the FDA's view, "virtually any material issued by or sponsored by a drug manufacturer as advertising."[59] Labeling includes material that accompanies the drug or that explains its use and has been construed to include books and reprints of journal articles distributed by pharmaceutical firms.[60] Advertising has not been defined, but certainly includes such traditional marketing vehicles as advertisements in medical journals and other media. The FDA generally views as advertising "anything, other than labeling, that promotes a drug product and that is sponsored by a manufacturer."[61]

1. The "Brief Summary"

The package insert, approved as part of the drug approval process, is a central document in the regulation of pharmaceutical marketing. The package insert must accompany all labeling in order to provide adequate directions for use. In most advertising, sellers must include a "brief summary," based on the package insert, identifying side effects, contraindications, warnings, and indications for use.[62] The brief summary typically occupies approximately one-half to three-quarters of a page of fine print in

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58 Malcolm Gladwell, *Firm to Recant Drug Claims; FDA Prevails in Demand for Ads of Retraction*, WASH. POST, Oct. 11, 1991, at 1.

59 Kessler & Pines, *supra* note 55, at 99. There is a persuasive argument, however, that the FDA's interpretation is overly broad. *See* Richard M. Cooper, *The Food and Drug Administration's Authority to Regulate Miscellaneous Statements by Pharmaceutical Manufacturers, in* PROMOTION OF PHARMACEUTICALS: ISSUES, TRENDS, OPTIONS (Dev S. Pathak et al. eds., 1992).

60 Kessler & Pines, *supra* note 55, at 2410.

61 *Id.*

62 21 C.F.R. § 202.1(e)(1) (1991). "Reminder" advertisements are exempt from the brief summary requirement. To qualify for the exemption, an advertisement cannot mention either the appropriate indications or the appropriate dosage for the product. Reminder advertisements must include the brand and generic names of the product and the generic name of each active ingredient. 21 C.F.R. § 202.1(e)(2)(i) (1991). Advertising is also exempt because it is not drug product advertising if it discusses an indication or condition without identifying a particular product. James M. Johnstone, *Special Problems in Direct-to-Consumer Advertising of Prescription Drugs*, 42 FOOD DRUG COSM. L.J. 315 (1987).

medical journal advertising. Because the average advertisement in the *Journal of the American Academy of Dermatology* was 1.4 pages in 1990,[63] the brief summary accounts for a significant portion of the total cost of journal advertising.

Although manufacturers have been willing to pay the added costs to reach physicians, in the higher cost consumer media, the brief summary requirement has severely restrained advertising that discusses specific uses of named products. Nonetheless, direct-to-consumer advertising has grown substantially, reaching an estimated $200 million in 1992.[64] Brand name advertising is largely confined to print, where the cost implications of the brief summary requirement are less dramatic. In broadcast advertising, advertising may discuss the condition without naming the product, or it can name the product without saying what it is for, but it cannot do both. Despite these limitations, direct-to-consumer advertising has had a significant impact. In 1992, seventy-eight percent of physicians said patients discussed symptoms they had seen mentioned in advertising and eighty-eight percent of physicians had patients request a drug by its brand name.[65]

In theory at least, the brief summary assures that physicians have a full picture of the benefits and risks of the advertised product. It has been described, however, as "an example of 'a yawnful concentration of legal jargon.'"[66] How often and how extensively physicians actually read the brief summary is open to question.[67] Surely, however, it is less well-read, and probably significantly so, than the remainder of the advertisement. In broadcast advertising on now-defunct Lifetime Medical Television, where the brief summary scrolled rapidly across the screen at the end of the program, it is unlikely that any physicians stayed tuned for the exciting conclusion.

In the context of consumer advertising, it is hard to imagine any benefits from the brief summary requirement. Instead, the requirement simply serves as a means to discourage, if not entirely

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63 Daniel J. Hogan et al., *An Analysis of Advertisements in the Journal of the American Academy of Dermatology, 1980 and 1990*, 28 J. AM. ACAD. DERMATOLOGY 993, 994 (1993). Although the studied journal may not be representative, there is no apparent reason to suspect systematic differences.

64 Winters, *supra* note 3, at 10.

65 *Trends and Forecasts*, MED. MARKETING & MEDIA, Mar. 1993, at 26. In 1989, 30% of physicians said patients discussed symptoms they had seen mentioned in ads and 45% had patients request a drug by brand name.

66 Hogan et al., *supra* note 63, at 996.

67 Fisherow, *supra* note 51, at 215. There do not appear to be published studies that address the extent of readership of the brief summary.

prevent, such advertising.[68] Rather than serving the theoretical purpose of providing more information, the result is that consumers have less information about both risks and benefits of various prescription drug products than would otherwise be available.[69]

Excessive information requirements can discourage the flow of truthful information even apart from the brief summary requirement. In a series of enforcement letters, the FDA challenged a number of broadcast advertisements directed to physicians, apparently asking that additional information be incorporated into the body of the commercials themselves. As with consumer advertising, requiring too much information may effectively prevent any communication at all.[70]

2. Unapproved Uses

Under current rules, advertising can only discuss product uses that have previously been approved for labeling. The significance of unapproved or off-label uses of drugs and the applicable regulatory standards are considered below in subsection a. Subsections b and c consider the benefits and costs of the current regulatory policy, respectively. Subsection d considers the additional costs and benefits applicable to discussions of off-label uses in the context of nontraditional promotional vehicles such as symposia and continuing medical education programs. Finally, subsection e offers a brief conclusion.

a. *The Significance and Regulation of Claims Regarding Unapproved Uses*

Unapproved or off-label uses of drugs are often an important part of medical therapy, particularly in rapidly changing fields such as oncology. A study by the General Accounting Office found that one-third of drug administrations in cancer patients were for off-label uses, and that fifty-six percent of all patients received as least one drug for an off-label use. All lung cancer patients in the sam-

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68 Johnstone, *supra* note 62.

69 For a discussion of the benefits of direct-to-consumer advertising, see Paul H. Rubin, *The FDA's Prescription for Consumer Ignorance*, J. REG. & SOC. COSTS 5 (1991); Alison Masson & Paul H. Rubin, *Matching Prescription Drugs and Consumers*, 313 NEW ENG. J. MED. 513 (1985).

70 Indeed, in the view of some observers, the result was the demise of Lifetime Medical TV as advertisers withdrew their commercials. Steven W. Colford, *FDA Blamed for Death of Lifetime Medical TV*, ADVERTISING AGE, July 19, 1993, at 3.

ple received at least one drug for an off-label use.[71] Most off-label product use was for indications that were identified in authoritative compendia of drug usage such as The American Hospital Formulary Service, the American Medical Association, and the United States Pharmacopeia.[72] Overall, an estimated one-fourth of all United States drug prescriptions are for unapproved uses.[73]

Despite their importance in medical practice, however, physicians cannot learn about off-label uses of products from advertising. FDA regulations specifically provide that an advertisement "shall not recommend or suggest any use that is not in the labeling accepted in such approved new-drug application or supplement."[74] To underline the point, an advertisement is "false, lacking in fair balance, or otherwise misleading" if it "[u]ses literature, quotations, or references for the purpose of recommending or suggesting conditions of drug use that are not approved or permitted in the drug package labeling."[75] Truth of the claim is not a defense; if the claimed use has not been previously approved for labeling, that use is prohibited in advertising.

Reliance on approved labeling to define permissible advertising claims cannot be defended on the grounds that the label gives a complete and accurate description of the state of knowledge about the drug. Particularly in areas where scientific knowledge is changing rapidly, the approved labeling necessarily lags behind the facts as reflected in the scientific literature. The problem of label lag is not confined to appropriate uses of the product. Knowledge of side effects and contraindications may also lag behind the approved labeling.[76]

Of course, manufacturers can, and sometimes do, seek approval to add claims for additional product uses to their labeling.

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71 Thomas Laetz & George Silberman, *Reimbursement Policies Constrain the Practice of Oncology*, 266 JAMA 2996 (1991).

72 Approximately three-fourths of off-label uses of drugs for cancer patients were recognized in the drug compendia. *Id.* at 2997.

73 *The FDA's Next Target: Drugs*, TIME, July 15, 1991, at 56.

74 21 C.F.R. § 202.1(e)(4)(i)(a) (1991).

75 21 C.F.R. § 202.1(e)(6)(xi) (1991).

76 In one Lanham Act case, for example, a comparative claim of fewer side effects was based on the approved labeling for both products. The judge found the claim deceptive and ordered corrective advertising because the approved labeling for the product claimed to have more side effects was not consistent with the current state of scientific knowledge. E.R. Squibb & Sons, Inc. v. Stuart Pharmaceuticals, Civ. No. 90-1178, 1990 WL 159909 (D.N.J. Oct 16, 1990). Thus, the court-ordered corrective message contradicted the labeling of the compared product and would have violated FDA regulations had it been disseminated by the manufacturer itself. It is hard to imagine a clearer case of regulatory failure.

Inevitably, however, not all will do so. The costs of the approval process itself are substantial, and, as discussed in more detail below, approval involves substantial delays. Moreover, the benefits of seeking approval for second indications are generally lower than the benefits of initial approval because the remaining patent life of the product is shorter.[77] Steps to reduce the cost and delays in obtaining approval for subsequent uses would increase the correspondence between approved labeling and the current state of scientific knowledge, but unapproved uses are likely to remain.

Nor is reliance on prior FDA approval of labeling essential to the regulation of advertising claims. In other areas product manufacturers are required to develop and maintain information and are responsible for its accuracy without prior approval. The Occupational Safety and Health Administration, for example, requires chemical manufacturers to prepare material safety data sheets summarizing information about chemical hazards and toxicity. The document must be reviewed periodically and updated whenever the manufacturer is aware of new information that makes the existing summary inaccurate. The material safety data sheets, in turn, provide the information that forms the basis for employer's programs for worker training in safe use of the chemicals and the development of emergency plans.[78] Thus, even vital health and safety information can be, and is, provided without prior regulatory approval of the information itself.

As with any other policy of requiring prior approval of the content of a communication, prohibiting claims about unapproved uses creates both benefits and costs. Without prior approval, in at least some instances, manufacturers, acting in the best of faith,[79] would make claims that the FDA would eventually conclude are not sufficiently supported by the evidence.[80] Prior approval prevents

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77 Paul H. Rubin, *From Bad to Worse: Recent FDA Initiatives and Consumer Health, in* BAD PRESCRIPTION, *supra* note 54.

78 Hazard Communication, 29 C.F.R. § 1910 (1993).

79 Reasonable scientists can and do differ over whether the evidence supports particular uses. Prior approval resolves all such disagreements in favor of the FDA.

80 The discussion that follows implicitly assumes that the FDA employs the ideal standard of approval. In fact, a substantial body of literature makes clear that the current approval standard for new drugs is itself too restrictive. *See, e.g.*, HENRY GRABOWSKI & JOHN VERNON, THE REGULATION OF PHARMACEUTICALS: BALANCING THE BENEFITS AND RISKS (1983); WILLIAM M. WARDELL & LOUIS LASAGNA, REGULATION AND DRUG DEVELOPMENT (1975); Sam Kazman, *Deadly Overcaution: FDA's Drug Approval Process*, 1 J. REG. & SOC. COSTS 35 (1990); Sam Peltzman, *An Evaluation of Consumer Protection Legislation: The 1962 Drug Amendments*, 81 J. POL. ECON. 1049 (1973). If the standard of approval is itself too cautious, the benefits of prior approval are reduced and its costs increased.

such claims and therefore offers benefits. The magnitude of these benefits depends on three factors: the likelihood that erroneous claims occur, the consequences to consumers when they do, and how effectively an ex post standard focusing on the accuracy of the claim could be policed. These factors are analyzed in the following subsection. Requiring prior approval also imposes costs, however, because claims that the FDA eventually determines are adequately supported are delayed pending review. The magnitude of those costs depends on the importance of the new use to patients and the length of time required for review. The costs of prior approval are considered in subsection c.

b. *Benefits of Prior Approval*

The first factor determining the benefits of the prior approval requirement is the likely incidence of claims for additional uses that the FDA would eventually reject. Assessing the likelihood of such claims is difficult. Few data are available that would provide objective evidence.[81] Instead, it is necessary to consider the factors likely to influence such claims.

There are strong incentives for advertisers in general, and pharmaceutical advertisers in particular, to assure that claims are truthful. In addition to the general market incentives for accuracy discussed in Section I, inaccurate claims about new uses for pharmaceutical products are likely to raise serious product liability risks. Moreover, manufacturers of competing products would surely bring inaccurate claims to the attention of the FDA, and the severity of the FDA's potential sanctions would serve as a deterrent.[82] Although the incentives for accuracy support the conclusion that there would not be a flood of false claims for off-label uses, they do not rule out the possibility that such claims could occur. Nevertheless, in cases where the FDA has challenged "pro-

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81 *See* Michael S. Wilkes et al., *Pharmaceutical Advertisements in Leading Medical Journals: Experts' Assessments*, 116 ANNALS INTERNAL MED. 912 (1992) (claiming to find evidence of widespread violations of FDA regulations in prescription drug advertising). A re-analysis of their data, however, finds that the pattern of results is not consistent with the assumption that there are widespread problems with the advertising. Instead, the results are more consistent with chance disagreements among individual expert reviewers. *See* J. Howard Beales & William MacLeod, *Experts Assessments of Pharmaceutical Advertisements: A Critical Analysis* (under review). For other criticisms of the study, see Rubin, *supra* note 77.

82 Indeed, the substantial risk that the FDA will disagree with a claim of effectiveness may well deter even accurate claims. If so, there would be little difference between the present requirement of prior approval and a policy based solely on the accuracy of the claims.

motional" activities such as sponsorship of symposia and continuing medical education, there have not been allegations that the off-label uses were inappropriate.[83]

The second factor influencing the benefits of the prior review requirement is the consequences to patients when deceptive claims for new uses occur. These consequences depend on the alternative treatments available. When there are effective alternative treatments, false claims that a product is effective will divert patients from a therapy that works.[84] Preventing such claims is the primary benefit of the prior approval requirement.

In other circumstances, however, there are no known effective therapies. Indeed, it is in precisely such cases that off-label uses are most common.[85] Presumably, claims that a product is effective for off-label uses would be most common in such instances as well.

If no drugs are approved for a particular condition,[86] physicians are choosing among alternatives that have not yet demonstrated effectiveness to the FDA. In such cases, physicians may treat patients with the best drug they know about rather than forgoing drug therapy. If so, there are no benefits from the prior approval requirement. Even if false claims occur, patients would have been treated with an unproven drug in any event. There is no gain from forcing physicians to choose the most effective drug in relative ignorance. Choices made with knowledge of the best case that competing manufacturers can make for their products, including the fact of the lack of FDA verification, are far more likely to advance patient welfare.

Third, the benefits of a prior approval requirement depend on the effectiveness of an ex post regulatory standard focused on

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[83] Of course, the FDA may simply not have addressed the question, because it does not need to do so under its view of the legal requirements.

[84] There may also be differences in the side effects profiles of the drugs. There is no reason to suspect, however, that side effects from an existing product in a new use would be systematically greater than the side effects of products already approved for that indication. Indeed, manufacturers would be more likely to make claims for off-label uses in situations where the side effects profile was either better or comparable to competing products because they would have a greater competitive advantage in such cases.

[85] Laetz and Silberman found that off-label uses for cancer patients were higher when there was no agreement on the best therapy and for specific cancers with no standardized chemotherapies. Laetz & Silberman, *supra* note 71, at 2997.

[86] Of the 17 new indications approved between 1984 and 1987, I have found that at the time of approval, there was no other drug approved for the same indication in seven instances. *See* Beales, *supra* note 18. If manufacturers are more likely to seek approval for conditions for which there are no direct competitors, lack of effective alternatives may be less common than these results suggest.

the accuracy of claims. That such a standard is workable and effective seems clear. For claims other than appropriate uses, ex post enforcement is the approach that the FDA currently employs. Claims about effectiveness, usefulness in a broad range of patients or conditions, safety, and claims about the incidence or severity of side effects and contraindications are acceptable if they are supported by substantial evidence or substantial clinical experience.[87] Similarly, comparative claims are permitted if supported by substantial evidence.[88] The FDA's success in achieving changes when it raises questions about advertising claims suggests that enforcing these requirements is not difficult.[89]

Accuracy has also proven to be a workable standard in Lanham Act cases involving comparative claims, even when complex scientific issues are involved. Most litigated cases have focused on whether the claim is "false on its face."[90] Courts have analyzed the scientific evidence presented by the parties to determine whether tests were "sufficiently reliable to permit one to conclude with reasonable certainty that they established the proposition for which they were cited."[91] Advertising has been enjoined because companies had no credible scientific evidence[92] or because the evidence that existed was not sufficiently reliable to support the claims.[93] In evaluating the evidence, courts have employed criteria very similar to those employed by the FDA to evaluate clinical studies, requiring, for example, qualified investigators, a protocol developed in advance and followed throughout, an objective methodology, placebo controls, blinding, and randomization.[94] Courts have also found claims false because they relied on obsolete scientific evidence, inconsistent with current knowledge and the state of scien-

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87 21 C.F.R. § 202.1(e)(6)(i) (1991).

88 21 C.F.R. § 202.1(e)(6)(ii) (1991).

89 If claims governed by the substantial evidence rules are inaccurate, the risks to patients from selection of an inappropriate therapy are very similar to those that would result from claims that an approved product is effective for another use for which there are approved competitors. Patients are diverted from the most appropriate therapy (which is presumably approved for the use) based on a deceptive claim.

90 *See* Charles J. Walsh & Marc S. Klein, *From Dog Food to Prescription Drug Advertising: Litigating False Scientific Establishment Claims Under the Lanham Act*, 22 SETON HALL L. REV. 389, 415 (1992).

91 Proctor & Gamble Co. v. Chesebrough-Pond's Inc., 747 F.2d 114, 120 (2d Cir. 1984) (comparative claims regarding hand and body lotions).

92 Thompson Medical Co., Inc. v. Ciba-Geigy Corp., 643 F. Supp. 1190 (S.D.N.Y. 1986) (claimed superiority of a weight loss medication).

93 Alpo Petfoods, Inc. v. Ralston Purina Co., 720 F. Supp. 194 (D.D.C. 1989), *aff'd in part, rev'd in part on other grounds*, 913 F.2d 958 (D.C. Cir. 1990) (claims that dog food reduced or eliminated canine hip dysplasia).

94 Walsh & Klein, *supra* note 90, at 430-34.

tific literature.[95] Although many cases have involved products that may be less sensitive than prescription drugs, courts have addressed the accuracy of claims about side effects of prescription drugs,[96] over-the-counter drugs,[97] and medical devices.[98]

The FTC has also demonstrated the workability of a standard that turns on the accuracy of advertising claims and whether the evidence is adequate to support a particular claim. Indeed, the Commission has successfully challenged claims for over-the-counter drugs that were, under FDA regulations, permitted on product labels.[99] It successfully challenged conflicting superiority claims for internal analgesics.[100] Similarly, it has successfully challenged unsubstantiated claims for medical devices.[101]

In short, although there are some benefits of a prior approval requirement, they appear quite limited. Benefits occur only if manufacturers make false claims that a product is effective for an off-label use when other effective (and approved) products are available. Even in such cases, the likely effectiveness of ex post enforcement against deceptive claims limits the benefits of prior approval.

c. *Costs of Prior Approval*

As with the benefits of a prior approval policy, the costs depend on the alternatives available to patients. When other drugs are approved for the same indication, physicians are likely to be aware of and use an effective treatment. Increased use of products that are eventually approved,[102] however, reflects physician determinations that the product is the most appropriate for those patients for whom it is prescribed.[103] Requiring prior approval means

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95 E.R. Squibb & Sons, Inc. v. Stuart Pharmaceuticals, Civ. No. 90-1178, 1990 WL 159909 (D.N.J. Oct. 16, 1990) (comparative side effects of hypertension drugs).

96 *Id.*

97 Thompson Medical Co. v. Ciba-Geigy Corp., 643 F. Supp. 1190 (S.D.N.Y. 1986).

98 Energy Four, Inc. v. Dornier Medical Sys., Inc., 765 F. Supp. 724 (N.D. Ga. 1991).

99 *Thompson Medical*, 104 F.T.C. 648 (1984), *aff'd sub nom.* Thompson Medical Co. v. F.T.C., 791 F.2d 189 (D.C. Cir. 1986), *cert. denied*, 479 U.S. 1086 (1987).

100 *In re* American Home Prods. Corp., 98 F.T.C. 136 (1981); *In re* Sterling Drugs, Inc., 102 F.T.C. 395 (1983); *In re* Bristol-Myers Co., 102 F.T.C. 21 (1983).

101 *In re* Removatron Int'l Corp., 111 F.T.C. 206 (1988).

102 The growth in share following approval is substantial. For the average drug approved for a new indication in 1984-1987, its share of patients increased 2.8 times by the fourth year after approval. *See* Beales, *supra* note 18.

103 The differences in effectiveness of competing drugs are often small compared to the differences in patient response to a particular drug. Thus, even if there is little difference in the average effectiveness of the newly approved product and existing

that in the interval between the development of substantial scientific support for the claim and its eventual approval by the FDA, a significant fraction of patients do not receive the therapy their physician believes is most appropriate.

The costs of prohibiting claims about unapproved uses are greater where there are no approved alternatives. In such instances, patients may not be treated with an effective therapy at all. Unable to learn about new developments from the source most likely to know, the product manufacturer, physicians must rely on other information sources such as reports from colleagues or their own reading of the medical literature. Individual articles, however, such as those reporting the results of controlled clinical trials, will inevitably give an incomplete picture of the use of the product. Studies may have employed samples too small to detect significant and therapeutically important advantages, and other studies may have yielded conflicting results. Reliance on the literature requires an assessment of the entire literature; a task requiring considerable investment of time and effort. Physicians in leading medical centers and research oriented institutions are likely to be well aware of the new use. Physicians in ordinary practice and their patients, however, are likely to suffer a significant information lag.

The costs of the prior approval policy also depend on the length of time between the development of substantial scientific support for a new use and FDA approval. In fact, the lag before a new use appears on a product label is substantial. On average, FDA review of a new drug application (NDA) takes two years after submission.[104] Although review of supplemental NDAs presumably involves less concern about side effects, because the product is already on the market, they receive lower priority than original NDAs.[105] As a result, review times for supplemental NDAs are essentially the same as for the original application for the drug.[106] For uses that have been approved for labeling, compendium recognition occurred on average at least 2.5 years prior to approval.[107]

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alternatives, the gain may be significant for the patients who receive it. *See* WARDELL & LASAGNA, *supra* note 80, at 104.

104 Frank E. Young, *From Test Tube to Patient: New Drug Development in the United States* (An FDA Consumer Special Report), Jan. 1988, at 5.

105 Rubin, *supra* note 77, at n.12.

106 Joseph A. DiMasi et al., *New Indications for Already-Approved Drugs: An Analysis of Regulatory Review Times*, 31 J. CLINICAL PHARMACOLOGY 205 (1991).

107 This result is based on a sample of 17 drugs approved for a new or expanded use during 1984-87. Past editions of US PHARMACOPEIA DRUG INFORMATION were examined to determine when the drug was first identified for the new use. No adjustment was made for the publication lag resulting from the fact that updates are only

Sufficient scientific evidence to make a sound case for the new use presumably appears even earlier.

Thus, prohibiting claims about off-label uses of approved drug products imposes significant costs. Costs are greatest when the off-label use involves conditions for which there are no effective alternative therapies because physicians and their patients are denied information about an effective treatment. Benefits are smallest under these same conditions because even erroneous claims do not divert patients from an approved therapy. In these instances at least, it seems clear that the costs of prohibiting claims about off-label uses outweigh the benefits.

Even when effective alternatives are available, the costs of prior approval appear to exceed the benefits. In effect, the policy requires physicians to make prescribing decisions based on something less than the best information available. Unless the incidence of false claims would be quite high and ex post enforcement against violations remarkably ineffective, the costs to patients denied the treatment their physician believes is most appropriate seem more substantial. Thus, the FDA should permit claims that a product is effective for off-label uses, provided the claims are supported by reliable evidence and disclose that the FDA has not approved the use.

A variety of policy changes could reduce the costs of the present prohibition on advertising claims about off-label uses. For example, claims could be allowed only if there are no approved alternative therapies for the new indication. This approach would narrow the current policy to the area where its benefits are greatest and its costs are lowest. Another approach would be to allow claims only if the use has been recognized in authoritative compendia of drug therapies.[108] Such a policy would reduce the likelihood of claims that the FDA would eventually determine were not adequately supported.

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published every other year. Excluding four products that were not listed in the compendium until after FDA approval, the average lag from listing to approval was 3.75 years, with a minimum lag of two years and a maximum lag of six years. *See* Beales, *supra* note 18.

[108] These approaches are not mutually exclusive. Allowing claims when there are no approved alternatives but only if the use is recognized in compendia is possible, but the latter restriction may have little influence on the types of claims manufacturers would be willing to make. Because the risk that a claim will be found inaccurate is lower, sellers are more likely to make claims that have already received third party recognition even without a requirement.

d. *Off-Label Uses, Symposia, and Other Promotional Activities*

Drug manufacturers have an obvious economic interest in assuring the rapid dissemination of information about effective uses of their products. That interest, which patients share, provides the motivation for advertising, detailing, and other promotional activities. Unable to inform physicians directly about the latest scientific information on uses that the FDA has not approved, it is perhaps not surprising that pharmaceutical companies have turned to other mechanisms to speed the diffusion of knowledge. Among those mechanisms has been sponsorship of symposia and other continuing education programs.

Unlike advertising and detailing, which involve purely the dissemination of information, symposia and other forms of scientific interchange also play a significant role in the production of knowledge. Interested researchers in any academic discipline gather regularly to hear one another's results and to debate, dissect, and discuss their accuracy and implications.[109] Such dialogues are an integral part of the scientific process and critical in the production of knowledge.

Symposium participants and attendees are likely to arrive in a skeptical frame of mind. The whole point of the meeting is often to debate and discuss ideas that are *not* established scientific facts. Participants come hoping to explore, and learn more about, the implications of results that are inherently uncertain. Areas of medicine or any other discipline where all results are well confirmed and agreed to by everyone are not the subject of conferences and symposia. Of course, participants expect that reported results are "true" in the sense that the experiments were not fudged. But they also understand that the replicability of the results and their practical implications are not yet established.

Although fair balance surely has a place in scientific presentations, it is quite a different fair balance than FDA regulations contemplate for prescription drug advertising.[110] Fair balance at a conference involves representing the range and divergence of sci-

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109 The phenomenon is hardly confined to the academic community. Trade associations of every stripe have regular meetings of interested members of the industry. Such events are generally profitable for the sponsoring organizations. And, not surprisingly, the participants in the programs have an economic interest in the topics they are discussing.

110 The regulations require a "fair balance" between presentation of a drug's effectiveness and its side effects or contraindications. 21 C.F.R. § 202.1(e)(5)(ii) (1991). Regulating conferences as a form of advertising would also require that they include the brief summary of prescribing information. The "brief summaries" that would be

entific opinion on the issue. For outsiders, however, evaluating "fair balance" is extremely difficult. For example, a conference may include only those pursuing one approach to an issue, excluding adherents of a different methodological or theoretical approach. Similarly, conferences are frequently dominated by a particular academic discipline, even if other academic disciplines are also interested in the issue and address it from different perspectives. Nonetheless, such conferences may be quite useful to participants pursuing the same set of issues, precisely because they focus on the issues that matter to the participants.

"Fair balance" in conferences, as in books, papers, and other forms of communication, is best judged by the recipients of the information. Conferences that do not present sufficient balance to be useful to those who attend will not be attended in the future. Organizers who present such conferences will find them increasingly difficult to assemble.

Considering purely the dissemination of information aspects of scientific conferences, continuing education programs, and the like, extending the prohibition of claims regarding off-label uses raises essentially the same set of costs and benefits discussed in the previous subsections. The magnitude of both costs and benefits is reduced, compared to off-label uses in advertising, simply because the number of participants who receive the information is generally much smaller. As argued above, however, the net effect of restricting the dissemination of information about off-label uses is harmful to patients. That conclusion applies as well to the regulation of nontraditional means of promotion.

Because of the information production aspects of scientific conferences, regulatory intervention poses substantial additional costs. The essence of the scientific method is to evaluate ideas based on their merits and the data supporting them, rather than on the basis of their source or their financing. A regulatory presence based on concepts of "independence" can hardly advance that objective and is far more likely to interfere significantly.[111]

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useful at conferences, however, are more likely to pertain to the presentations, not prescribing information.

[111] Moreover, there is no apparent reason why a concern about "independence," if valid in the context of conferences, should end there. If the "independence" of conference participants is important enough to restrict or regulate their participation, is their independence any less critical in their individual journal articles? Alternatively, if financial support from a pharmaceutical manufacturer converts speeches at scientific meetings into promotional pieces, it would appear to suffice to make journal articles by those same people promotional pieces as well.

Regulatory oversight of conferences based on who participates may lead to the absence of legitimate experts who are, in the FDA's view, "too closely" associated with a particular drug's manufacturer. Many skilled scientists are actually employed by pharmaceutical companies; it is hard to see how their employer reduces the value of their contribution to scientific exchange. Moreover, dedicated professionals who would prefer not to be subject to such scrutiny may simply choose not to participate. In either case, the result would be a loss of expertise to conference participants, potentially less effective presentation of a point of view that may be vital, and a less effective process for creating scientific and medical knowledge. It would require only limited interference in the production of scientific knowledge to far outweigh any plausible benefit of further constraining the dissemination of the latest knowledge about unapproved uses of prescription drugs.

Regulatory oversight of conferences and education may also result in less financial support from pharmaceutical manufacturers for such activities. The result would be less dissemination of other information now provided in such programs. Fewer symposia and conferences would also mean reduced opportunities for face to face scientific interchange and further reductions in the efficiency of producing scientific knowledge.

e. *Conclusion Regarding Claims for Unapproved Uses*

The real issue in evaluating advertising claims for unapproved uses is whether the claim is accurate. Whether approved by the FDA or not, truthful claims that a product is effective against a particular condition advance patient welfare, by assuring that physicians make their choice with the best information available. Inaccurate claims reduce patient welfare, because misinformed physicians will make inappropriate choices. Uninformed physicians, however, will also make inappropriate choices. Focusing on accuracy, rather than prior approval, would reduce these costs.

Similarly, the issue in evaluating claims for off-label uses in scientific meetings and symposia is the accuracy of the information provided. The scientific method itself, however, with its insistence on reproducible results, is a far better mechanism to assure accuracy than oversight by any government agency, with far less risk of suppressing important facts.

III. CONCLUSION

Regulatory intervention in markets is often justified because information is imperfect. When facts are misrepresented, or significant drawbacks of a particular product are not revealed, consumers are likely to make inferior choices. Moreover, with products such as prescription drugs, inaccurate or incomplete information about product limitations can result in serious health and safety risks to consumers. Sound regulatory policies can prevent these problems and enhance consumer welfare.

Consumers also make inferior choices, however, if they choose without adequate knowledge of the benefits of particular products. Moreover, ignorance of the benefits of products, such as prescription drugs, can also create serious health and safety risks, because inappropriate treatment decisions are the likely result. Regulatory policies that deny consumers important information about product benefits can therefore create the very problems they are presumably intended to solve.

An important mechanism for disseminating information about product benefits in a market economy is advertising. The ability of sellers to advertise spurs competition among alternative products and alternative providers. The ability to advertise tends to reduce prices in markets for consumer goods and services as well as in markets for prescription drugs. Moreover, advertising tends to improve the product alternatives available to consumers and to produce better matching between individual consumers and the best product to serve their needs.

Regulatory restrictions on advertising can sacrifice these important benefits. Requirements for too much information can effectively prohibit advertising in certain media, with adverse effects on the consumers they are intended to protect. Prohibitions on truthful claims mean that consumers must make choices in relative ignorance.

Prescription drug advertising regulations suffer from both problems. The brief summary requirement, particularly in the context of direct-to-consumer advertising, offers no plausible benefits. It is not brief, not a summary, and for many consumers not intelligible. It severely limits the ability of pharmaceutical advertisers to use broadcast media, still the best way to reach large numbers of consumers.

The rules limiting advertising claims about product uses to those that the FDA has already approved effectively prohibit truthful claims. Particularly when no alternative therapies have been

approved, the requirement does not even serve to reduce the use of ineffective medicines. Instead, physicians who are not completely current with the relevant literature are forced to choose therapies without the benefit of the best available information. The requirement itself should be eliminated or substantially narrowed. Extending the current policy to nontraditional forms of promotion such as scientific meetings and symposia offers very limited additional benefits. It does so, however, at the considerable risk of damaging the process of developing and disseminating scientific knowledge.