

Consumer-Directed Advertising of Contraceptive Drugs: The FDA, Depo-Provera, and Product Liability

WILLIAM GREEN, J.D., PH.D.*

I. INTRODUCTION

Pharmaceutical manufacturers have advertised prescription drug products to the public for over a decade. These consumer-directed advertisements often are promoted, like those for other consumer products, with appeals to vanity, insecurity, and pain. Prescription drug advertisements possess certain unique features, most notably a statement that consumers must visit their doctor before purchasing the product. These advertisements also encourage consumers to obtain more detailed information from the manufacturer, often by using 800 numbers to phone in requests for free video tapes, brochures, and information packets.

Depo-Provera is one of these prescription drugs. Since the Food and Drug Administration (FDA) approved the three-month injectable contraceptive in October 1992, Upjohn, the drug's manufacturer, has marketed the drug widely.¹ The Depo-Provera advertisement provides the opportunity to explore several questions about prescription drug advertising. Does the FDA have the authority to regulate consumer-oriented prescription drug advertising? If the agency has the authority to protect consumers against deceptive advertisements, do the Depo-Provera advertisements fairly represent the contraceptive's risks and benefits? If the advertisements produce a more informed consumer, do they expose Upjohn to product liability? If they do, will the company be able to successfully defend itself by employing the learned intermediary rule and the federal doctrine of preemption? If Upjohn is unable to rely upon these defenses, what are the product liability consequences of its Depo-Provera advertisement? These questions generally address the FDA's authority, Upjohn's liability, and the consequences for women who choose an elective drug. Initially, the answers are defined by the parameters of, and controversy over, a pharmaceutical risk regulation system in which federal and state laws govern public availability and individual use of prescription drugs.

The FDA, drug companies, physicians, and patients are responsible for regulating pharmaceutical risk. But patients find it difficult to make an informed decision about using a prescription drug because the FDA, drug companies, and physicians are not members of an integrated system of risk regulation, but are participants whose involvement in defining risk is structured by the Federal Food, Drug, and Cosmetic Act (FDCA),² by state tort law, and ultimately by the federal Constitution. These laws create the frame-

* Dr. Green is Professor of Government, Morehead State University, Morehead, Kentucky.

This article is a revised, abbreviated, and updated version of a paper presented at the 1994 Annual Meeting of the American Political Science Association. The author wishes to thank Ernest J. Yanarella, Professor of Political Science, and Richard C. Ausness, Professor of Law, University of Kentucky, for their helpful suggestions, and Rowena Green, M.A., for her insights in the analysis of the Depo-Provera consumer-oriented advertising materials.

¹ See, e.g., Michael Klitsch, *Injectable Hormones and Regulatory Controversy: An End to the Long-Running Story?*, 25 FAMILY PLANNING PERSPECTIVES 37 (1993); and William Green, *The Odyssey of Depo-Provera*, 42 FOOD DRUG COSM. L.J. 567 (1987).

² Pub. L. No. 75-717, 52 Stat. 1040 (1938), as amended 21 U.S.C. §§ 301 et seq. (1988).

work for a dual system of regulation and two levels of risk management.³

Whether drugs should be made publicly available, the first level of risk regulation, is the legal responsibility of the FDA. The agency manages this risk through its control over experimental drug research and drug marketing. This control includes its authority to approve a drug's package insert, which is the official labeling that describes the drug's approved uses, warnings, precautions, side effects, and contraindications.

The second level of risk regulation, which asks whether the drug should be used by an individual, is the responsibility of physicians who decide to prescribe a drug for patient use based on medical knowledge of the patient and the drug. A physician's knowledge of a drug may be based on the drug's FDA-approved labeling, but FDA authority does not extend to physician prescription practices.⁴ If a physician fails to regulate prescription drug risk, the patient's recourse is governed by state medical malpractice law.

Unlike those of physicians, pharmaceutical company risk regulation practices are governed by both federal and state law. Drug companies are required to comply with the FDA's labeling regulations, changes in the labeling of previously approved drugs, and orders to remove drugs from the market. Drug companies are also required to comply with FDA regulation of their marketing practices, including advertising, and to notify the agency about adverse reactions to their drugs. At the same time, pharmaceutical companies are bound by state product liability law, which entitles patients to claim that a drug's manufacturer failed to warn a physician about the drug's risks and that this failure to warn caused them injury.

This article will explore the personal consequences of this dual system of risk regulation for a woman who reads the Depo-Provera advertisement, consults with her physician and receives an injection. Part II will analyze the advertisement and its compliance with FDA regulations. Part III will explore the product liability consequences of the Depo-Provera advertisement. Here attention will focus on a hypothetical case based on *Upjohn v. MacMurdo*,⁵ and the ability of Upjohn to avoid liability by relying on the learned intermediary rule and the federal constitutional doctrine of preemption.

II. THE DEPO-PROVERA ADVERTISEMENT

The FDA relies on the 1962 amendments to the FDCA⁶ to regulate prescription drug advertising. Section 502(n) of the Amendments contains the "brief summary" requirement, which provides that a prescription drug is misbranded unless its advertisements contain "information in a brief summary relating to side effects, contraindications, and effectiveness as shall be required in [FDA] regulations."⁷ Section 502(n)'s requirement was enacted to better inform physicians about prescription drugs, not to protect consumers against deceptive advertising.⁸ In the early 1980s, pharmaceutical companies began to advertise their prescription drug products directly to the general public. The FDA responded in 1985 by extending its section 502(n) authority "to regulate

³ See Henry Grabowski, *Product Liability in Pharmaceuticals*, in *THE LIABILITY MAZE* 360-66 (Peter W. Huber & Robert E. Litan, eds. 1991).

⁴ See 37 Fed. Reg. 16,503 (1972).

⁵ 562 So. 680, 681-82 (Fla. 1990).

⁶ Pub. L. No. 87-781, 76 Stat. 780 (1962).

⁷ 21 U.S.C. §§ 352(n).

⁸ See *infra* note 56.

prescription drug advertising, regardless of its intended audience.”⁹

Pharmaceutical advertisements for prescription drugs aimed at the general public have raised questions about the new duties manufacturers may assume under state product liability law.¹⁰ Do the advertisements resemble those for other products? Do they fairly represent the drug’s risks and benefits? Do they comply with section 502(n)’s brief summary requirement? Are the company’s promotional claims limited to those approved in the labeling? Are the virtues of the product stated in bold print? Are the warnings contained in the advertisement, and, if so, are they prominent and easy to understand or are they in technical language and small print? If the warnings appear on subsequent pages, are there references in the advertisement to these pages? Do the warnings comply with section 502(n)’s brief summary requirement? Do the advertisements encourage women to seek additional product information from the manufacturer? Do the advertisements tell consumers to visit their doctor in order to purchase the product? These questions frame the following analysis of the Depo-Provera advertisement, its accompanying patient information, and its 800 number information.

A. *The Advertisement*

Upjohn’s multi-page advertisement for Depo-Provera has appeared in major national news, health, and women’s magazines.¹¹ Overall, the advertisement employs the distinctive features of prescription drug advertisements. The first page introduces the product’s basic appeal to convenience. In deep pink and mauve tones is a wristwatch with months characteristic of the four seasons printed on the face: March at 3:00, June at 6:00, September at 9:00, and December at 12:00. On the second page, this soothing image is transformed into a clear statement of the drug’s basic appeal. In large print at the top of the page, the advertisement announces, “Introducing Birth Control You Think About Just 4 Times a Year.” The corollary appeal appears in smaller print immediately below, saying “Many women wish they didn’t have to remember their birth control every day.” After this generic comparison with the contraceptive pill, the advertisement directly addresses the potential consumers, saying “If you’re one of them, you might want to know about Depo-Provera.” Thereafter, the advertisement has three major themes that roughly mirror the drug’s FDA labeling: its benefits, side effects, and contraindications.

The description of Depo-Provera’s benefits begins by repeating the advertisement’s

⁹ 50 Fed. Reg. 36,667 (1985).

¹⁰ See, e.g., Nancy L. Buc, *Current Regulatory Issues in Marketing Prescription Drugs: Comparative Claims and Advertising to Consumers*, 37 FOOD DRUG COSM. L.J. 402 (1982); Mark Novitch, *Direct to Consumer Advertising of Prescription Drugs*, 39 FOOD DRUG COSM. L.J. 306 (1984); Paul Rheingold, *Expanding Liability of the Drug Manufacturer to the Consumer*, 40 FOOD DRUG COSM. L.J. 135 (1985); Elisabeth Rosenthal, *Drug Makers Set Off a Bitter Debate With Ads Aimed Directly at Patients*, N.Y. TIMES, Mar. 3, 1991, at 17; and Lance Gilgore, *A Consideration of Direct-to-Consumer Advertising of Prescription Drugs and Potential Legal Problems With the Brief Summary: Is the FDA’s Regulatory Authority Illusory?*, 46 FOOD DRUG COSM. L.J. 849 (1991).

¹¹ The Upjohn Company, “Introducing Birth Control You Think About Just 4 Times a Year” (1993) (Depo-Provera consumer-directed advertisement).

Variations on the Depo-Provera advertisement make similar appeals to convenience. A recent one and a half-page advertisement in *Woman’s Day* magazine features a mother and her three children. On the picture is printed the basic appeal: “With three kids, who has time to think? So I picked birth control I only have to think about 4 times a year.” WOMAN’S DAY, Feb. 1, 1995. The remaining half page contains the text of the advertisement. Aside from these variations in visual appeals to convenience, the texts of the advertisements appear to contain only minor nonsubstantive differences.

appeal to convenience, linking it to physician availability and emphasizing the drug's reliability, informs the reader that since the drug is 99% effective in preventing conception it is "one of the most reliable contraceptives available." Safety is addressed tangentially by presenting a positive image of the drug's worldwide use. The advertisement notes the product's lengthy use by "millions of women" in Western European nations "like England, France, and Sweden," which have a major commitment to personal health, but does not mention that the drug's most extensive use includes millions of women in Third World nations like Kenya, India, Thailand, Chile, and Costa Rica. Then the advertisement turns to Depo-Provera's reversibility, saying that a woman "can usually become pregnant" once she stops taking the drug, but does not mention that a woman's return to fertility can vary from six to eighteen months. Cost, the final benefit described in the advertisement, is said to be "about the same per year as birth control pills." This rather generic comparison, although accurate, may leave the impression that a woman would be well advised to choose Depo-Provera for convenience or economic reasons, but obscures the fact that the higher payment for each individual injection of Depo-Provera might be beyond the means of a lower income woman.

The advertisement identifies four side effects in declining order of importance: menstrual bleeding, weight gain, amenorrhea, and osteoporosis. The advertisement notes that "most" women who use Depo-Provera experience irregular, unpredictable menstrual bleeding and weight gain; "many women stop having monthly periods;" and some "may" experience "a decrease in the amount of minerals stored in . . . [their] bones." None of these side effects is described as serious. Women are told that amenorrhea is "not a medical problem,"¹² but they are not informed that weight gain and the likelihood of the drug causing osteoporosis is doubly qualified.¹³ Women are told in the advertisement not to be concerned about irregular and unpredictable menstrual bleeding, but they are not informed about a major finding of a study by Upjohn researchers, Drs. Paul Schwallie and J. Robert Assenzo, that the drug's use causes prolonged menstrual bleeding.¹⁴

Under the heading "Depo-Provera is not right for every woman," the advertisement clearly describes four of Depo-Provera's contraindications: "Women with a family or personal history of breast cancer, blood clots, liver disease, or those who think they might be pregnant, should not use Depo-Provera." The advertisement also makes it clear from the outset that Depo-Provera is available only through a physician. Thereafter, it emphasizes four times the need to discuss contraceptive "risks and benefits" with a physician. At the bottom of the advertisement, however, its reference to the accompanying patient information and the need to discuss it with a physician appears in very small print.

B. *The Patient Information*

"Depo-Provera Contraceptive Injection," the patient information statement, ap-

¹² *Id.* The advertisement states: "Your doctor can explain why this happens and that it is not a medical problem."

¹³ *Id.* The advertisement states: "Use of Depo-Provera *may* be associated with a decrease in the amount of minerals stored in your bones, which *may* be considered among the risk factors for development of osteoporosis." (emphasis added).

¹⁴ Paul Schwallie & J. Robert Assenzo, *Contraceptive Use: Efficacy Study Utilizing Medroxyprogesterone Acetate Administered as an Intramuscular Injection Once Every Ninety Days* 24 *FERTILITY AND STERILITY* 331, 334 (1973).

pears on the page following the advertisement.¹⁵ Largely based on the drug's FDA-approved labeling, its format is reader-friendly; its nine bold-type headings speak directly to a woman in a question-and-answer format; and under its numbered subheadings, it details in small print the drug's common risks, possible side effects, and precautions in neither overly complicated nor technical language. A woman is advised to consult her health provider in making a contraceptive choice, and, after using Depo-Provera, if she suspects she is pregnant, misses a period, or experiences the specified side effects.

Menstrual bleeding is mentioned specifically in the patient information statement under three headings: under "What are the Possible Side Effects of Depo-Provera?" it states that "some women reported . . . [i]rregular menstrual bleeding" in clinical trials; under "What Symptoms May Signal Problems While Using Depo-Provera?" it lists unusually heavy vaginal bleeding; and under "What are the Risks of Using Depo-Provera?" it mentions unusually heavy or continuous bleeding, but asserts (without any reference to research findings) that this is "not a usual effect of Depo-Provera." In all three instances, a woman is told explicitly to call or see her health care provider, but she is not told about a major finding from the Schwallie and Assenzo study: 26.9% of women who received their first Depo-Provera injection experienced excessive bleeding, i.e., bleeding and/or spotting from twelve to thirty days per month for three months.¹⁶

C. The 800 Number Information

The Depo-Provera advertisement encourages women who want more information to call an 800 number. This information includes a copy of the patient labeling and two brochures, one on Depo-Provera and one comparing methods of birth control. The patient labeling adds little to a woman's knowledge about Depo-Provera, because it is only a slightly reconfigured version of the patient information accompanying the advertisement.¹⁷ The Depo-Provera brochure, which is based on the advertisement's format and appeal, provides more information than the advertisement about the drug and its benefits, side effects, and contraindications.¹⁸ The brochure also provides new information on the painfulness of the injection, the importance of receiving timely injections, and the need for additional protection against sexually transmitted diseases. The brochure does not contain any more information about the menstrual bleeding side effect than the advertisement. The brochure on "Choosing a Birth Control Method," which briefly describes and compares barrier methods, the intrauterine device (IUD), the Pill, Norplant, and Depo-Provera,¹⁹ is meant to be read in conjunction with the back page of the Depo-Provera brochure that advises a woman to talk with her physician about birth control methods, and concludes with the suggestion that it is the woman who chooses: "Once you have all the information you need, you will be able to make the choice which

¹⁵ The Upjohn Company, *Depo-Provera Contraceptive Injection* (1993) (patient information included with Depo-Provera consumer advertisement).

¹⁶ See *supra* note 14.

¹⁷ The Upjohn Company, *Depo-Provera Contraceptive Injection, Patient Labeling* (1993) (patient labeling included with the two Depo-Provera 800 number brochures).

¹⁸ The Upjohn Company, *Contraceptive Confidence 3 Months at a Time*, (1993) (Depo-Provera 800 number brochure).

¹⁹ Association for Reproductive Health Professionals, *Choosing a Birth Control Method* (Jan. 1994) (800 number brochure briefly describing and comparing the average success rate, length of protection, average cost, return to fertility, privacy of use, and protection against sexually transmitted diseases of barrier methods, the IUD, the Pill, Norplant, and Depo-Provera).

is best for you.”

D. Summary

The Depo-Provera advertisement, given its subtle tone and serious character, does not resemble advertisements for other consumer products, other than in its appeal to convenience. The advertisement and its accompanying patient information and 800 number materials may comply with section 502's brief summary requirement. The issue here is whether the advertisement, because it is aimed at the general public, creates new duties for Upjohn under state product liability law.

III. THE DEPO-PROVERA ADVERTISEMENT'S PRODUCT LIABILITY CONSEQUENCES

Once the FDA has approved a drug, the agency has answered one part of the risk regulation equation: whether the drug should be made publicly available. The other part of the equation is whether the drug should be used by a particular patient. This decision turns, in part, on a physician's knowledge of the drug and its FDA-approved labeling. If a patient believes that a pharmaceutical company has failed to warn a physician about the drug's risks, and she has suffered harm as a result, the patient may initiate a product liability claim against the manufacturer. In a product liability case, attention will focus on the drug's labeling and the issue will be whether the label information was adequate to warn the consumer about the risks inherent in the drug and the harm that could follow from its use.²⁰

The Depo-Provera advertisement has the potential for generating a wide array of product liability actions. This analysis will not examine this world of potential litigation, but will focus on one major short-term side effect not sufficiently identified in the advertisement: heavy and prolonged menstrual bleeding. It will first examine *Upjohn v. MacMurdo*,²¹ the leading product liability case on this issue prior to the drug's contraceptive approval. Then, the article will consider a hypothetical case based on *MacMurdo* and the drug's advertisement, will explore two defenses drug manufacturers frequently raise — the learned intermediary rule and federal preemption doctrine — , and will conclude with an evaluation of Upjohn's potential liability for the advertisement's warning about menstrual bleeding.

A. *Upjohn v. MacMurdo*

Depo-Provera's use as an unapproved contraceptive was the subject of medical malpractice and product liability suits in the quarter century prior to its approval in 1992. Women who experienced a variety of debilitating short-term side effects from using the drug sued their physicians and Upjohn, but their cases were dismissed or settled. Only Anne MacMurdo's product liability case was tried, appealed, and reviewed by a state supreme court.²² Anne MacMurdo received two injections of Depo-Provera

²⁰ Lars Noah, *The Imperative to Warn: Disentangling the "Right to Know" from the "Need to Know" About Consumer Products Hazards*, 11 YALE J. REG. 293, 326-32 (1994).

²¹ 562 So. 680 (Fla. 1990).

²² See William Green, *Miscarriage of Justice: Depo-Provera Case May Insulate Drug Makers*, 27 TRIAL 61 (1991).

in 1974. The injections produced heavy and prolonged menstrual bleeding, which her obstetrician ended by performing a hysterectomy. At trial in 1986, MacMurdo's attorney argued that the Depo-Provera package insert had failed to warn her physician that the use of the drug could produce excessive and prolonged bleeding. The trial court jury found that Upjohn had been negligent in failing to provide adequate package insert warnings.²³ An intermediate appellate court affirmed the trial court's finding that "there was . . . substantial evidence presented that the drug . . . caused MacMurdo's bleeding problems, that the warnings were insufficient to alert her physician of this risk, and that her hysterectomy was performed to treat the bleeding condition."²⁴

On appeal, the Florida Supreme Court held that the adequacy of drug warnings was governed by *Felix v. Hoffmann-La Roche, Inc.*,²⁵ which had held that the adequacy of a manufacturer's warning about the dangers of a drug is often "a question of fact, . . . [but] it can become a question of law where the warning is accurate, clear, and unambiguous."²⁶ Applying the *Felix* standard, the *MacMurdo* court held that because package insert warnings were directed at physicians, their adequacy to inform had to be proven by expert testimony. After rejecting the plaintiff's expert because he was a Ph.D. pharmacologist, and selectively using the obstetrician's testimony, the court concluded that "[n]o medical expert testified that the package insert was insufficient to put a doctor on notice that the symptoms displayed by MacMurdo . . . could result from the use of Depo-Provera."²⁷ As a consequence, the claim that the Depo-Provera package insert failed to warn against prolonged bleeding was held insufficient to present a jury question. Because "the insert [had] warned of the possibility of abnormal bleeding outside the menstrual period," the court held that these warnings, in light of *Felix*, were accurate, clear, and unambiguous as a matter of law.²⁸

B. A Hypothetical Depo-Provera Product Liability Case

Suppose that after the product's approval another Anne MacMurdo read the Depo-Provera advertisement, including the accompanying patient information and 800 number materials, visited her doctor and discussed the risks and benefits of birth control options, and chose Depo-Provera. Suppose that her doctor, who may have read the physician advertising material on Depo-Provera,²⁹ consulted the *Physicians' Desk Reference (PDR)* entry on the drug,³⁰ gave her a physical examination, and then an injection. Subsequently, the patient experienced prolonged menstrual bleeding, which was

²³ *MacMurdo v. Upjohn*, No. 78-8497 CL (Broward Cir. Ct. Fla. 1986).

²⁴ *Upjohn v. MacMurdo*, 536 S.2d 337, 339-40 (Fla. Dist. Ct. App. 1988).

²⁵ *Upjohn v. MacMurdo*, 562 So. at 681-82, citing *Felix v. Hoffmann-La Roche, Inc.*, 540 So.2d 102 (Fla. 1989).

²⁶ *Felix*, 540 So.2d at 105.

²⁷ *Id.*

²⁸ *Id.*

²⁹ The Upjohn Company, *Depo-Provera Contraceptive Injection. Contraceptive Confidence 3 Months at a Time*, 18 THE FEMALE PATIENT (Nov. 1993). Physician information is included with the Depo-Provera physician advertisement. The Upjohn Company, *We'll Help Her Learn About the First 3-Month Contraceptive. You'll Help Her Decide*, 18 THE FEMALE PATIENT (Nov. 1993).

Two recent full-page health care provider and physician-directed advertisements titled "Contraceptive Confidence 3 Months at a Time" feature the wristwatch picture in deep pink and mauve tones. In very small print at the bottom of the page, the advertisement identifies two contraindications and requests the reader to "[p]lease see [the] brief summary of prescribing information on [the] adjacent page." 27 FAMILY PLANNING PERSPECTIVES (Mar./Apr. 1995) and 86 OBSTETRICS AND GYNECOLOGY (Aug. 1995).

³⁰ PHYSICIANS' DESK REFERENCE, *Depo-Provera Contraceptive Injection* 2543-46 (49th ed. 1995).

terminated by a hysterectomy.

Suppose that this hypothetical woman sued Upjohn, claiming that the drug's consumer and physician-oriented advertising materials and the *PDR* were inadequate to inform her and her physician that heavy and prolonged menstrual bleeding was a likely side effect from the drug's use, because Upjohn, knowing the results of the Schwallie and Assenzo study, included it in the *PDR* list of references, but failed to provide in the *PDR* and the physician's and consumer-oriented advertising material a major finding of the Schwallie and Assenzo study: 26.9% of women bled from twelve to thirty days per month during the first three months of drug use.³¹

Suppose finally that this hypothetical physician, like Anne MacMurdo's, testified at trial that when the woman complained of abnormal bleeding, he did not consider that Depo-Provera was causing her problem because the *PDR* identified it as an unusual or rare side effect. Given these suppositions, would the legal outcome be different than the one in Anne MacMurdo's case? The answer would likely depend on the applicability of the learned intermediary rule, the doctrine of preemption, and the state product liability law to consumer-oriented prescription drug advertisements.

C. Learned Intermediary Defense

If a woman brought a product liability action claiming the Depo-Provera advertisement failed adequately to warn her against heavy and prolonged menstrual bleeding, Upjohn would be likely to raise a learned intermediary defense. State and federal courts first recognized the learned intermediary rule in the 1966 case of *Sterling Drug, Inc. v. Cornish*.³² The rule protects drug manufacturers if they "direct their warnings to prescribing physicians who, in turn, are expected to serve as 'learned intermediaries' for the manufacturer and provide the necessary warnings to their patients."³³ Subsequently, the FDA challenged the assumptions of the learned intermediary rule when it required patient inserts for oral contraceptives in 1970 and IUDs in 1975.³⁴ Some courts have recognized exceptions to the learned intermediary rule in cases involving contraceptives, but the contraceptive exception is limited to the Pill and IUD. So far, state and federal courts have been unwilling to create an exception for advertising. Would the courts extend the contraceptive exception to include Depo-Provera? Are these courts likely to recognize a learned intermediary exception for advertising prescription drugs, including Depo-Provera?

Judicial recognition of an exception for the Pill and IUD cases could be expanded to support an exception for Depo-Provera. A court relying on *Stephens v. G.D. Searle & Co.*³⁵ and *Hill v. Searle Laboratories*,³⁶ two cases that recognized exceptions for the contraceptive pill and IUD, could reject the learned intermediary rule in a case involving the injectable drug. A court could reason that women who receive an injection of

³¹ See *supra* note 14. The Schwallie and Assenzo study also found that, after the second injection, 20.5% of the women continued to experience bleeding from eleven days to every day per month during the second three months.

³² 370 F.2d 82 (8th Cir. 1966).

³³ Teresa M. Schwartz, *Consumer-Directed Prescription Drug Advertising and the Learned Intermediary Rule*, 46 FOOD DRUG COSM. L.J. 829 (1991).

³⁴ See, e.g., Teresa M. Schwartz, *Consumer Warnings for Oral Contraceptives: A New Exception to the Prescription Drug Rule*, 41 FOOD DRUG COSM. L.J. 241 (1986); and Howard Rowe, *Patient Package Inserts: The Proper Prescription?*, 50 FOOD AND DRUG L.J. 95 (1987).

³⁵ 602 F. Supp. 379 (E.D. Mich. 1985).

³⁶ 884 F.2d 1064 (8th Cir. 1989).

Depo-Provera, like those who receive the Pill and IUD, are more likely to have decided to use that birth control method before visiting their physician, and will have only infrequent contact with a physician over a long period of time (three months) after receiving the injection. A court also could reason that Depo-Provera, like the Pill and IUD, has serious side effects, that FDA regulations require its manufacturer to provide direct warnings to patients by means of patient package inserts, and that the drug is marketed directly to patients. Taken together, these factors that distinguish contraceptives from other prescription drugs could be made applicable to Depo-Provera.

The *Stephens* and *Hill* cases also suggest that Depo-Provera might qualify for a consumer-directed advertising exception, but it is less likely that a court would recognize this exception. A key question would be whether the court believes that the Depo-Provera advertisement has "significantly affected the nature of the doctor/patient relationship."³⁷ A woman who reads the advertisement is told that her doctor is the principal source of medical information about the drug. The advertisement states that "before . . . you consider any birth control method, you should discuss the risks and benefits with your physician."³⁸ The advertisement also encourages the woman, albeit in very small print at the bottom of the page, to discuss the accompanying patient information with her doctor.

The patient information emphasizes that her physician is the learned medical intermediary who "will help you compare Depo-Provera with other contraceptive methods and give you the information you need in order to decide which contraceptive method is the right choice for you."³⁹ The patient information also tells the woman to inform her doctor about medications she is taking and her personal and family medical history related to use of the drug. Finally, the Depo-Provera 800 number brochure, after advising a woman to talk with her physician about birth control methods, states that it is she who chooses: "Once you have all the information you need, you will be able to make the choice which is best for you."⁴⁰

The Depo-Provera advertisement clearly encourages a woman to play an active role in making a contraceptive decision. Has this advertisement thereby altered the doctor-patient relationship sufficiently to create an advertising exception? Some courts would be unpersuaded if they "consider[ed] only one issue — whether a doctor prescribed the product for the patient — and ignore[d] other circumstances such as the nature of the product and whether the patient is actively involved in choosing the product."⁴¹ Other courts may be persuaded by the decisions in *Hensigen v. Bloomfield Motors*⁴² that "a manufacturer's duty runs directly to the consumer when it markets products directly to the consumer;"⁴³ *Stephens v. Parke-Davis*⁴⁴ that heavily advertised prescription drugs (i.e., those that are overpromoted to physicians) rendered FDA-approved warnings inadequate; and by *Stephens* and *Hill*, that abandoned the learned intermediary rule, in part because the drug manufacturers had aimed their advertising directly at the public. For these courts, the issue would not be who writes the prescription, but who decides to take the drug. If that decision is made by a patient, largely on the basis of

³⁷ See Schwartz, *supra* note 33, at 839.

³⁸ See *supra* note 11.

³⁹ See *supra* note 15.

⁴⁰ See *supra* note 18.

⁴¹ See Schwartz, *supra* note 33, at 840.

⁴² 161 A.2d 69 (N.J. 1960).

⁴³ See Schwartz, *supra* note 33, at 841.

⁴⁴ 507 P.2d 653 (Cal. 1973).

Upjohn's patient-directed Depo-Provera advertisement, before she visits her doctor, these courts would be likely to conclude that any conversation she had with her doctor about risks and benefits of contraceptive methods was merely a formulaic exercise for her to receive the injection.

D. Preemption

Upjohn would have another defense against a state product liability suit if a court extended the contraceptive exception or recognized an advertising exception to exempt Depo-Provera from the learned intermediary rule. The drug company could argue that recovery under a product liability theory is preempted by its compliance with the brief summary requirement of section 502(n) of the FDCA.⁴⁵ Federal law may override state law if a congressional statute expressly preempts state law, if the statute impliedly preempts state law by establishing a pervasive regulatory scheme that occupies the entire field, and if the state law, although it is neither expressly nor impliedly preempted, actually conflicts with the statute.⁴⁶

Since Upjohn would have to concede that the FDCA does not expressly preempt state tort law, including a product liability cause of action,⁴⁷ the drug manufacturer would have to base its preemption arguments on implied occupation of the field and actual conflict theories.⁴⁸ Even so, Upjohn in this case would face an "uphill battle."⁴⁹ As the Supreme Court observed in *Hillsborough County v. Automated Medical Laboratories*,⁵⁰ Upjohn would have to demonstrate that its compliance with section 502(n) was strong enough to overcome the presumption that state product liability suits based on the manufacturer's consumer-directed advertising could "constitutionally co-exist with federal regulation."⁵¹ In fact, *Abbott Laboratories v. American Cyanamid*⁵² and *Mazur v. Merck*⁵³ emphasized that the "presumption against preemption is even stronger when state regulation of matters related to health and safety are involved and when federal regulation would work to preempt state tort law remedies."⁵⁴ These federal courts would not be disposed to find preemption if Upjohn's compliance with section 502(n) would enfeeble a state's ability to protect its people from the dangers of contraceptive use and leave women harmed by Depo-Provera without a remedy at law.

Upjohn may argue that the FDA has occupied the field of drug safety regulation by pervasively and comprehensively regulating the labeling and advertising of contraceptive drugs. The FDA's regulations, Upjohn may further argue, require that extensive information be included in Depo-Provera's labeling and that the drug's consumer advertising be written in compliance with Section 502(n). Courts, however, would be reluctant to infer preemption from the comprehensiveness of the FDCA and FDA regu-

⁴⁵ See 21 U.S.C. § 352(n).

⁴⁶ Richard Ausness, *Federal Preemption of State Products Liability Doctrines*, 44 S.C. L. REV. 187, 193 (1993).

⁴⁷ See *Hillsborough County v. Automated Med. Labs.*, 471 U.S. 707, 714 (1985).

⁴⁸ See Noah, *supra* note 20, at 351-61. See also Brian Donato & Mary Beth Neraas, *Federal Preemption of Product Liability Claims Involving Drugs and Medical Devices Regulated Under the Federal Food, Drug, and Cosmetic Act*, 45 FOOD DRUG COSM. L.J. 305, 317 (1993).

⁴⁹ *Hillsborough*, 471 U.S. at 714.

⁵⁰ *Id.* at 707.

⁵¹ *Id.* at 716.

⁵² 844 F.2d 1108 (4th Cir. 1988).

⁵³ 742 F. Supp. 239 (E.D. Pa. 1990).

⁵⁴ *Id.* at 246.

lations, because that would be “tantamount to saying that whenever a federal agency decides to step into a field, its regulation will be exclusive.”⁵⁵ Courts would, therefore, be likely to follow *Spychala v. Searle*, which held that federal regulation did not preempt state tort law unless there was “statutory or regulatory language or legislative history that lends support to the conclusion that Congress intended to exclude state tort law.”⁵⁶

In the case of section 502(n), neither its language nor its legislative history suggest that Congress, in granting the FDA authority to regulate prescription drug advertising, intended to preempt state tort law. If a court examined the FDA’s section 502(n) claim of authority to regulate prescription drug advertisements irrespective of their audience,⁵⁷ it would find that for the first twenty years, the FDA limited its section 502(n) regulation to advertisements directed at physicians. In 1983, however, the agency responded to drug company plans to advertise their prescription drug products to the public by calling for a temporary moratorium to discuss and study the subject.⁵⁸ Two years later, the FDA withdrew the memorandum and stated in a *Federal Register* announcement that it would “continue to regulate prescription drug advertising regardless of audience in accordance with section 502(n).”⁵⁹

A court could find that the FDA’s extension of section 502(n) to direct-to-consumer advertisements is unsupported by the statute’s legislative history and the contemporaneous comments by FDA administrators, which suggest that section 502(n) was enacted “to provide physicians with better and more adequate information about drugs.”⁶⁰ Moreover, the FDA’s request for a moratorium in 1983 did not follow the Administrative Procedure Act’s (APA’s) notice-and-comment rulemaking procedures,⁶¹ nor those of FDCA section 701(e).⁶² In fact, the FDA’s 1985 *Federal Register* announcement withdrawing the moratorium is legally problematic, because the agency “merely reported its decision to regulate direct-to-consumer advertising under section 502(n).”⁶³ Since federal appellate courts have been willing to strike down the FDA’s extension of regulations to related, but new, areas without following informal rulemaking procedures,⁶⁴ it is quite possible to “foresee a situation where the agency’s attempt to regulate direct-to-consumer advertising under section 502(n) . . . is legally challenged and adjudged improper.”⁶⁵ Even if a federal court resolves this issue and requires the FDA to follow APA informal rulemaking procedures in regulating of consumer-directed prescription drug advertisements, state product liability law will continue to provide a critical drug risk regulation mechanism for the consumer, because Congress did not intend to preempt state tort law when it enacted section 502.

Upjohn also may argue that there is an actual conflict between state product liability law and section 502(n) on frustration of federal purpose grounds. The company could claim that a state product liability damage award based on the drug’s failure to

⁵⁵ *Hillsborough*, 471 U.S. at 716.

⁵⁶ 705 F. Supp. 1024, 1030 (D.N.J. 1988).

⁵⁷ See Gilgore, *supra* note 10, at 850.

⁵⁸ FDA Statement of Policy: Direct-to-Consumer Advertising of Prescription Drugs, Moratorium and Cover Letter (Sept. 2, 1983). See also Novitch, *supra* note 10, at 306; 50 Fed. Reg. at 36,677.

⁵⁹ 50 Fed. Reg. at 36,677.

⁶⁰ S. Rep. No. 1744, 87th Cong., 2d Sess. 33 (1962) (views of Sen. Kefauver).

⁶¹ See 5 U.S.C. §§ 551-559, 701-706 (1988 and Supp. 1993).

⁶² 21 U.S.C. § 371(e).

⁶³ Schwartz, *supra* note 33, at 857.

⁶⁴ *Id.*

⁶⁵ *Id.* at 858.

warn about heavy and prolonged menstrual bleeding conflicts with the FDA's finding of an adequate warning, thereby frustrating the agency's effective communication of the drug's labeling to physicians. A Depo-Provera advertisement written in compliance with section 502(n), Upjohn may argue further, could expose the company to potentially ruinous state product liability for its failure to adequately disclose the drug's risks. To provide a more inclusive warning, Upjohn might suggest, would produce an advertisement so overloaded with information that it might fail to adequately inform consumers.

Upjohn is likely to be disappointed by the judicial response to this argument. Courts have not been persuaded by frustration of federal purpose arguments, and would be likely to respond, as the Supreme Court did in *Hillsborough County* and as the federal courts did in *Abbott* and *Mazur*, by rejecting the argument that FDA regulations have not struck a balance between drug safety and availability. Instead, these courts have decided that the agency's labeling regulations merely establish minimum standards and allow the states to strike a balance by supplementing federal regulations.⁶⁶ As the *Mazur* court recognized, federal regulation and state tort law serve distinct purposes. "Essentially, federal regulation serves a deterrent purpose by limiting the manufacture of inherently dangerous products to those applicants who meet certain stringent safety standards, while state tort law serves the equally important purpose of compensating individuals injured by those very same products."⁶⁷ Together, they create a dual system of drug risk management in which "compliance with FDA regulations will not ensure that a manufacturer's products will not cause injury . . . [and w]hen those products do cause injuries, the state tort system provides a means of compensation."⁶⁸

Since Depo-Provera's labeling does not effectively communicate to physicians the significance of the Schwallie and Assenzo findings of prolonged menstrual bleeding, a court could find that state product liability law is "free to demand more" so that physicians can act as learned intermediaries.⁶⁹ It would be a small step for a court to reason that section 502(n)'s extension to consumer-directed advertising in 1985 has made the role of product liability law in the dual system of drug risk management even more important. In the case of Depo-Provera, a court could find that the consumer-directed advertisement and its accompanying patient information are not adequate for the purpose of informing women because the advertisement does not mention the Schwallie and Assenzo findings and because the patient information misrepresents the findings by saying that heavy and prolonged menstrual bleeding is not a usual effect.⁷⁰ As a consequence, a more detailed advertisement would lead not to information overload, but to the disclosure of one significant side effect (heavy and prolonged menstrual bleeding) that would allow a woman to make an informed contraceptive choice.

E. Depo-Provera's Product Liability in the Hypothetical Case

Assuming that a court rejects Upjohn's learned intermediary and preemption arguments in the hypothetical case, the outcome of the litigation will be governed by state product liability law. Here the issue will be whether the warnings about Depo-Provera

⁶⁶ *Mazur*, 742 F. Supp. at 247.

⁶⁷ *Id.*

⁶⁸ Richard Cooper, *Drug Labeling and Products Liability: The Role of the Food and Drug Administration*, 41 FOOD DRUG COSM. L.J. 233, 235 (1986).

⁶⁹ Schwallie & Assenzo, *supra* note 14.

⁷⁰ See Upjohn advertisement, *supra* note 11.

contained in the advertisement are adequate for the average woman consumer. Adopting this general legal standard, there are several questions the attorney for the woman in our hypothetical case would ask about the Depo-Provera advertisement: Are the warnings about excessive and prolonged menstrual bleeding prominently displayed in the advertisement? Are the warnings easy to understand or are they detailed in small type and technical language? If the warnings are not in the advertisement, are they contained on a separate page and easy to understand? A trial jury's answers will determine whether Upjohn has met its obligation adequately to inform the consumer that Depo-Provera can cause heavy and prolonged menstrual bleeding in 26.9% of women during the first three months of use.

In the Depo-Provera advertisement, menstrual bleeding is the first of four side effects identified under the heading "Some of the side effects of Depo-Provera."⁷¹ In the same type as all the other drug information, it states: "Most women experience irregular and unpredictable menstrual bleeding."⁷² There is no other reference to menstrual bleeding in the advertisement, nor does the advertisement specifically state that there is more detail about this warning on the next page. It merely states: "Please read the accompanying patient information and discuss it with your physician."⁷³

In the patient information, a bold heading, identical to the other nine headings, asks "What are the Risks of Using Depo-Provera Contraceptive Injection?" Irregular menstrual bleeding, as listed in the advertisement, is the first side effect identified. In small type, identical to the other patient information, the following explanation is provided:

The side effect reported most frequently by women who use DEPO-PROVERA for contraception is a change in their normal menstrual cycle. During the first year of using DEPO-PROVERA, you might have one or more of the following changes: Irregular or unpredictable bleeding or spotting, an increase or decrease in menstrual bleeding, or no bleeding at all. Unusually heavy or continuous bleeding, however, is not a usual effect of DEPO-PROVERA, and if this happens, you should see your health care provider right away.⁷⁴

No other information is given about heavy and continuous menstrual bleeding under this heading or in the remainder of the patient information. If a woman called the 800 number, the brochure would provide the same brief statement about irregular and unpredictable menstrual bleeding and the patient labeling would provide a statement identical to the one in the patient information. A physician is provided with no more substantial information. The Upjohn physician information states under the heading *Bleeding Irregularities*: "DEPO-PROVERA Contraceptive injection disrupts menstrual bleeding patterns in most women, irregular or unpredictable bleeding or spotting or, rarely, heavy or continuous bleeding may occur."⁷⁵ This statement is taken almost verbatim from the *PDR*.⁷⁶ In its reference section, the *PDR* cites the 1973 *Fertility and Sterility* article by Schwallie and Assenzo, but the article's title, "Contraceptive Use-Efficacy Study Utilizing Medroxyprogesterone Acetate Administered as an Intramuscular Injection Every 90 Days," does not indicate its relevance to heavy and prolonged menstrual

⁷¹ *Id.*

⁷² *Id.*

⁷³ *Id.*

⁷⁴ *Id.*

⁷⁵ See *supra* note 29.

⁷⁶ See *PDR*, *supra* note 30, at 2544.

bleeding.⁷⁷

Neither the Depo-Provera advertisement nor the 800 number brochure makes any reference to heavy and prolonged menstrual bleeding. The patient information accompanying the advertisement and the patient labeling from the 800 number materials state only that "heavy or continuous bleeding is not a usual effect."⁷⁸ Even the physician advertisement and the *PDR* characterize this bleeding as a rare occurrence. None of these materials discloses the Schwallie and Assenzo findings about severe bleeding. It seems clear that Upjohn has known for twenty years that Depo-Provera causes severe menstrual bleeding, yet the company did not inform physicians about this side effect when it wrote the drug's 1974 package insert. In 1986, a Florida trial jury found Upjohn negligent for its failure to warn Anne MacMurdo's physician about the prospect of heavy and continuous bleeding. In its Depo-Provera labeling and subsequent drug advertisement, the company did not disclose the Schwallie and Assenzo findings.

If, therefore, the woman in this article's hypothetical case read the Depo-Provera advertisement, the accompanying patient information, and the 800 number materials, and then visited her physician and received an injection for contraception, she should be able to prove that Upjohn negligently failed to warn her that the drug causes heavy and prolonged menstrual bleeding, and that she made an uninformed decision to her detriment. But if she wishes to prevail in her product liability suit, she also will have to establish not only that the warning was inadequate, but that it caused her injury. On the issue of causation, Upjohn would not be able to claim that the physician had "the opportunity to provide the patient with information about the prescription product, and, thereby, break the causal link between manufacturer's failure to warn and the patient's injury."⁷⁹ Allowing this defense would reinstate the learned intermediary rule. If, however, "a doctor *actually provides* a plaintiff with information missing from the advertisement, then the causal chain is broken by the doctor and the plaintiff should not recover."⁸⁰ Given the absence in the Upjohn physician advertising material and the *PDR* information on severe menstrual bleeding, it is unlikely that a physician would have been able to supply the additional drug labeling information.

IV. CONCLUSION

Prescription drugs have been advertised directly to the public for over a decade. The Upjohn consumer advertisement for Depo-Provera has provided the opportunity to raise several questions about the FDA's authority over advertising. FDCA section 502(n) grants the FDA authority to regulate advertisements to physicians, but the agency's authority to regulate consumer-directed prescription drugs is legally questionable, and its judicial disposition uncertain. Until this issue is decided, the Depo-Provera advertisement appears to comply with section 502(n)'s brief summary requirement and may fairly represent the drug's benefits. Whether the advertisement fairly represents the drug's risks has been the focus of this analysis.

The Depo-Provera advertisement, it has been argued, could expose Upjohn to state product liability suits because the advertisement does not disclose, for example, one serious short-term side effect: heavy and prolonged menstrual bleeding. In a product liability suit, the company might raise the learned intermediary defense, but that de-

⁷⁷ *Id.* at 2545. See also Schwallie & Assenzo, *supra* note 14.

⁷⁸ See Schwartz, *supra* note 33, at 847 (emphasis in original).

⁷⁹ *Id.* (emphasis added).

⁸⁰ See Schwartz, *supra* note 33, at 848 (emphasis added).

fense may fail if a court were willing to extend the contraceptive exception or create a new advertising exception to the learned intermediary rule. Even if a court were unwilling to extend the contraceptive exception or create an advertising exception, it would be likely to reject Upjohn's claim that the FDCA preempts state product liability claims. As a consequence this analysis suggests that the woman in the hypothetical case is likely to prove that Upjohn negligently failed to warn her about the drug's risks.

In sum, this article has examined the FDA's regulation of consumer-oriented prescription drug advertising within the wider context of the agency's participation in a dual system of risk regulation. This study casts some doubt on the argument that the courts and state product liability law do not have a prominent risk regulation role and that drug risk regulation ought to be the sole providence of the FDA. In fact, this analysis suggests that the current dual system provides for a comprehensive approach to risk reduction in which the FDA's regulatory process uses scientific experts to conduct an *ex ante* probabilistic evaluation of a drug's benefits versus risks, and a judicial regulatory process relies on state trial judges and lay juries who focus on a drug's *ex facto* risks in determining whether that drug caused the adverse event.⁸¹

⁸¹ See Grabowski, *supra* note 3, at 361-64.