LIMITING PHYSICIAN FREEDOM TO PRESCRIBE A DRUG FOR ANY PURPOSE: THE NEED FOR FDA REGULATION

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Since 1962, federal regulation of prescription drugs under the Federal Food, Drug, and Cosmetic Act\(^1\) has contained a regulatory anomaly which deprives some drug consumers of the protection of the Act. Under the Act, before a drug distributor may sell a drug through interstate commerce to a pharmacy, the drug must be licensed by the Food and Drug Administration (FDA).\(^2\) The FDA can grant such a license only if the drug is safe and efficacious to treat a certain illness.\(^3\) By comparison, a physician may order the pharmacy to dispense the drug in intrastate commerce for any illness, whether or not FDA has licensed the drug as safe and efficacious.

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2 See notes 8-19 and accompanying text infra.
3 See note 11 and accompanying text infra.
The prescription of drugs for purposes not approved by FDA has been the subject of a continuing controversy between the agency, physicians, and representatives of physician organizations. For example, in 1972, the FDA proposed extensive regulations to solve what it then regarded as health hazards posed by prescriptions for purposes not approved by the agency. After vehement opposition by the medical community, the FDA allowed its proposals to lapse. Recently, with the proposal of the Drug Regulatory Amendments of 1978, the agency once again has made proposals designed to alleviate problems it sees as associated with the prescription of drugs for nonapproved purposes.

The following discussion analyzes what kind of health hazards are posed by the present regulatory anomaly and what kinds of solutions—regulatory or nonregulatory—have been proposed. The proposed solutions involve issues such as what role malpractice liability, informed consent, peer review, and patient-package inserts should play in medical practice. These are then analyzed to determine which might be the most appropriate methods by which to proceed.

**Definition of the Problem of Nonapproved Drugs**

**The FDA Approval Process**

The Federal Food, Drug, and Cosmetic Act (FDCA) provides that no new drug may be sold in interstate commerce unless that drug has been approved by the FDA. The FDA may only approve the drug if its sponsor establishes for the therapeutic use or uses for which the sponsor proposes to advertise the drug that the

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4 See notes 44-50 and accompanying text infra.
5 See notes 284-85 and accompanying text infra.
6 See notes 286-88 and accompanying text infra.
7 See notes 289, 348, 379, 399, 422 and accompanying text infra.
9 New drugs are defined as drugs whose composition is not generally recognized as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling of the drug, or as drugs whose composition has been so recognized as a result of investigations, but which have not been used to a material extent or for a material time. 21 U.S.C. § 321(p) (1976). For a discussion of the difficulty faced in interpreting this section, see Weinberger v. Bentex Pharmaceuticals, Inc., 412 U.S. 645, 652-54 (1973); J. Mashaw & R. Merrill, Introduction to the American Public Law System 463-66 (1975).
10 The FDCA provides that no person shall introduce into interstate commerce any new drug without premarket approval from the Secretary of Health, Education, and Welfare. 21 U.S.C. § 355(a) (1976). This and all other delegable functions vested in the Secretary by the Act have been delegated to the FDA Commissioner. 21 C.F.R. § 5.1 (1977).
drug is safe and that there is substantial evidence that it is effective.\textsuperscript{11} Substantial evidence of effectiveness must include at least two "adequate and well-controlled investigations," which are studies that involve the use of formal experimental controls to establish the statistical reliability of the observations.\textsuperscript{12}

As the FDCA has been interpreted by the FDA, meeting the two requirements involves a rigorous process consisting of both animal and human testing.\textsuperscript{13} First, the drug's sponsor must submit to the FDA a Notice of Claimed Investigational Exemption for a New Drug (IND) containing information—including the results of animal studies on the pharmacological and toxic effects of the drug\textsuperscript{14}—from which the FDA can determine whether the drug appears reasonably safe and effective for human users.\textsuperscript{15} If human testing is then allowed,\textsuperscript{16} it consists of three phases which commence with the testing of healthy human volunteers to determine the drug's safety and chemical effects. The testing culminates with the treatment of large numbers of ill humans, to assess the drug's safety, effectiveness, and most desirable dosage.\textsuperscript{17} All this information, along with any information about health dangers posed by the drug as re-

\begin{itemize}
  \item \textsuperscript{11}21 U.S.C. § 355(d) (1976).
  \item \textsuperscript{12}21 U.S.C. § 355(d) (1976) provides:
  \begin{quote}
  "The term ‘substantial evidence’ means evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof.
  \end{quote}
  The statute, by rejecting the use of uncontrolled studies, anecdotal reports, and clinical testimonials to gain new drug approval, adopted the scientific viewpoint that, in light of the unpredictable course of many diseases and the biases and expectations of both patients and physicians, quantification of therapeutic benefit was not possible without formal experimental controls. Weinberger v. Hynson, Westcott & Dunning, 412 U.S. 609, 617-20 (1973); Upjohn Co. v. Finch, 422 F.2d 944, 951-54 (6th Cir. 1970). See also Lasagna, The Pharmaceutical Revolution: Its Impact on Science and Society, 166 Sci. 1227, 1231 (1969).
  \item \textsuperscript{13}21 C.F.R. §§ 310-314 (1977).
  \item \textsuperscript{14}21 C.F.R. § 312.1(a)(2) (1977). Other information includes: the chemical composition of the new drugs; a detailed protocol intended to be used in initial human studies (called clinical studies); the qualifications of the clinical investigators who will carry out the studies; an agreement by the sponsor to notify the FDA and all participating investigators of any adverse effects which arise during animal or human testing; an agreement by the sponsor that it will obtain the consent of the person on whom the drug is to be tested; and an agreement to submit annual progress reports. Pines, A Primer on New Drug Development, FDA Consumer, Feb. 1974, at 12.
  \item \textsuperscript{15}21 C.F.R. § 312.1(a)(2) (1977); Pines, supra note 14, at 12.
  \item \textsuperscript{16}The sponsor may initiate human studies unless the FDA prohibits it from doing so within 30 days of receiving the IND. 21 C.F.R. § 312.1(a)(2) (1977).
  \item \textsuperscript{17}Pines, supra note 14, at 12-14. For a detailed description of these phases, see J. Gibson, Medication, Law and Behavior 125-45 (1976).
\end{itemize}
revealed by the testing, is submitted to the FDA in the form of a New Drug Application (NDA). If the application is approved, the sponsor may market the drug.

Besides its requirements regarding the licensing of new drugs, the FDCA also provides certain requirements concerning the labeling and advertising of prescription drugs. For prescription drugs, a drug will be considered "misbranded" and therefore subject to withdrawal from the market unless the drug, as it is shipped to the pharmacist for dispensing, is accompanied by a label or a package insert bearing certain required information. A drug also will be considered misbranded unless advertisements about the drug contain in a summarized fashion the information required to be in the drug label or package insert. For new drugs, the label or package insert must be approved by the FDA before it can be used.


19 The FDA has 180 days in which to approve or disapprove an NDA, although that period is often extended. 21 U.S.C. § 355(c)(1) (1976); Shapiro, Divorcing Profit Motivation From New Drug Research: A Consideration of Proposals to Provide FDA With Reliable Test Data (to be published in Duke Law Review). If the NDA is not approved, the FDA must give the sponsor "notice of an opportunity for a hearing . . . on the question of whether such application is approvable," 21 U.S.C. § 355(o)(2) (1976), after which the FDA issues a final order either approving or refusing to approve the NDA. 21 U.S.C. § 355(d) (1976). Unfavorable decisions may be appealed by the sponsor to the appropriate United States court of appeals. 21 U.S.C. § 355(h) (1976).


22 21 C.F.R. § 201.100(c)-(d) (1977). For a description of the information required, see notes 39-43 and accompanying text infra.

While the FDCA requires certain information to be on the label of any drug product purchased by a consumer, 21 U.S.C. § 352 (1976), prescription drugs are exempted from most, but not all of these requirements. 21 U.S.C. § 353 (1976). To qualify for these exemptions, the FDA has required that certain other requirements pertaining to providing information to the physician, rather than patient, be met. One of these requirements is that the drug package sent to the pharmacist either must be labeled or the drug's package must contain an insert, called a package insert. 21 C.F.R. § 201.100(c)-(d) (1977). While the physician is unlikely to see either the drug label or the package insert, their contents are reprinted in sources usually read by physicians. See notes 101, 102, and accompanying text infra.


The information required to be present in the package insert, the label, and in drug advertisements (in summarized fashion) is information derived from the testing process. It includes the indications, or uses, for which the manufacturer provided data to establish the safety and efficacy of the drug. The required information also includes information found by the testing about recommended dosages and about possible health hazards associated with the drug. To understand the nature of these latter hazards, it is necessary to examine the risk/benefit decisions which the FDA makes with regard to each drug it approves.

Every drug has the potential to cause a set of physiological effects in the body, some of which are beneficial and some of which are adverse. The latter effects, often termed adverse reactions or side-effects, can range in seriousness from a relatively mild result, such as drowsiness, to a fatal result. One governmental estimate, for example, has put the number of deaths in the United States of hospital patients caused by adverse drug reactions at 130,000 persons annually.

Because of these potential serious consequences, no drug can be considered absolutely safe. As a result, when the FDA judges a drug to be safe during its licensing process, the agency makes a relative decision that the benefit of the drug, in terms of its expected therapeutic effect, outweighs the risk that one of the nonbeneficial side-effects may occur. If the test on a drug leads the FDA to the conclusion that the drug is, on the whole, beneficial, then the drug is

26 Id. §§ 201.100(c)(1), (d)(1), 202.1(d)(2).
27 Id. §§ 201.100(c)(1), (d)(1), 202.1(e)(1).
28 J. Gibson, supra note 17, § 8.1.1, at 86; M. Dixon, Drug Product Liability § 6.10[5], at 46 (1977). The dysfunctional aspects result from the fact that a drug may react with some other body structure than the one for which it has been designed. Dubos, On the Present Limitations of Drug Research, in Drugs in Our Society 41 (P. Talalay ed. 1964).
29 M. Dixon, supra note 28, § 6.10[4], at 45.
30 J. Gibson, supra note 17, § 8.1.1, at 91. The most infamous side-effect of any drug may have been the deformities in new born infants caused by the tranquilizer Thalidomide. D. Harney, Medical Malpractice § 9.6, at 321 (1973).
33 J. Gibson, supra note 17, § 8.1.1, at 96.
considered "safe" for its intended use.\textsuperscript{34}

The risk/benefit decision for a drug is particularly complex because, among other reasons, the question of the drug's benefit always depends on the particular use or uses to which the drug will be put.\textsuperscript{35} For example, medical evidence now has established that an antibiotic called "Chloromycetin" will cause a fatal blood disease in one out of every 24,000 persons who take it.\textsuperscript{36} Thus, given the wide variety of alternative methods of treating mild infections, the use of Chloromycetin for such infections cannot be considered safe.\textsuperscript{37} By comparison, it is generally medically accepted that the drug's use to treat typhoid is safe since the mortality rate of the disease, without use of the drug, is about twenty percent.\textsuperscript{38}

Given that the risk/benefit ratio can vary so widely, the FDA is faced with a dilemma. On the one hand, the drug is needed to treat typhoid. On the other hand, it may be dangerous when used against other diseases. To resolve this kind of problem, the FDA requires that the drug label, the package insert, and drug advertisements (in summarized form) all contain sufficient information about the hazards of a drug like Chloromycetin to alert the physician to the shifting risk/benefit ratios posed by the drug.\textsuperscript{39}

This information about potential health hazards is conveyed to the physician by the use of several descriptive categories. One such category, "contraindications," tells the physician that the drug should not be given to certain types of patients if an alternative method of treatment exists.\textsuperscript{40} There will also be information pertaining to "precautions" which can be taken to avoid the occurrence

\textsuperscript{34} \textit{Interim Report: Risk}, supra note 32, at 9. Unfortunately, the FDA's initial risk/benefit decision may turn out to be incorrect since many side-effects will not become evident until a drug has been widely used. \textit{U.S. Dept of Health, Education, and Welfare, Task Force on Prescription Drugs, The Drug Prescribers} 3-4 (1968) [hereinafter cited as \textit{Task Force on Prescription Drugs}].

\textsuperscript{35} \textit{Interim Report: Risk}, supra note 32, at 7. Other reasons for the complexity of a risk/benefit decision for a drug are discussed in B. Barber, \textit{Drugs and Society} 178-85 (1967).


\textsuperscript{37} Gaddum, \textit{A Perspective on Pharmacology}, in \textit{Drugs in Our Society}, supra note 28, at 25.

\textsuperscript{38} Id.

\textsuperscript{39} J. Gibson, supra note 17, § 9.1, at 160; M. Dixon, supra note 28, § 6.10[4], at 39. For a description of the label presently used for Chloramphenicol, see id. § 6.10[4], at 42-43.

\textsuperscript{40} J. Gibson, supra note 17, § 9.2.1, at 169. For the categories of individuals listed as contraindicated, test data would have established that there is an anticipated risk/benefit ratio which is unfavorable, or which is unfavorable if alternative treatment is available. \textit{Id}. 
of a side-effect. The physician will also be informed of other facts relevant to his prescribing decision under a heading of “warnings.” Finally, there will be a list of side-effects apparently caused by the drug as it was observed in the testing process.

**Origins of Nonapproved Prescriptions**

Once a drug is marketed pursuant to the FDA license, with its approved package insert and accompanying advertising, the physician may prescribe the drug for the purposes or indications for which it was approved based on the information contained in those sources or based on other information. The physician, however, is not limited to those uses and instead may prescribe the drug for any other use the physician deems fit. To understand the physician’s authority in this matter, the jurisdiction of the FDA over physician prescribing must be reviewed.

**FDA Jurisdiction Over Prescriptions.**—In *United States v. Phelps Dodge Mercantile Co.*, a challenge to the legality of a FDA food seizure was upheld on the grounds that the FDA failed to establish, as was required by the FDCA, that the food was adulterated when introduced into interstate commerce, even though the food, still in the original cans, was adulterated when seized. In the Miller Amendment, enacted in 1949, Congress reacted to this decision by changing the food adulteration and misbranding provisions of the Act to extend the FDA’s jurisdiction to food stored after interstate shipment.

Since these amended food sections are distinct provisions from the nonamended new drug sections, the FDA has read those developments to mean that its new drug jurisdiction is at an end after an approved drug is shipped in interstate commerce with the approved package insert and neither the shipper nor the recipient intends that the drug be used for a purpose not approved by the agency. This means that

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41 Id. § 9.2.1, at 169-70; M. Dixon, supra note 28, § 6.10[4], at 44.
42 J. Gibson, supra note 17, § 9.2.1, at 170. These might include information such as “safety in pregnancy is not known” or “drug may mask signs of infection.” Id.
43 Id. § 9.2.1, at 170-71.
44 157 F.2d 453 (9th Cir. 1946), cert. denied, 330 U.S. 818 (1947).
45 157 F.2d at 455.
48 Notice of Proposed Rulemaking, Legal Status of Approved Labeling for Prescription
once the new drug is in a local pharmacy, . . . the physician may, as part of the practice of medicine, lawfully prescribe a different dosage for his patient, or may otherwise vary the conditions of use from those approved in the package insert, without informing or obtaining the approval of the Food and Drug Administration. 49

The agency does have one means of indirect jurisdiction over such prescribing, but it would not be viable for most instances of the nonapproved use of a drug. If the agency believed that the nonapproved use of a drug was posing a health risk to consumers, it would seek to withdraw its previous approval of the drug. 50 To do so, however, would mean that the drug would be denied to patients for the approved purpose or purposes. Consequently, the agency could use this authority only in rare cases where removal of the approved use would not be detrimental to patients.

Because of this lack of FDA jurisdiction, physicians will prescribe drugs for purposes other than those approved by the FDA. To understand the health problem that could be posed, the origins of such a practice will need to be analyzed.

How Nonapproved Prescriptions Originate.—The Holdover Origin.—If a new drug is marketed for certain purposes, physicians may eventually prescribe that drug for other purposes in any of several different ways. One of these instances, the so-called "holdover" situation, involves circumstances where a drug has been approved for a particular use, among others, but based on later arriving safety or efficacy evidence, the FDA withdraws approval for that use. 51 Although the FDA will accompany this decision by individually mailing warnings to all physicians of the change, experience has shown that, since the drug remains on the market for other uses, physicians will continue to prescribe the drug for the disapproved purpose. 52 In one recent case, despite newspaper publicity and mailed notice warnings that FDA had withdrawn its approval to use estrogen/progesterone combination drugs to prevent miscarriages and to treat other pregnancy-related illnesses, a market survey a year after the mailings indicated that 533,000 prescriptions were written for

Drugs; Prescribing for Uses Unapproved by the Food and Drug Administration, 37 Fed. Reg. 16,503 (1972) [hereinafter cited as Notice of Proposed Rulemaking].

49 Id.

50 Id. at 16,505. For the difficulties in accomplishing such a withdrawal, see notes 82-83 and accompanying text infra.


52 Id.
these uses—only ten percent less than the number written in the year in which such uses originally were approved.\(^{53}\)

The New Discovery Origins.—The other origins of nonapproved prescribing concern the discovery of a new use for a drug, rather than the withdrawal of an old use. For example, a physician may consider using a drug for a nonapproved purpose based on a report of that use in another country.\(^{54}\) The physician may then be tempted to try the drug on a patient, especially one whose condition has been unresponsive to the various drugs approved in this country to treat the condition of the patient.\(^{55}\)

The physician may also decide to use a drug for an unapproved purpose premised on a case report in the medical literature.\(^{56}\) The reports originate in instances where the patient is suffering from two illnesses and it is discovered that the drug apparently successfully treats both, although the drug is only being administered to treat the one illness for which it is approved.\(^{57}\)

A third route by which a drug may be used for a nonapproved purpose involves a patient whose condition has proved difficult to resolve. Based on some sort of theorizing by the physician, but without the assistance of any formalized testing, the physician may elect to try the drug on his patient.\(^{58}\)

\(^{53}\) Id.


\(^{55}\) Franklin & Lowell, supra note 54, at 1076.

\(^{56}\) See, e.g., Hearings on Use of Advisory Committees by the Food and Drug Administration Before a Subcomm. of the House Comm. on Government Operations, 93d Cong., 2d Sess. 62 (1974) [hereinafter cited as Hearings on Use of Advisory Committees].

\(^{57}\) For example, a drug named "Propranolol" was found useful in the treatment of angina pectoris at the time it was being used for the approved purpose of treating cardiac arrhythmia in patients who suffered from both diseases. Id.

\(^{58}\) See, e.g., Bishop, Drug Used to Relieve Gout May Prevent Sudden Death Months After Heart Attack, Wall St. J., Feb. 9, 1978, at 13, col. 1. In this instance, Anturane, a drug used to treat gout, was tried to treat heart attack victims because there was some evidence that the drug prevented certain red blood cells, called platelets, from clumping together to form clots.

This situation also often occurs in the pediatric use of drugs. Because new drugs are
Whatever the initial causation, prescriptions for a nonapproved purpose spread through reports in the medical literature and through discussions by physicians at medical meetings and elsewhere.\textsuperscript{59} As a consequence, some nonapproved uses become widespread among physicians long before the use is approved by the FDA.\textsuperscript{60}

The total extent of nonapproved prescribing is in doubt. Two factors, however, suggest that it may be considerable. First, there have been numerous prominent examples of nonapproved prescribing in the last few years, covering almost every area of medical practice. For example, for heart disease, five different drugs recently have been touted by physicians as being important therapeutic advances although none were approved at the time by the FDA for that purpose.\textsuperscript{61} The most prominent of these, Propranolol, was acknowledged by the FDA to have widespread use.\textsuperscript{62} Drugs used for nonapproved purposes also have become popular in the treatment of hypertension,\textsuperscript{63} contraception,\textsuperscript{64} infectious diseases,\textsuperscript{65} epilepsy,\textsuperscript{66} psoriasis,\textsuperscript{67} and enuresis (bed wetting).\textsuperscript{68}

Besides these widely varying examples of nonapproved prescribing, a recent empirical study also suggests that nonapproved us-


\textsuperscript{60} Temple, Legal Implications of the Package Insert, 58 MED. CLIN. AM. 1151, 1157 (1974).

\textsuperscript{61} Rheinstein, Drug Labelling As a Standard For Medical Care, 4 J. LEGAL MED. 22, 24 (1976) (Lidocaine); Bishop, supra note 58, at 13, col. 1 (Anturane); Archer, A Guide Into Chaos; Resist It, 227 J.A.M.A. 1397, 1398 (1974) (Xylocaine and Dilantin); Temple, supra note 60, at 1157 (Propranolol).

\textsuperscript{62} Hearings on Use of Advisory Committees, supra note 56, at 128.

\textsuperscript{63} Archer, supra note 61, at 1397 (Propranolol).

\textsuperscript{64} Hearings on Quality of Health Care, supra note 59, at 20 (Depo-Provo), 44 (Diethylstilbestrol (DES)) (1973) (statement of Charles C. Edwards, M.D.).


\textsuperscript{66} Archer, supra note 61, at 1397-98 (Valium and Tegretol).

\textsuperscript{67} Id. at 1398 (Methotrexate).

\textsuperscript{68} Temple, supra note 60, at 1157 (Imipramine); "Therapeutic Orphans," supra note 58, at 811-12 (Togranil).
age can be widespread. In reviewing the prescription of three medications for over 300 hospital patients, one group of researchers found that the three drugs were prescribed for nonapproved purposes for over fifty percent of the usage of each drug.

These latter origins of a nonapproved prescription are unlikely ever to be eliminated since there is an unavoidable lag between the time a new use for a drug is discovered and the time that use is approved by the FDA. The lag results in part from the fact that FDA approval is based on substantial evidence of efficacy and proof of safety derived from rigid scientific testing. By comparison, the physician may decide to prescribe the drug long before such testing can be completed. In fact, new drug testing for FDA purposes is a very time-consuming process, in some cases lasting years.

Whatever lag is caused by the process of testing for FDA approval, the time which may elapse between recognition of a new use and FDA approval also is increased by another factor. The distributor or manufacturer of a drug may not start its FDA testing until some time after a new use for a drug is recognized by at least some physicians. It has been asserted that this lag occurs because the drug's sponsor may have an insufficient economic incentive to begin testing until considerable sales of the drug for the nonapproved purpose become evident. The fact that the manufacturer is already benefitting from sales attributable to the unapproved use may also

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69 Mundy, supra note 65, at 1744.
70 The drugs were Cephalexin, Allpurinol, and Propranolol. Id.
71 Temple, supra note 60, at 1155; Archer, supra note 61, at 1397.
72 For any change which would alter the conditions of use, labeling, safety, effectiveness, strength, quality or purity of a drug, a drug manufacturer must submit a supplemental drug application for FDA approval. 21 C.F.R. § 314.8(a)(2) (1977). This application must contain the evidence which would have been required if the change had been part of the original application for the drug. 21 C.F.R. § 314.8(a)(1) (1977). For changes in indications or uses, this means that there must be substantial evidence of efficacy and acceptable evidence of safety for the new use. See note 11 and accompanying text supra.
73 One commentator has aptly described this result as follows: The most important feature of the package insert, the one that distinguishes it from other sources of information and makes possible its use as an authoritative reference source, is that its content must be based on substantial evidence. The labeling cannot simultaneously meet this requirement and be fully up to date. It cannot be authoritative and avant-garde. There will be reasonable uses of the drug, especially new ones, which will not appear in the labeling because they are not yet supported by substantial evidence available to FDA.
74 Id. at 1157.
75 See notes 76-77 infra.
76 Archer, supra note 61, at 1397; Rheinstein, supra note 61, at 22. Cf. Temple, supra note 60, at 1155 (investigative and financial resources of the industry are channeled elsewhere).
contribute to its lack of incentive to seek FDA approval, although those sales cannot be increased by advertising or promotion for the nonapproved purpose.

Since the FDA lacks authority to order a manufacturer to include a new use for the drug in the insert, even if it has been tested and found useful, considerable numbers of patients for considerable periods of time may be administered a drug which is not approved. As a result, these patients may be exposed to a significant health risk. The nature of the risk is examined in the next section.

**Health Consequences of Nonapproved Prescribing**

*The Nature of Physician Risk/Benefit Decisions.*—A prescription of a drug for an unapproved purpose is not necessarily an improper use of that drug. To understand why, the nature of the decision to approve the drug by the FDA must be compared to the nature of the decision made by a physician to prescribe a drug for a particular patient.

When the FDA approves a drug as safe and efficacious for the treatment of some particular illness, the agency has decided that there is authoritative evidence that the drug can be used, subject to the qualifications which may be contained in the package insert, by any physician for any patient with that illness. As such, the agency's analysis is based on a risk/benefit decision for a class of patients.

Under the present regulatory framework, that decision by the FDA is likely a conservative one in the sense that the FDA will require a very high quantum of proof of safety and efficacy. This agency frame of mind results from three regulatory facts of life.

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77 Rheinstein, *supra* note 61, at 23, 26, 27 (1975). Peck, *FDA Approval: When Should Your Judgment Outweigh It?*, CURRENT PRESCRIBING, Dec. 1975, at 26, 27. Another reason suggested for a manufacturer's reluctance to seek a change in the labeling may be that, once a change is sought, the FDA has ruled it will review the entire package insert. H. Dowling, *MEDICINES FOR MAN: THE DEVELOPMENT, REGULATION, AND USE OF PRESCRIPTION DRUGS* 240-41 (1970). Since the package insert may have been the result of a compromise between the FDA and the manufacturer in the first instance, the manufacturer may be reluctant to reopen the previous decisions.

78 See notes 10-11 and accompanying text *supra*.

79 "Therapeutic Orphans," note 58 *supra*.

80 See notes 33, 34, and accompanying text *supra*.

First, once the FDA approves a drug, the drug can be withdrawn from the market only through the use of cumbersome and time-consuming legal procedures. Consequently, if the drug poses a health danger, the FDA may not be able to act as quickly as it desires to remove the drug from the market.

The second factor is related to the first. Almost all medical experts agree that the United States lacks a reliable system by which adverse reactions caused by drugs are reported to the FDA. Thus, the FDA may not learn about certain dangers posed by a drug until some time after those dangers pose a considerable public health threat.

The final factor leading to the conservatism of the FDA's decisions relates to congressional oversight of FDA actions. Because such oversight always concerns drugs which the FDA has approved which some time later prove to have unacceptable dangers, the FDA has made two important efforts to speed its withdrawal process. First, it often successfully reaches an informal agreement with the manufacturer or sponsor to voluntarily withdraw the drug. Second, it may invoke its power not to grant a hearing unless there are disputed issues of fact.

If a hearing is adverse to the manufacturer or sponsor of a drug, it may appeal the FDA's order for judicial review. Even if the FDA obtains an order favorable to its decision, however, the manufacturer or sponsor may decide to market the drug in violation of the order. In such circumstances, the FDA must seek a judicial order of seizure in each jurisdiction where the drug is located.

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officials must know that they are most vulnerable to this type of political criticism when they incorrectly release a drug for marketing.87

By comparison, because a physician is making the decision only for one patient, instead of the class of patients for which the FDA is making the decision, the physician may view the use of a drug as appropriate before the time the FDA would be ready to make a similar decision.88 In other words, the risk/benefit ratio of a drug might be favorable for a patient, given that patient’s unique needs, even though the risk/benefit decision for a class of similar patients might not be favorable.89 Similarly, a physician could decide to be more therapeutically venturesome than the FDA in the sense that the physician would require a lesser quantum of proof of safety and efficacy to prescribe the drug.90 This might occur, for example, in instances where available alternative methods of therapy have proven to be unsuccessful.

Because of these differences in the functions of individual physicians and the FDA, the decision to prescribe a drug for a nonapproved purpose is not necessarily improper. For that reason, the FDA has eschewed seeking authority to completely ban all prescribing for nonapproved purposes.91 Nevertheless, the possibility that such a decision, on given occasions, might be improper must be carefully examined.

The Possibility of Mistaken Risk/Benefit Decisions.—The Difficulty of the Prescribing Decision.—While a physician can reach a mistaken risk/benefit decision regarding any use of a drug, the decision to prescribe for a nonapproved purpose may be especially vulnerable to such an error. Part of the cause of this increased vulnerability is the fact that the decision to adopt a nonapproved use may involve a more difficult risk/benefit analysis than for an approved drug.

products that entail physical risk—regardless of what benefit they provide. No FDA official has ever been publicly criticized for refusing to allow the marketing of a drug. Many, however, have paid the price of public criticism, sometimes accompanied by an innuendo of corruptibility, for approving a product that could cause harm.

Merrill, Can The FDA Do Anything Right?, VA. L. SCH. REP., Summer 1978, at 22.
87 For an example of one such incident of intense congressional criticism concerning the drug Parnate, see Merrill, supra note 36, at 12-15.
88 Franklin & Lowell, supra note 54, at 1076.
89 TASK FORCE ON PRESCRIPTION DRUGS, supra note 34, at 4.
90 The FDA’s standards, because of its functions, are very strict. See notes 81-87 and accompanying text supra.
To understand this difference, a recent study on physician prescribing habits is helpful.\textsuperscript{92} The study, which analyzed all of the previously published studies on the same subject, concluded that the doctor's decision to prescribe a drug occurs in several stages.\textsuperscript{93} In the first of these stages, the physician becomes aware of and interested in the drug.\textsuperscript{94} In the latter stages, the physician evaluates the qualities of the drug and then tries it on some patients.\textsuperscript{95}

The difficulty of the physician's evaluation differs depending on whether the drug is approved or not. If the drug is approved, the physician knows that large scale human testing to rigid scientific standards has established that the drug is safe and effective for certain classes of patients.\textsuperscript{96} Hence, besides eliminating alternative choices of treatment,\textsuperscript{97} the doctor's decision concerns whether a given patient is different in some regard so that the FDA's general decision about safety and efficacy is inappropriate for that particular patient.\textsuperscript{98}

If the drug is not approved by the FDA, the nature of this latter decision is different. The physician must make a primary decision about the safety and efficacy of the drug to treat the patient's illness without the benefit of the FDA's class decision.\textsuperscript{99} Since this decision is an absolute one, rather than the comparative decision made for approved uses, it would seem to call for greater knowledge and expertise on the part of the physician.


\textsuperscript{93} Miller, \textit{Parts I-III, supra} note 92, at 493-94.

\textsuperscript{94} \textit{Id.} at 493.

\textsuperscript{95} \textit{Id.} at 493-95.

\textsuperscript{96} Temple, \textit{supra} note 60, at 1154.

\textsuperscript{97} When the FDA approves a drug, it usually makes no judgment about whether that drug is more effective than other available drugs in the treatment of a given illness. As a result, neither the package insert nor pharmaceutical advertising contains any information about relative efficacy—how the efficacy of the drug being advertised compares to other drugs.

\textsuperscript{98} \textit{Hearings on Competitive Problems In the Drug Industry Before the Subcomm. on Monopoly of the Senate Select Comm. on Small Business}, 90th Cong., 2d Sess. 3709 (1968) [hereinafter cited as \textit{Hearings on Competitive Problems}] (statement of Phillip Lee, M.D.).

Because the nature of the decision may be more difficult, the chance of a mistaken decision would seem greater. Moreover, the possibility of a mistake in such a situation is likely increased because, as the following discussion indicates, there is less useful information available to the physician concerning a nonapproved drug than for an approved drug.

Availability of Prescribing Information.—Studies indicate that the physician’s evaluation of the quality of a drug is apparently two-fold. First, the physician will try to decide whether the drug would be useful therapy. For information on that question, physicians normally consult their colleagues, read journal articles, and attend medical meetings—not necessarily in that order. Second, having decided to use the drug, the physician acquires factual data on proper dosages, contraindications, and other information such as warnings and side-effects, from two sources: the Physician’s Desk Reference, and to a lesser extent pharmaceutical advertising.

For an unapproved use, these two sources of information are not available. Since neither package inserts nor other drug advertisements may contain any information about uses not approved by the FDA, the physician considering such prescriptions lacks the usual sources of information. To replace these sources, the physician has several options. One possibility is that the physician can extrapolate the necessary information from the data in the package insert for the approved purpose. A physician, however, may lack the expertise to make the necessary extrapolations, if the extrapolations

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100 Miller, Parts I-III, supra note 92, at 493.
101 The Physician’s Desk Reference is a compilation of FDA package inserts for those drugs for which advertising fees have been paid. Miller, Parts VII-VIII, supra note 92, at 89. It is sent to all physicians in the United States free of charge. H. Dowling, supra note 77, at 271.
103 D’Andrade, Communicating with Physicians: A Regulatory Overview, 29 Food Drug & Cosm. L.J. 154, 157 (1974). See notes 22, 88, and accompanying text supra. Medical treatises are not limited to approved purposes, but often may be out of date. Hearings on Competitive Problems, supra note 98, at 3712 (statement of Philip R. Lee); Temple, supra note 60, at 115. Moreover, some treatises contain essentially only the same information as the package insert. J. Gibson, supra note 17, § 10.4.2, at 243.
104 B. Barber, supra note 35, at 40; Harelik, Johnston, Rivers, & Ryan, Pharmacist and Physician Evaluation of Drug Information Sources, 32 Am. J. Hosp. Pharm. 594, 594-95 (1975) [hereinafter cited as Harelik]. One commentator has expressed the matter this way: “It is my
can even be made.\textsuperscript{105} Most drug testing is done by physicians specially qualified as clinical pharmacologists, who have advanced training in pharmacology and in some aspect of specialized medicine.\textsuperscript{106}

A second option faced by the physician would be to consult colleagues. Many such consultants may also lack the necessary expertise, however, or may have expertise only in irrelevant clinical areas. Most often, other physicians are not conveniently available for advice.\textsuperscript{107} Thus, the primary source of information would seem to be the third alternative—medical journal articles.\textsuperscript{108}

The use of such articles also presents possible problems. First, little information may be available if there have not yet been numerous studies made of the new use. Second, even if such studies have been made, the physician lacking expertise in clinical pharmacology may not be able to make any independent judgment of the quality of the work reported in the articles.\textsuperscript{109} This is the function which the FDA serves when it approves drugs.\textsuperscript{110} Independent judgment in certain cases is necessary. Studies have shown that some medical journal articles report on research that was not scientifically rigorous enough to be considered reliable.\textsuperscript{111}

\textsuperscript{105} Hearings on Quality of Health Care, supra note 59, at 261 (statement of James L. Goddard, M.D.).

\textsuperscript{106} Miller, Parts VII-VIII, supra note 92, at 89. Many physicians may receive little training in pharmacology in medical school. Hearings on Competitive Problems, supra note 98, at 3712-13 (statement of Phillip R. Lee, M.D.); Task Force on Prescription Drugs, supra note 34, at 6-8; B. Barber, supra note 35, at 41; H. Dowling, supra note 77, at 271-72. Contra, Examination of the Pharmaceutical Industry, supra note 99, at 319. Moreover, the country presently has a deficit of some 200 clinical pharmacologists. Mirkin, supra note 58, at 112.

\textsuperscript{107} Miller, Parts VII-VIII, supra note 92, at 89.

\textsuperscript{108} Hearings on Quality of Health Care, supra note 59, at 261 (statement of James L. Goddard, M.D.).

\textsuperscript{109} See notes 104 & 106 supra.

\textsuperscript{110} See notes 12-19 and accompanying text supra.

Many physicians believe that the importance of the necessity for such scientific rigor cannot be overemphasized.112 One prominent medical expert explained this importance as follows:

[A]n evaluation of a drug depends upon dozens, sometimes hundreds of variables that are not intrinsic in the drug or its dosage . . . .

Given these variables, the only accurate way to decide on the efficacy of a drug is to treat patients under conditions that will control as many variables as possible and to determine whether statistically significant differences can be obtained between patients who have received the drug and those who have not.113

This necessity, besides requiring proper testing, has another effect. It means that even if the physician successfully prescribes a nonapproved use for his patients, the drug in the future still may not be safe or efficacious for all similarly situated patients.114

The potential that a physician might make an improper risk/benefit decision has important consequences for drug consumers. Past experience with physician prescribing practices for nonapproved purposes suggests that the adverse reactions which result from prescribing mistakes can pose serious public health consequences.

The Consequences of Mistaken Risk/Benefit Decisions.—There are two types of evidence on the extent or scope of injuries which may be caused by the prescription of a drug for a nonapproved purpose. The first type of evidence, which consists of data which directly associates patient injuries with the prescription of a drug for a nonapproved purpose, suggests that a considerable number of patients each year may be harmed by such prescribing. The second type of evidence, which consists of reports on the extent of mistaken risk/benefit decisions by physicians, but without any indication as to what harm may have resulted, supports the initial conclusion.

Because the financial resources necessary to properly test an unapproved drug may be considerable, serious scientific testing may not occur until the manufacturer of the drug undertakes to sponsor such testing. Temple, supra note 60, at 1157; TASK FORCE ON PRESCRIPTION DRUGS, supra note 34, at 9. As a result, the lag between discovery of the new use and FDA approval becomes greater. See notes 71-79 and accompanying text supra.


113 H. Dowling, supra note 77, at 127. The variables include such facts as the time of day the drug was taken, with what foods, with what other drugs, whether the patient exercised afterwards, the patient's general health, the condition of the patient's liver, kidneys, and other organs affected by the drug and whether the patient took the drug as directed. Id.

114 Id. at 128.
Evidence On Adverse Reactions.—The fact that at least some prescriptions for nonapproved purposes can pose serious therapeutic dangers is documented by a congressional investigation into the use of Methotrexate,115 a drug approved by the FDA for the treatment of acute childhood leukemia and for other types of cancer.116 The investigation revealed that, beginning in 1958, there were reports appearing in the medical literature which supported the use of Methotrexate to treat psoriasis and that by 1967 the drug became the standard dermatological treatment for severe psoriasis.117 By 1971, although Methotrexate prescriptions for psoriasis had declined, for many physicians it was still standard practice to prescribe the drug.118 Thus, for a considerable number of years, the use of Methotrexate for the treatment of psoriasis was widespread.

When Methotrexate was approved for the treatment of acute leukemia, it was discovered that the drug posed a considerable number of serious side-effects.119 Nevertheless, the risk/benefit ratio was favorable because of the lethal nature of acute leukemia.120 By comparison, psoriasis is rarely lethal.121 As a consequence, when the FDA had sufficient information to approve the use of Methotrexate for treatment of psoriasis, it did so only for cases of severe and disabling psoriasis, apparently finding that the danger of the drug was too great for a more widespread use.122

Before FDA approval, with its suggested limitations on the drug's use, the FDA believed that physicians had failed adequately to perceive the dangers associated with the use of Methotrexate and

116 Id. at 13 (statement of James Grant). Methotrexate also was approved to treat choriocarcinoma and lymphosarcoma. Id.
117 Id. at 15 (statement of James Grant), 108 (statement of Henry Roenigk, Jr., M.D.).
118 Id. at 108 (statement of Henry Roenigk, Jr., M.D.). At its highpoint in usage, a 1967 survey indicated that 87% of those surveyed used Methotrexate, while another study showed that by 1971 usage had declined to 68% of those surveyed reporting they had used Methotrexate. Id.
119 Id. at 2-3 (copy of the package insert), 14 (statement of James Grant). Among the side-effects which were associated with Methotrexate were ulcerative stomatitis, diarrhea, hemorrhagic enteritis, hepatic dysfunction, cirrhosis and liver failure, renal disease, monosuppression, teratospermia, fetal abnormalities, pneumonitis, alopecia, skin rashes, and combinations of these effects. Id. at 14.
120 Id. at 17 (statement of James Grant).
121 Id. at 116 (statement of Henry Roenigk, Jr., M.D.).
the need to monitor carefully patients undergoing therapy. The consequence of these mistakes was severe. During this period, the FDA identified fifteen deaths which were reported in the medical literature and elsewhere as resulting from the prescription of Methotrexate for psoriasis in combination with other drugs. One medical expert believed that the effects of the other drugs could be disassociated in nine of those cases so that Methotrexate could be said to have directly caused those deaths. Because of the lack of any reliable adverse reaction reporting system, other evidence and expert opinion presented during the investigation indicated that the number of Methotrexate-related deaths could be significantly higher than presented by these reports.

Another example of the potentially serious consequences of mistaken prescribing decisions concerning nonapproved purposes involves the antibiotic Chloromycetin, now approved only to treat typhoid and a few other rare indications. In 1952, three years after the drug's introduction and after temporarily removing it from the market as unsafe, the FDA recommended to physicians that, because the drug caused a usually fatal blood disorder, its use be carefully limited and that it not be used indiscriminately for minor infections. Later evidence indicated that this disorder would occur in one of every 24,000 persons who took the drug. Nevertheless, despite the FDA's actions and an almost constant stream of medical journal articles recommending limited usage, a study found that the drug was still prescribed in one year for over four million patients—only 400 of whom had any disease for which the drug was recommended for use. Reports of Chloromycetin-caused fatalities and other data indicate that eighty percent of those

123 Methotrexate Hearings, supra note 115, at 18 (statement of James Grant), 31 (statement of Gail Goodrich).
124 Id. at 15 (statement of James Grant), 21 (statement of James Grant, Appendix A, Mortality).
125 Id. at 116 (statement of Henry Roenigk, Jr., M.D.).
126 Nyfors, Methotrexate in Psoriasis, 2 Lancet 1251 (1968), cited in Methotrexate Hearings, supra note 115, at 77 n.5; Methotrexate Hearings, supra note 115, at 122 (statement of Henry Roenigk, Jr., M.D.).
128 Merrill, supra note 36, at 18, 27.
129 M. Mintz, By Prescription Only 8, 12-13 (1967).
130 Id. Other estimates put the incidence of the blood disorder anywhere from one in 60,000 to one in 225,000. Campbell, supra note 127, at 129.
131 H. Dowling, supra note 77, at 279; M. Mintz, supra note 129, at 14-15.
132 Hearings on Competitive Problems, supra note 98, at 2487 (statement of Dr. James T. Weston), cited in J. Gibson, supra note 17, at 357.
fatalities were in patients given the drug for other than medically accepted indications, often a common cold.133

Evidence of Mistaken Risk/Benefit Decisions.—Besides the information on adverse reactions caused by drugs used for nonapproved purposes, other investigations and studies show that the incidence of such improper prescribing decisions may be considerable. The studies and investigations reaching that result are both quantitative and qualitative in nature.

The quantitative studies attempted to measure the extent to which the prescribing practices of physicians were in conformity with expert medical opinion. Those studies found little conformity for at least several kinds of drugs, primarily antibiotics.134 Two studies in the early 1970s, for example, agreed that less than one-third of all antibiotic prescriptions could be considered unquestionably correct or “rational.”135 Studies of other drugs reached similar results. A 1974 study of the hospital use of three drugs, for example, found that two of the drugs were administered for nonapproved purposes in variance with the medical literature respectively seventy-eight percent and fifty-eight percent of the time.136

Qualitative information from 1973 congressional hearings similarly suggests that there may have been misuse of two drugs for a nonapproved purpose of contraception. One of these drugs, Diethylstilbestrol (DES), when finally approved by the FDA, was limited to use in emergency situations requiring contraception, such as rape or incest, because it was found that, if the drug was not effective, female offspring could develop cancer.137

Despite these dangers, before the FDA approved DES as a postcoital contraceptive, it was used in at least fifteen university

133 Merrill, supra note 36, at 27.
136 Mundy, supra note 65, at 1749.
137 Hearings on Quality of Health Care, supra note 59, at 44 (statement of Charles Edwards, M.D.), 216 (statement of Peter Greenwald, M.D.). This consequence was particularly disastrous for some children since for a time DES was given to pregnant women to prevent miscarriages. The danger to the resulting children became so serious that in 1971 the FDA wrote all physicians in the country warning them not to use DES for pregnant women. Id. at 201-02 (reprinting HEALTH RESEARCH GROUP, REPORT ON THE MORNING AFTER PILL 1-2 (1972)).
health centers where apparently little or no effort was made in most cases to determine whether the pregnancy was an emergency situation, whether the woman was already pregnant, or whether there was a family history of breast or genital cancer, circumstances which increase the likelihood of the unfavorable effect. Moreover, in most cases the women given the drug were not informed about its dangers, including the wisdom of an abortion should the drug prove to be ineffective for that patient.

A similar situation was revealed concerning the use of Depo-Provera. When the IND testing of the drug for FDA approval revealed that it caused cancer in animals, use of the drug was carefully limited and patients were required to sign consent forms acknowledging the risk of cancer. Despite these developments, unapproved use of the drug as a contraceptive was found in Tennessee and was thought to exist widely elsewhere under circumstances which raised questions concerning the appropriateness of the prescriptions and of the quality of the informed consent obtained, if any such consent was obtained.

The foregoing studies on physician prescription errors do not establish the scope of such errors or the degree of harm which is caused to patients as a result. Definitive information of that sort must await the FDA's development of a comprehensive system of adverse reaction reporting, which is probably years away. Nevertheless, it seems likely that adverse effects, in considerable numbers, are caused by inaccurate physician decisions.

To the extent patients are harmed by the prescription of drugs for nonapproved purposes, the present regulatory system offers those

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139 *Id.* at 199-200 (statement of Sidney Wolfe, M.D.). The use of DES was being studied under carefully controlled circumstances at university health centers other than those surveyed. *Id.*
140 *Id.* at 194-96 (statement of Anita Johnson).
141 *Id.* at 21, 42-44 (statement of Charles Edwards, M.D.).
142 *Id.* at 82, 86 (statement of Robert Hutcheson, Jr., M.D.), 94-95 (statement of James Brown, M.D.).
143 *Id.* at 62 (statement of Nathan Kase, M.D.).
144 *Id.* at 56-57 (statement of Marcia Greenberger), 57-60 (statement of Anna Burgess), 60-61, 66-68 (statement of Nathan Kase, M.D.). *Contra, id.* at 78-82 (statement of Leonard Brooks, M.D.), 85-87 (statement of Robert Hutcheson, Jr., M.D.).
145 See note 84 *supra.*
146 J. Gibson, *supra* note 17, § 13.9.4, at 371; cf. Mirkin, *supra* note 58, at 106 (adverse reaction problems derive from cultural passion for drug use, from unsatisfactory testing of drugs, and from doctors' poor therapeutic training).
patients the opportunity to sue the physician for malpractice. A review of the judicially developed malpractice system will demonstrate that the system is ineffective in controlling or preventing drug injuries resulting from prescriptions for nonapproved purposes.

**Malpractice Liability for Nonapproved Prescribing**

Since the FDA lacks regulatory authority over nonapproved prescribing, the principal means for societal control over how physicians use drugs for that purpose is the tort negligence system. But the tort system, involving liability both for negligence and for failure to obtain a patient’s informed consent, does not constrain physicians’ use of drugs for nonapproved purposes.

*Negligence Liability*

*The Traditional Standard of Care.*—For a favorable verdict, the malpractice plaintiff must establish that a physician owed the patient a duty to meet a certain standard of care and that the physician’s failure to meet that standard of care caused the plaintiff harm. The latter requirement, causation, involves a “but-for” test (But for the defendant’s conduct, would the plaintiff have sustained damages?) coupled with a “proximate cause” test (Was defendant’s conduct a proximate cause of plaintiff’s injury?).

The following discussion assumes that a plaintiff could meet the causation requirement. In reality, proof of facts sufficient to make out causation may be a difficult matter.

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147 The only other important mechanism, physician peer review, does not presently exist for physician prescribing practices. See note 309 and accompanying text infra. Severe and continuous abuses might subject a physician to review of the license for authority to practice. See, e.g., Kansas State Bd. of Healing Arts v. Foote, 200 Kan. 447, 436 P.2d 828 (1968).


149 D. HARNEY, supra note 30, § 4.1.

150 Rheingold, Causation Issues in Medical Malpractice, Cases, in MODERN TRENDS IN MEDICAL MALPRACTICE 55, 57 (1978).

151 D. HARNEY, supra note 30, § 4.1. The matter is difficult because the effects of medical negligence need to be distinguished from the results of the disease or injury from which the patient is suffering. 1 D. LOUISELL & H. WILLIAMS, MEDICAL MALPRACTICE § 11.29, at p. 11-77 (1977). Consequently, expert medical testimony usually is required. Id. at p. 11-83. It has been suggested that the drug package insert also be accepted as evidence of causation. Comment, Package Inserts For Prescription Drugs as Evidence in Medical Malpractice Suits, 44 U. CHI. L. REV. 398, 448 (1977) [hereinafter cited as CHICAGO Comment]. Since the FDA demands a certain level of proof that the information contained in the insert is accurate, it is believed the information in the inserts is at least as good as most expert testimony. Id. at 448.
tiff can meet this burden, the extent of protection offered by the malpractice system can more readily be examined.

The standard of care is normally the degree of skill and knowledge possessed by similar physicians in the same, or in some jurisdictions, similar communities.\(^{152}\) Under this definition, if a physician chooses a drug therapy which is not used by any other physician, there should be liability for any injuries which are caused inasmuch as the physician is not giving the patient the same care which would be given by other similarly situated physicians. Since the 1871 decision in *Carpenter v. Blake*,\(^ {153}\) in which a physician was charged with departing from normal medical practice in setting a dislocated elbow, the case law has supported this result.\(^ {154}\) There are some important qualifications to this general rule, however.

One of the qualifications is that a medical procedure need not be used by a majority of comparable physicians for the courts to consider it within the standard of care owed a patient. To so hold, it has been decided, would discourage the use of new therapies which generally may be beneficial to patients.\(^ {155}\) Consequently, a procedure may be proper if it is used only by a "minority of respectable medical practitioners."\(^ {156}\)

A second qualification to the general rule is that, even if the therapy has not been used by at least a minority of similar physicians, the doctor can still avoid liability by justifying the reasonableness of the treatment.\(^ {157}\) This may be done by showing that a

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\(^{152}\) D. Harney, supra note 30, § 3.3.

\(^{153}\) 60 Barb. 488 (N.Y. Sup. Ct. 1871), rev'd on other grounds, 50 N.Y. 696 (1872).

\(^{154}\) D. Harney, supra note 30, § 3.10, at 158-59; Campbell, supra note 127, at 1310; Note, *Torts: Physicians and Surgeons: Malpractice: Liability for Medical Experimentation*, 40 Calif. L. Rev. 159, 160 (1952) [hereinafter cited as California Note].


This represents a change in attitude. At one time, some courts considered any departure from established procedures which resulted in patient injury to be malpractice. California Note, supra note 154, at 160-61. Consequently experimentation of any sort was judicially condemned. See, e.g., Owens v. McCleavy, 313 Mo. 213, 223, 281 S.W. 682, 685 (1926); Carpenter v. Blake, 60 Barb. 488, 514, 523, 524 (N.Y. Sup. Ct. 1871), rev'd on other grounds, 50 N.Y. 696 (1872); Sawdey v. Spokane Falls & N. Ry. Co., 30 Wash. 349, 350, 70 P. 972, 975 (1902).

\(^{156}\) D. Harney, supra note 30, § 3.10, at 159; Campbell, supra note 127, at 311. See, e.g., Leech v. Bralliar, 275 F. Supp. 897, 902 (D. Ariz. 1967); Baldor v. Rogers, 81 So. 2d 658, 660 (Fla. 1954).

similar physician, possessing the same skill and knowledge, would have used the innovative therapy under the circumstances. To the extent that other comparable therapies do not exist to treat the illness, the physician can more easily make this showing.

The most striking example of the second qualification involved the first and only implantation of an artificial heart in a human being. After the patient's death, the surgeon was sued on several grounds, including the allegation that the surgery constituted negligence in the form of impermissible "experimentation" since no other physician had previously engaged in this form of treatment. The United States Court of Appeals for the Fifth Circuit, which affirmed the district court's direction of a verdict for the defendant surgeon, found that the record contained no evidence that the physician's actions were inconsistent with "how a reasonably careful and prudent physician would have acted under the same or similar circumstances." The record included extensive testimony that, without the transplant, the patient faced imminent death.

**Application to Prescriptions for Nonapproved Purposes.**—As a result of the foregoing legal developments, in the most common situation where a physician prescribed a drug for a nonapproved purpose in the same manner as other similar physicians would have done, it is likely the patient could not recover damages if the drug caused a harmful adverse reaction. This result is likely for two reasons. First, the size of the minority of physicians who use a particular method of treatment may not need to be very large in order to establish a standard of care. For example, in *Leech v. Bralliar*, a physician was sued for using a method to treat "whiplash" injuries caused by an automobile accident which was used by only "a small minority of physicians in the United States." While the physician was found liable for the injuries he caused, it was because he improperly used the treatment method. The court specifically found

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158 *Id.*
159 CALIFORNIA NOTE, supra note 154, at 164. *Contra*, Baldor v. Rogers, 81 So. 2d 658, 661 (Fla. 1954).
160 Karp v. Cooley, 493 F.2d 408, 415 (5th Cir. 1974).
162 Karp v. Cooley, 493 F.2d 408, 423 (5th Cir. 1974).
164 493 F.2d at 423.
165 *Id.* at 417.
167 *Id.* at 899.
that the method itself was an acceptable standard of care.\textsuperscript{168}

Second, prescriptions for unapproved purposes pose the greatest danger when use becomes widespread.\textsuperscript{169} In such circumstances, the possibility that a physician with inadequate knowledge will prescribe a drug is the greatest.\textsuperscript{170} At the same time, in such circumstances, the physician's protection from an adverse malpractice verdict is the greatest since at least a minority of other physicians will be engaged in a similar practice.

*Alternatives to the Traditional Legal Standards.*—In a situation of widespread use for a nonapproved purpose, therefore, the patient may win his suit only if he convinces the court that what is a common practice among physicians is not the standard of care which appropriately is owed to the patient. There are two possible methods by which to make that argument: (1) that the drug is being used by dissimilar physicians, who have greater training and expertise than the physician in question, and (2) that the common use of the drug represents unsound medical practice. In the latter argument, the patient may try to use the FDA-approved medical insert as evidence of the proper standard of care which is owed. The probable lack of success of these arguments is explained below.

*Differentiating Standards of Care.*—Knowledge about a nonapproved use of a drug usually comes to physicians from the research work done by other physicians.\textsuperscript{171} Through publications and seminars, some physicians educate others to innovative therapies. Much of this early work with a new use for a drug typically occurs at university hospitals or other research institutions.\textsuperscript{172} At such locations, therapy is conducted by teams of physicians and scientists who represent a wide spectrum of skills and who are trained in a medical speciality denoted as clinical investigation.\textsuperscript{173} Moreover, patients are kept under close and frequent observation.\textsuperscript{174} The standard of care owed the patient at such institutions is said to be that degree of skill present at other similar institutions.\textsuperscript{175}

\textsuperscript{168} *Id.* at 902.
\textsuperscript{169} See notes 69-70 and accompanying text *supra*.
\textsuperscript{170} See notes 92-99 and accompanying text *supra*.
\textsuperscript{171} Morse, *supra* note 155, at 760-61.
\textsuperscript{172} *Id.*
\textsuperscript{173} *Id.*
\textsuperscript{174} *Id.* at 761.
\textsuperscript{175} *RESTATEMENT (SECOND) OF TORTS* § 229A (1965); *W. PROSSER*, *supra* note 148, § 32, at 164.
If a new drug use has been limited to such research institutions, it can be argued the practicing physician should not be able to defend his own use for the new purpose based on its prior use. Since the practicing physician may lack the resources and training of his clinical counterpart, it could be argued that the prior use was not made by similarly situated physicians. Consequently, under this line of argument, the duty of care which the practicing physician owes his patient is not to use the drug.\textsuperscript{176}

There are two problems with such an argument. If the argument was to be given judicial sanction, it might limit the spread of innovative therapy, restricting such therapy to university hospitals.\textsuperscript{177} In the long run, such restrictions could injure the public health if use of promising therapies were curtailed.

More significantly, the difference in skill level between clinical investigators at research institutions and practicing physicians is not an absolute one, but a spectrum. For example, persons engaged in medical specialities or subspecialities might possess skill near to, equal to, or in excess of the skill level of the research clinical investigator. At least some nonresearcher practicing physicians could successfully argue that they have the skills necessary to be compared to the researchers.

In addition, as more information is learned and published concerning therapeutic innovations, arguably the number of physicians who are skillful enough to allow use of the drug increases. When this happens, even physicians far removed in skill level from their research colleagues may be able to successfully claim that their use of the drug should be compared to its use by their colleagues. Accordingly, the courts may view the differences in skill levels as less important.

Nevertheless, a practicing physician's use of an innovative therapy might be contrasted with research use if the therapy has not been used to any extent outside of research institutions. Even if this theory were judicially recognized, it may not offer much protection to injured patients. The greatest dangers are posed when the unapproved use becomes widespread.

The Package Insert as the Standard of Care.—Because the standard of care practiced by a community of physicians in certain cir-

\textsuperscript{176} Cf. \textit{Restatement (Second) of Torts} § 229A, comment \textit{d}, at 74 (1965) (doctor who does not claim superior skill is not held to the higher standard). \textit{See} notes 104-06 and accompanying text \textit{supra}.

\textsuperscript{177} \textit{See} notes 88-91 and accompanying text \textit{supra}.
cumstances may constitute an unacceptable medical practice, some courts will allow a plaintiff to try to establish that a different standard of care was owed. Otherwise, the medical profession becomes, in effect, the judge of its own culpability.

In those jurisdictions, a plaintiff can try to claim that the FDA package insert constitutes the acceptable medical standard of care and that any departure from it, even if common among similar physicians, constitutes negligence. That argument, to date, has not been accepted. Nevertheless, the insert may still be used by plaintiffs in some courts as nonconclusive evidence of the standard of care which was owed the patient. To understand the implications of these decisions, they must be examined in some detail.

Previous Case Law.—Because attempts to introduce the package insert as evidence of a physician's standard of care involve the use of declarations made out of court offered for their truth, many courts have held the insert inadmissible as hearsay. Nevertheless, in some of these jurisdictions, the insert may be used as the basis for expert testimony and as the source of questions for cross-examination if the expert being cross-examined will recognize the insert as medically authoritative. But, because the insert is hearsay, in neither instance can the factfinder use it to support a judgment for the party presenting the evidence.

By comparison, since the insert will constitute hearsay only if it is offered for the truth of the statements contained therein, other jurisdictions have admitted the insert to be used by the factfinder as proof that the physician had notice of the information contained in the insert. For example, in a case involving a warning contained

178 D. Harney, supra note 30, at § 3.1(B).
179 Id.; W. Prosser, supra note 148, § 32, at 165.
181 See notes 192-98 and accompanying text infra.
183 Chicago Comment, supra note 151, at 419 n.105.
in the insert that a drug was not for pediatric use, the court admitted
the insert not to prove the drug "was unsafe for use upon a child,"
but as "evidence of a warning which the physician disregards at his
peril, and his disregard of it is relevant upon the issue of his use of
reasonable care, where other evidence shows the drug is, in fact, dan-
gerous to a child."187

Contrary to the results in the previous cases, some courts have
admitted the insert for proof of the statements contained therein,
usually without an explanation of why the evidence, so used, is not
hearsay.188 One court which did address the issue of hearsay found
that the insert could be admitted because it was objective—in the
sense that the manufacturer was not a party to the law suit—and it
was reliable—in the sense that the manufacturer's potential liability
for a failure to adequately warn physicians about use of the drug
promoted honesty.189 Most jurisdictions which admit the insert

187 Koury v. Folio, 272 N.C. 366, 376, 158 S.E.2d 548, 556-57 (1968). The need for in-
dependent evidence that the information contained in the insert is in fact true was emphasized
in Sharpe v. Pugh, 21 N.C. App. 110, 113, 203 S.E.2d 330, 333, aff'd without opinion by an

170, 180 (1957); Julien v. Barker, 75 Idaho 413, 423, 272 P.2d 718, 724 (1954); Ohligschlager v.
Proctor Community Hosp., 55 Ill. 2d 411, 417-18, 303 N.E.2d 392, 396 (1973); Nolan v. Dillon,
261 Md. 516, 540, 276 A.2d 36, 49 (1971); Mulder v. Parke Davis & Co., 288 Minn. 332, 338,
181 N.W.2d 882, 887 (1970); Marchese v. Monaco, 52 N.J. Super. 474, 487, 145 A.2d 809, 816
(App. Div. 1958), cert. denied, 28 N.J. 565, 147 A.2d 609 (1959); Crouch v. Most, 78 N.M. 406,
408, 432 P.2d 250, 252 (1967).

88 S.D. 446, 453, 221 N.W.2d 39, 42-43 (1974). A detailed academic consideration of the
hearsay dangers of the package insert concluded the insert was reliable. CHICAGO Comment,
supra note 151, at 422-26, 449. First, since most information in the insert is based on "well-
controlled clinical studies," see note 12 and accompanying text supra, the four testimonial
dangers of hearsay (sincerity, memory, perception, and narration) are significantly reduced by
the scientific basis of studies. Temple, supra note 60, at 1155; CHICAGO Comment, supra note
151, at 423. Second, to the extent some information like adverse reactions is from nonscien-
tific sources such as physician observations, physician training should guarantee accurate per-
ception, although sincerity may be a problem since by making such reports the physician may
subject himself to negligence liability. Id. at 423-24. Third, the marketing incentives of the
drug company and the cautionary posture of the FDA ease sincerity problems that may arise
when the two sides negotiate what information the insert will contain. Id. at 424. Finally, the
narration risk that the jury will misunderstand the information in the insert, while great, is
ameliorated by the availability of physician testimony in most suits. Id. at 426. Balanced
against these considerations, the need for evidence may be sufficiently compelling to justify its
admission. That need arises from the difficulty plaintiffs have in obtaining expert physician
testimony and the considerable expense of such testimony. Id.

Given these indices of reliability, it can be argued the package insert is admissible as one
of several hearsay exceptions. It has been suggested the inserts could qualify as public records
and reports, as commercial publications, as learned treatises, or as otherwise reliable to the
same degree as other exceptions, all categories of hearsay exceptions recognized by at least the
Federal Rules of Evidence. Comment, Evidentiary Aspects of Manufacturer Recommendations
have limited the weight to be accorded it by holding that the insert alone is insufficient proof to establish a prima facie case of what standard of care the physician owes to the patient.\textsuperscript{190} Commonly, no explanation is offered for that decision.\textsuperscript{191} One such court did, however, mention counsel's arguments that the inserts were not sufficiently current, were overcautious, and were viewed by most physicians as supplemental to their clinical experience in furnishing information about a drug.\textsuperscript{192}

If the insert alone is insufficient to prove the physician's standard of care, in most of these jurisdictions the plaintiff would have to present additional evidence in the form of expert testimony.\textsuperscript{193} In a few jurisdictions, however, the additional evidence need not be expert in origin if the jury can easily understand the nature of the standard of care which is owed.\textsuperscript{194}

In a minority of three jurisdictions, there is no need for any additional evidence to prove a standard of care, expert or not. In these jurisdictions, the package insert is sufficient to establish a prima facie case.\textsuperscript{195} As a result, once the insert is accepted into evidence, it be-


\textsuperscript{193} W. Prosser, supra note 148, § 32, at 164.

\textsuperscript{194} Monk v. Doctors Hosp., 403 F.2d 580, 583 (D.C. Cir. 1968) (where the manufacturer's instructions directed the location on the patient's body for attachment of an electrosurgical machine, the testimony of the defendant physician, combined with the instructions, were sufficient to take the case to the jury because of their nontechnical nature); Sanzari v. Rosenfeld, 34 N.J. 128, 140, 167 A.2d 625, 633 (1960) (where the administration of Epinephrine for minor dental surgery was counterindicated in the insert for patients with high blood pressure, the jury's common knowledge that drugs can be harmful combined with the insert was sufficient evidence to avoid dismissal).


Where a drug manufacturer recommends to the medical profession (1) the conditions under which its drug should be prescribed; (2) the disorders it is designed to relieve; (3)
comes incumbent upon the physician to sufficiently explain the reasons for his departure from the recommendations of the insert. Failure to do so successfully will result in a verdict against the physician.\textsuperscript{196}

One court explained the decision against requiring evidence in addition to the insert as turning on the difficulties which malpractice plaintiffs have in obtaining favorable expert testimony.\textsuperscript{197} These difficulties have often resulted from a "conspiracy" by physicians not to testify against each other, often called the "conspiracy of silence."\textsuperscript{198}

Application to Prescriptions for Nonapproved Purposes.—The survey of the treatment of the package insert by the courts shows that the insert in fact will be of little assistance to prove that the community standard of care is not the one by which to measure the care owed the patient. This conclusion corresponds to the advice being given physicians by their attorneys. One prominent malpractice lawyer has advised: "[T]he legal significance of the package insert . . . does vary among the different jurisdictions. . . . It seems reasonable to assume, however, that even under the most rigid legal interpretations, the physician may on his own responsibility, . . . administer a drug for an unapproved use . . ., providing he can establish a reasonable medical rationale."\textsuperscript{199}

\textbf{Informed Consent Liability}

Since it is believed that most physicians do not inform patients that they are receiving a drug for a purpose not approved by the FDA,\textsuperscript{200} a plaintiff might also seek damages under the doctrine of

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\textsuperscript{197} Id. at 336, 181 N.W.2d at 885.


\textsuperscript{199} Hirsh, \textit{The Medicolegal Implications of the Package Insert}, CASE & COMMENT, Jan.-Feb. 1977, at 14, 16, 18.

\textsuperscript{200} This belief is derivative. Long-time commentators on informed consent are of the opinion that few physicians disclose any meaningful information, including presumably the nonap-
informed consent for injuries suffered. The following discussion analyzes why such potential relief would be unlikely.

**Applicable Legal Tests.**—Consistent with the notion that a battery—the unauthorized touching of another—was cognizable as a tort for which damages could be recovered, the courts early made two important decisions regarding medical treatment. First, it was decided that a physician committed a battery if a patient was treated without the consent of the patient to that treatment. Second, the physician also was found to have committed a battery when he engaged in treatment which was beyond the scope of the consent which was obtained. By such decisions, the courts effectuated a principle of self-determination that a patient had the right to determine what should be done with the patient’s own body.

It became apparent, however, that the patient’s right of self-determination could be invaded in another manner. Unless a physi-
cian disclosed to a patient a reasonable amount of information concerning both the diagnosis and the nature and risks of a particular form of treatment, the viability of any consent which might be given would be questionable. To protect the patient from this more subtle invasion of a right to self-determination, a duty of reasonable disclosure was created with the failure of the duty constituting negligence. As a consequence, a traditional negligence rubric of tests arose: (1) did the physician, as measured by the prevailing medical practice in the community, fail to adequately inform the patient of the reasonably foreseeable risks involved in the treatment that would be received; (2) was the failure of the physician the proximate cause of an injury to the patient measured by whether or not the patient would have submitted to the treatment if given adequate information; and (3) did the injury result in damages in the form of an injury to the patient.

When judges, however, were made aware of physicians' concerns that disclosure of some medical information might be therapeutically counterproductive in a given instance of an emotionally

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206 It could be argued that unless sufficient information is provided to a patient for the patient's decision concerning treatment to be informed, any consent which is given is not consent at all. 2 D. LOUISELL & H. WILLIAMS, supra note 151, § 22.08, at 594.58. If this theory were followed, the physician's action would constitute a battery. See note 210 and accompanying text infra. It has not been followed, and most courts instead view the matter as one concerning negligence. This has been explained on the ground that there was a consent given, but, in obtaining that consent, the doctor failed to meet his due care duty to disclose pertinent information. Cobbs v. Grant, 8 Cal. 3d 229, 240-41, 502 P.2d 1, 8, 104 Cal. Rptr. 505, 512 (1972). It has been suggested that courts were motivated to put relief on a negligence basis for a number of reasons including: the social stigma of the battery claim on the physician; the possibility that malpractice insurance policies did not cover battery; an unwillingness to allow punitive damages associated with battery; the lack of hostile intent, a usual battery component, on the part of the physician; and the longer statute of limitations for negligence actions. Trogun v. Fruchtman, 58 Wis. 2d 569, 599-600, 207 N.W.2d 297, 313 (1973); Riskin, supra note 204, at 592-95; DRAKE Note, supra note 202, at 701. Such a basis, however, has placed a more complicated burden of proof on plaintiffs than would an action based on battery where the burden of proof consists only in proving lack of consent and a touching. G. ANNAS, L. GLANTZ, & B. KATZ, supra note 161, at 29; Riskin, supra note 204, at 585; see note 56 and accompanying text supra.

207 Note, Informed Consent—A Proposed Standard for Medical Disclosure, 48 N.Y.U. L. Rev. 548, 549-52 (1973) [hereinafter cited as N.Y.U. Note]. For a listing of recent cases adopting this standard, see DRAKE Note, supra note 202, at 704 n.57. The standard of disclosure is subject to two important qualifications. First, the courts require only reasonable, not full, disclosure of all the possible consequences of treatment. See, e.g., Williams v. Menehan, 191 Kan. 6, 8, 379 P.2d 292, 294 (1963). Second, a physician is required only to disclose pertinent risks of which he has actual knowledge or reason to know. DRAKE Note, supra note 202, at 705.
unstable or unduly apprehensive patient, many courts refined the first test of the rubric.\textsuperscript{208} Physicians were allowed a “therapeutic privilege” defense to the failure to disclose necessary information when it could be established by a preponderance of the evidence that disclosure of the information would have increased the risks of treatment, foreclosed a rational decision by the patient, or posed psychological damage to the patient.\textsuperscript{209}

Moreover, realizing that most plaintiffs who do sue would testify on the causation question in their favor by asserting that but for the inadequate information they would not have agreed to the medical procedure, most courts also modified the second test of the rubric.\textsuperscript{210} To counter this tendency, an objective test to measure proximate cause came to be used: that is, would the average prudent person in the plaintiff’s position, if properly informed, have foregone the treatment?\textsuperscript{211}

In a minority of jurisdictions, these developments, which made it more difficult for a plaintiff to prevail,\textsuperscript{212} were countered by another development which worked to favor plaintiffs. Some courts were troubled by what they saw as a logical inconsistency in the prevailing community practice standard. The theory of informed consent was to protect a patient’s interest in self-determination so that


\textsuperscript{209} Canterbury v. Spence, 464 F.2d 772, 789 (D.C. Cir. 1972); Cobbs v. Grant, 8 Cal. 3d 229, 246, 502 P.2d 1, 12, 104 Cal. Rptr. 505, 515-16 (1972); YALE Note, \textit{supra} note 204, at 1564. Normally, a physician establishes the defense by use of expert testimony that his medical judgment was justified under the circumstances. \textit{Id.} at 1565.

\textsuperscript{210} \textit{E.g.}, Cobbs v. Grant, 8 Cal. 3d 229, 245, 502 P.2d 1, 11-12, 104 Cal. Rptr. 505, 515-16 (1972).

\textsuperscript{211} Canterbury v. Spence, 464 F.2d 772, 787 (D.C. Cir. 1972); Cobbs v. Grant, 8 Cal. 3d 229, 245, 502 P.2d 1, 11-12, 104 Cal. Rptr. 505, 515-16 (1972); DRAKE Note, \textit{supra} note 202, at 706-07; N.Y.U. Note, \textit{supra} note 207, at 550. This requirement has been criticized as inconsistent with protecting an individual’s right of self-determination. Capron, \textit{supra} note 204, at 420. For one thing it offers no protection to the patient who desires to make an unreasonable decision. DRAKE Note, \textit{supra} note 202, at 713. Moreover, the belief that there is some one “reasonable” or “prudent” response to every medical situation has been called “nonsense,” both from the point of view of the physician and from that of the patient. Katz, \textit{supra} note 200, at 163.

Reforms which have been advocated include: giving physicians the burden of proving lack of causation, Riskin, \textit{supra} note 204, at 604-06; adopting a causation standard: had the withheld information been given, would it have been a “substantial factor” in the plaintiff’s decision to forgo treatment, DRAKE Note, \textit{supra} note 202, at 713; adopting a subjective standard of causation, Capron, \textit{supra} note 204, at 421; and eliminating the causation requirement altogether, Riskin, \textit{supra} note 204, at 601-03.

\textsuperscript{212} For a further discussion of these events and their possible cause, see notes 384-86 and accompanying text \textit{infra}.  

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the patient could make a rational decision whether to undergo the proferred therapy. Yet, under the prevailing standard, the test of whether information had to be provided bore no relationship to the patient's need for the information. It was based instead on the custom of physicians in the community.\textsuperscript{213}

As a result, these minority-rule courts have replaced the prevailing professional standard of care standard with a test which determines whether the information not disclosed was "material" to the patient. Information will be considered material when "a reasonable person, in what the physician knows or should know to be the patient's position, would be likely to attach significance to the risk or cluster of risks in deciding whether or not to forego the proposed therapy."\textsuperscript{214} While the foregoing test is objective, at least one court, without explicitly so declaring, may have adopted a subjective approach. It would ask if the information was material not to a "reasonable person," but to the "particular patient" involved in the law suit\textsuperscript{215}.

\textsuperscript{214} Id. at 787. Accord, Wilkinson v. Vesey, 110 R.I. 606, 627, 295 A.2d 676, 689 (1972). For an extensive listing of courts which purportedly have followed the minority standard, see Riskin, supra note 204, at 587 n.46; Drake Note, supra note 202, at 713 n.57. It is not clear, however, that all of these courts have adopted the materiality standard to the same degree and with the same lack of qualifications as Canterbury and Wilkinson. See Comment, New Trends In Informed Consent?, 54 Neb. L. Rev. 66, 86-88 (1975) [hereinafter cited as NEBRASKA Comment].

The materiality standard, like its majority counterpart, has been criticized. For example, the choice of an objective standard, rather than a subjective test of whether the particular patient would have attached significance to the information had it been given, has been seen as a retreat from protecting individual self-determination, which is one of the purposes of informed consent. Capron, supra note 204, at 408.

In addition, since the minority courts recognize the therapeutic privilege, it has been noted that the minority viewpoint is not as far reaching as it first appears. In this view, the therapeutic privilege is seen as a procedurally different method of invoking the professional standard of care. Thus, the plaintiff is thought to be under the same disadvantages as with the majority rule. Katz, supra note 200, at 157. See also note 213 and accompanying text supra. The distinction between the two standards as a result has been termed "meaningless." Katz, supra note 200, at 168.

Finally, since the ambit or scope of the materiality standard is unlimited, physicians are left uncertain as to its effect and scope. Drake Note, supra note 202, at 711; N.Y.U. Note, supra note 207, at 554. For this problem two reforms have been urged: adoption of the FDA consent standards for a new drug experiment, id. at 555-63, or creation of a prima facie violation if a physician failed to give information concerning certain topics specified in advance. Yale Note, supra note 204, at 1561.

\textsuperscript{215} Cobbs v. Grant, 8 Cal. 3d 229, 245, 502 P.2d 1, 11, 104 Cal. Rptr. 505, 515 (1972). The case has been read as involving a subjective test in Capron, supra note 208, at 407; Drake Note, supra note 202, at 711. For a contrary interpretation, see Nebraska Comment, supra note 214, at 81.
Nondisclosure of Nonapproved Status as the Basis for Liability.—Because of the manner in which the law of informed consent has developed, one commentator was moved to this pessimistic assessment of the protection offered to patients: “[T]he doctrine of informed consent remains a symbol which despite widespread currency has had little impact on patient decision making, either in legal theory or medical practice.” Consistent with that assessment, under both the majority and minority tests for informed consent disclosure, it is not likely that nondisclosure of the nonapproved status of a drug often would be found to be a violation of the informed consent doctrine. Application of these tests to this situation makes this clear.

Application of the Majority Test.—Under the majority view, where the scope of disclosure is measured by the practice of similarly situated physicians as to disclosure, the patient would have little chance of winning an informed consent law suit for several reasons. First, if it is correct that presently few physicians engage in disclosure of the nonapproved nature of some drug treatment, the community standard would not be favorable to the patient’s case. Second, even if some physicians in the community did engage in such disclosure, a physician, to be exonerated, would need only to establish the likelihood that a reasonable minority of physicians did not engage in that practice. Finally, even if the patient got past those two hurdles to establishing the physician’s liability, the physician might still be able to interpose the therapeutic privilege as a defense.

Application of the Minority Test.—Under the minority test, where the factfinder measures the scope of disclosure by a “materiality” standard, the result is not as predictable. Since most often the factfinder would be the jury, the jury’s natural tendency to find for a

216 Katz, supra note 200, at 139.
217 See note 207 and accompanying text supra.
218 See note 205 and accompanying text supra.
219 Under the majority test, the plaintiff assumes the burden of proving that the physician’s failure to disclose material information was in violation of the prevailing medical practice in the community by production of expert medical testimony. Drake Note, supra note 202, at 702; Yale Note, supra note 204, at 1557 & n.67. Failure to meet this burden mandates a finding that the physician was under no duty to make the sought after disclosure, and he cannot be found liable. Id. Hence, unless a plaintiff could establish that some relevant segment of the medical community does disclose the nonapproved status of a drug, liability could not be established.
220 See W. Prosser, supra note 148, § 32, at 163.
221 See note 209 and accompanying text supra.
plaintiff\textsuperscript{222} might lead it to find that failure to disclose the nonapproved status of a prescription was a material omission.

Nevertheless, in many cases, an opposite result can be expected. The defendant physician will be able to develop strong testimony that information about the nonapproval of a drug bears no relevancy to the safe use of that drug.\textsuperscript{223} This, of course, is the belief which many physicians hold. Unless a plaintiff developed counter-evidence that a drug’s nonapproved status affects the risk of taking the drug,\textsuperscript{224} a jury may lack the perspective to know that they could find for the plaintiff on the issue of materiality.

\textit{The Necessity For An Alternative To Malpractice}

\textit{Viability of the Existing System.—}The twofold purpose of the tort negligence system in regulating drug prescribing is to compensate patients who are injured by physician negligence and to create thereby an incentive to physicians to avoid further injuries.\textsuperscript{225} Concerning nonapproved prescribing, the system fails in both regards.

For all prescription drugs, there is some risk that an adverse reaction will occur.\textsuperscript{226} The best protection against such an occurrence is an accurate risk/benefit appraisal by the physician of the drug for the patient.\textsuperscript{227} Because of several difficulties inherent in the existing process of drug regulation, however, that protection may not exist in the case of a drug prescribed for a nonapproved purpose.\textsuperscript{228}

Nevertheless, under the existing state of malpractice law, if the physician has committed nothing more than an error in judgment concerning the risk/benefit decision, it is unlikely that the patient can recover damages. Under a community standard of practice, the physician is entitled to prescribe a drug in the same manner as the physician’s colleagues, which includes the possibility of making such errors.\textsuperscript{229} Alternatively, the patient can seek compensation by alleging a lack of informed consent, but the failure to inform a patient of the nonapproved status of the drug prescription would potentially constitute liability only in a minority of jurisdictions and then only

\textsuperscript{222} R. Rabin, Perspectives on Tort Law 35 (1976).
\textsuperscript{223} See notes 88-90 and accompanying text supra.
\textsuperscript{224} See notes 94-114 and accompanying text supra.
\textsuperscript{225} Ball, supra note 111, at 574; Schwartz & Komesar, Doctors, Damages and Deterence: An Economic View of Medical Malpractice, 298 New Eng. J. Med. 1282 (1978).
\textsuperscript{226} See notes 28-32 and accompanying text supra.
\textsuperscript{227} See note 39 and accompanying text supra.
\textsuperscript{228} See notes 94-114 and accompanying text supra.
\textsuperscript{229} See notes 148-99 and accompanying text supra.
on a sporadic basis.\textsuperscript{230}

Since physicians will usually not be held liable for errors in judgment, little legal incentive exists for them to become better prescribers. Moreover, even if this assessment of the law underestimates the degree of physician liability, or the patient could recover because the physician did commit an act recognized as negligent, there are other impediments which probably prevent victims from being compensated. Many potential litigants will not sue because they will not realize that their injuries were drug-related side-effects.\textsuperscript{231} Others will be discouraged by the difficulty of obtaining a lawyer, even on a contingent fee basis, especially if the potential of winning compensation is not great.\textsuperscript{232}

Studies have demonstrated the considerable occurrence of these effects. A 1974 California analysis of 24,000 malpractice incidents detected in hospital records showed that no more than 4,000 injured patients filed claims.\textsuperscript{233} Similarly, it has been reported that forty percent of the file entries held by insurance companies of potentially compensable mishaps reported by physicians are never pursued by the patient.\textsuperscript{234} Despite numerous fatalities caused by the dangerous drug Chloromycetin, one commentator has concluded: "[Chloromycetin] has had the potential for generating many more law suits than have actually been brought to the attention of lawyers."\textsuperscript{235}

Nevertheless, perhaps only a small number of deserving plaintiffs are actually deterred from bringing suit. However, even in these circumstances, the malpractice system may not promote fair compensation. Often, the damage award which is received is less than the medical expenses and lost earnings incurred.\textsuperscript{236} In addition, an attorney's fee must usually be paid out of that award.\textsuperscript{237}

\textsuperscript{230} See notes 200-24 and accompanying text supra.
\textsuperscript{231} Merrill, supra note 36, at 89.
\textsuperscript{232} Hearings On The Quality Of Health Care, supra note 59, at 75 (statement of Marcia Greenberger).
\textsuperscript{233} Schwartz & Komesar, supra note 225, at 1286. Similarly, a study of records of patients discharged from two hospitals during 1972 revealed that of the large number of significant injuries resulting from malpractice, only one in every 15 led to malpractice claims. \textit{Id.} at 1286.
\textsuperscript{234} \textit{Id.} at 12.
\textsuperscript{235} J. Gibson, supra note 17, § 13.9.1, at 358.
\textsuperscript{236} Schwartz & Komesar, supra note 225, at 11 (estimating the average patient receives one-third to two-thirds of actual losses).
\textsuperscript{237} O'Connell, An Alternative To Abandoning Tort Liability: Elective No-Fault Insurance For Many Kinds of Injuries, 60 Minn. L. Rev. 501, 506-12 (1975-76) (estimating that the malpractice tort system returns 28 cents of the premium dollar to injured patients, of which only 12.5 cents reimburses the patient for losses not otherwise compensated).
Furthermore, if deserving patients sue, there will not necessarily be accident avoidance, since not all negligent physicians will be found liable. Furthermore, a recent Rand Corporation study shows that, because of the nature of malpractice insurance ratemaking, payment of compensation to victims, even in the high amounts which have led to calls for reform of the system, may not lead physicians to reform their practices. Since malpractice premiums, which are based on class ratings, are rarely influenced by a physician's record of claims, settlements, and verdicts, no individual physician has more than a slight pecuniary incentive to reduce the expected losses resulting from that physician's behavior. The study may, however, overstate this effect, since the notoriety alone of a malpractice suit may encourage physicians to avoid accidents.

Finally, the system fails in another important respect. As a society, we have chosen to try to prevent personal injury, even at considerable expense, in addition to compensating for injuries not prevented. This choice represents a commitment to the importance of the quality of human life and reflects a judgment that for many of our citizens the award of monetary damages is a poor substitute for lives that have been lost or bodies that have been damaged.

**Absolute Liability As An Alternative.**—Because of the largely noncompensable nature of drug injuries at present, Professor Richard Merrill, among others, has proposed that either the manufacturer or physician be absolutely liable for drug-caused injuries. Of the two, Professor Merrill has argued persuasively that the manu-

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238 Ball, *supra* note 111, at 575. This consequence has been described as having the following effects:

A court's failure to recognize negligent behavior has the effect of reducing the expected loss and thus permits physicians to set their investment in mishap avoidance below the ideal level. At the same time, the malpractice system as a whole is made more expensive because the proceeding raises administrative costs but yields no benefit.


241 *Id.*

242 1 D. LOUISELL & H. WILLIAMS, *supra* note 151, § 1.01, at 5-6.


244 *See* J. GIBSON, *supra* note 17, § 13.71, at 353.

facturer is in a better position to assume such an obligation. Manufacturers, unlike physicians, would be able to spread the cost of accidents over a large group of consumers who benefit from the use of drugs. Moreover, manufacturers, because of their ability to test drugs and gather and disseminate performance data are in a superior position to avoid accidents. Finally, insurance (or self-insurance) would be less expensive for manufacturers since, unlike physicians, manufacturers would be able to predict with some accuracy that certain drugs would be used.

Absolute liability, however, would not necessarily decrease the number of such drug-caused injuries since physicians would lack any incentive to engage in accident avoidance. To redress this problem, Professor Merrill proposes that any physician negligence which caused the injury would release the manufacturer from its absolute liability. To further ensure physician carefulness, Professor Merrill would have the courts treat any departure from the FDA’s package insert as prima facie evidence of negligence. This would give the package insert in all jurisdictions the same evidentiary status it now has in just three states.

While preferable to the existing system, Professor Merrill’s proposal applied to nonapproved prescribing has several distinct disadvantages. Under the proposal, since package inserts do not contain any prescribing information about nonapproved uses, manufacturers could claim that the prescription itself was negligent. Although as a result the physician in almost every case would be compelled to defend the prescription, many of these prescriptions would be medically proper. This may have the effect of generally discouraging nonapproved prescribing, possibly to the medical detriment of some patients.


246 Merrill, supra note 36, at 107. Accord, Reiter, supra note 245, at 49-54.
247 Merrill, supra note 36, at 108.
248 Id. at 108-10.
249 Id. at 108. Physicians who prescribe hundreds of drugs yearly are unable to predict which products might be used. Id.
250 Id. at 107, 111. A manufacturer would also escape liability if it established patient negligence. Id. at 108.
251 Id. at 108, 111-12.
252 See notes 195-98 and accompanying text supra.
253 The physician would be either called as a witness by the manufacturer, or, more likely, impleaded by the plaintiff.
254 See notes 80-91 and accompanying text supra.
Moreover, the physician would probably be able to successfully defend the prescription on the basis that it was consistent with community standards. If so, physicians would be in their present position, with little incentive to engage in more accurate risk/benefit analysis.

To avoid its absolute liability, the manufacturer could also litigate the issue of whether the risk/benefit decision which was made regarding the specific patient was negligent. Even if the manufacturer escaped liability on that basis, however, the patient could not be benefited. Unless the existing law changed, although the manufacturer escaped liability, the physician would not be liable to the patient for such an error in judgment. Of course, existing negligence law in such circumstances might change to favor patients, but even then patients may still not be compensated because of the other infirmities in the system.

Need For Preventative Efforts.—Because of the limitations of the tort negligence system, even if extended to absolute liability, consideration should be paid to whether there are methods by which injuries caused by nonapproved prescribing could be prevented. The following analysis examines proposed solutions, regulatory and nonregulatory, to determine which might be the most appropriate.

Preventative Solutions for Nonapproved Prescribing

Two categories of solutions have been proposed to help solve the problem that physicians who prescribe drugs for nonapproved purposes may lack or be unable to use necessary prescribing information. Solutions of the first type seek to create more careful physician use of existing, but limited, prescribing information, while other solutions are intended to increase the amount and quality of that information. Both kinds of solutions could lead to more accurate risk/benefit assessments by physicians of nonapproved drug uses.

Improved Use of Existing Prescribing Information

Better Dissemination of Information.—More careful physician use of existing, but limited information about nonapproved uses could be promoted most easily by better dissemination of the existing information. This might be done under two existing FDA mechanisms—the drug package insert or the FDA Drug Bulletin—or by a proposed federal drug compendium.
The most logical source for disseminating prescribing information is the drug package insert. The insert, as the authoritative statement of the results of the human and animal testing performed by a drug sponsor to gain FDA approval,\textsuperscript{255} includes information about potential side-effects and steps physicians can take to diagnose and avoid those side-effects.\textsuperscript{256} By law, however, the information in the insert must pertain to the approved use of the drug.\textsuperscript{257} Hence, any information about nonapproved uses, if not relevant to the approved use, could not be included.\textsuperscript{258}

As an alternative, the FDA could increase its efforts to include information about nonapproved uses in the \textit{FDA Drug Bulletin}, an agency periodical read by many physicians.\textsuperscript{259} The information could be in the nature of a cautionary note and could include a progress report on the status of the FDA’s evaluation of the nonapproved use for approval,\textsuperscript{260} if such approval is being sought.\textsuperscript{261}

While such reports would be beneficial, there may be a limitation to their usefulness. The \textit{FDA Drug Bulletin} competes with a host of other sources of drug information for the physician’s atten-

\textsuperscript{255} See notes 21-24 and accompanying text \textit{supra}.
\textsuperscript{256} See notes 25-27 and accompanying text \textit{supra}.
\textsuperscript{257} The Act, however, dictates a different standard for warnings. Dr. Richard Crout, as director of the FDA Bureau of Drugs has stated: “Substantial evidence is not required for a warning . . . [because] a warning is something that properly is given at an early stage . . . .” Rheinstein, \textit{supra} note 61, at 24.
\textsuperscript{258} The FDA believes it would be unwise for the present prohibition to be eliminated:

The Commissioner concludes, however, that it is neither lawful nor in the interest of good patient care for the package insert to contain references to indications or usages for which substantial evidence of safety and effectiveness is not available. Physicians clearly have access to new information on drugs through the medical literature, scientific meetings, postgraduate courses, and professional contacts with colleagues. The package insert is not intended under the law to serve as a totally current repository of all such information. It is intended instead to be an authoritative document which contains only those indications and usages based upon substantial evidence of safety and effectiveness. Notice of Proposed Rulemaking, Labeling For Prescription Drugs Used in Man: Proposed Format for Prescription-Drug Advertisements, 40 Fed. Reg. 15,392, 15,393 (1975).

\textsuperscript{259} Ruskin, \textit{Survey of Drug Information Needs and Problems Associated with Communications Directed to Practicing Physicians—Pt. 1: Physician Information Survey} 47 (1974). In one survey, 79% of the responding physicians indicated regular or occasional readership of the periodical. \textit{Id.} This represented the largest audience of any medical periodical publication. \textit{Id.} The periodical reaches over 600,000 physicians, dentists and other health professionals. \textit{Examination of the Pharmaceutical Industry, supra} note 99, at 575 (statement of Charles C. Edwards, M.D.).

\textsuperscript{260} Review Panel Final Report, \textit{supra} note 54, app. 1, at 3.

\textsuperscript{261} There may be a considerable lag between the time the nonapproved use of a drug becomes widespread and the manufacturer commences testing to gain FDA approval for that use. \textit{See} notes 71-73 and accompanying text \textit{supra}. For a solution to this lag, see notes 395-417 and accompanying text \textit{infra}.
tion and therefore may not be read. In addition, the physician may lack access to, or not remember, a relevant article at the time the prescription decision is being made. Undoubtedly, the popularity of the Physician’s Desk Reference as a source of drug information is related to its accessibility as a one-volume compendium of package inserts.

To present governmentally originated drug information in a manner more convenient for physicians, successive FDA officials, governmental studies, and proposed congressional legislation have recommended creation of a federal drug compendium. Like the Physician’s Desk Reference, the compendium would be a compilation of the information presently contained in the drug package inserts. But its proponents see the compendium as having several advantages. It would contain information about all drugs, instead of just those for which a sponsor pays for inclusion. It would include additional information such as the costs of the drug to the patient. Finally, the compendium would be organized according to therapeutic category to allow a physician to find at one location in the book information concerning all drugs approved to treat a certain illness.

Present proposals for the compendium would also allow the FDA to include “such additional relevant information [as it] determines would promote proper use of [a drug].” The compendium could then be used to disseminate information about nonapproved prescribing. Since, like the Physician’s Desk Reference, the compendium should be an easily accessible source of drug prescribing information, the included information would probably come to the physician’s attention.

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263 RUSKIN, supra note 259, at 55.
264 Hearings on Quality of Health Care, supra note 59, at 32 (statement of Charles C. Edwards, M.D.); Crout, supra note 91, at 144-45; Goddard, The Drug Establishment, ESQUIRE, March 1969, reprinted in Hearings on Quality Of Health Care, supra note 64, at 330.
267 Crout, supra note 91, at 145.
268 Hearings on Competitive Problems, supra note 98, at 3715.
269 Id. (statement of Phillip Lee, M.D.).
270 Crout, supra note 91, at 145.
271 S. 2755, supra note 266, § 155(b), at S3892.
272 See Moser, supra note 262, at 1336; Temple, supra note 60, at 1158.
Despite this advantage, critics of the compendium argue that it would be counterproductive. They fear it eventually would come to be regarded as the "official" standard for prescribing, thereby discouraging necessary innovation.\textsuperscript{273} Moreover, it is contended that a compendium could place physicians at a greater risk of adverse malpractice decisions if they disagreed with the recommendations of the compendium.\textsuperscript{274}

These fears seem overstated. The FDA has indicated that any compendium which it produces will be done in consultation with the medical community.\textsuperscript{275} Moreover, nothing in the concept of a compendium would force a physician to follow its recommendations. Presently, many physicians do not follow the package insert recommendations and presumably they would treat a compilation of inserts in the same manner.\textsuperscript{276} Finally, as a compilation of inserts, the compendium would stand on the same evidentiary footing as the present package insert. As previously discussed, the insert poses an insignificant evidentiary threat for physician malpractice defendants.\textsuperscript{277}

In fact, the most significant limitation of the compendium is that, like a package insert, it may contain only what information is available. As previously discussed, in some instances that information may be inadequate for some physicians safely to prescribe a drug. Consequently, limitations on what drugs certain physicians may prescribe have been proposed.

\textit{Limitations on Physician Prescribing}.—Safer prescribing for nonapproved purposes might also be promoted by limiting such prescribing to those physicians who would most likely have the expertise to use the drug safely.\textsuperscript{278} These would be physicians, who

\textsuperscript{273} See Letter from American Society of Internal Medicine to FDA Commissioner Donald Kennedy (Aug. 9, 1977) (comments on REVIEW PANEL FINAL REPORT, note 54 supra); Coyne, \textit{Washington's New Malpractice Threat: Package Inserts and a Modest Proposal from the FDA}, PRIVATE PRACTICE, Apr. 1975, at 44. \textit{See also} Moser, \textit{supra} note 262, at 1338.

\textsuperscript{274} See Letter from Pharmaceutical Manufacturers Association to FDA Hearing Clerk, at 28 (Aug. 15, 1977) [hereinafter cited as PMA Letter] (comments on REVIEW PANEL FINAL REPORT, note 54 supra); Coyne, \textit{supra} note 273, at 44.

A former FDA commissioner has argued that pharmaceutical company opposition is based on the added competition the companies would face if the government proposed a compendium for which companies did not have to pay to be included. In such a compendium, physicians would be alerted to drugs produced by companies which cannot afford to advertise in the \textit{Physician's Desk Reference}. Goddard, \textit{supra} note 264, at 330.

\textsuperscript{275} Crout, \textit{supra} note 91, at 145.

\textsuperscript{276} See notes 51-58 and accompanying text \textit{supra}.

\textsuperscript{277} See notes 180-98 and accompanying text \textit{supra}.

\textsuperscript{278} Address by Herbert L. Ley, Jr., M.D., Harvard Medical School Alumni Day (June 4,
because of prior training or experience, would be better able to evaluate what limited information is available. The limitations could be imposed by FDA or through a physician peer review mechanism.

The choice is of great concern to organized medicine. In the past, the medical community has opposed any attempt at what it perceived as FDA regulation of medical practice, while promising additional efforts on its own behalf. Usually, the opposition has been adamant.

In 1967, for example, a prominent physician leader criticized the FDA after it proposed to a medical author that he amend his textbook to warn that a dosage he recommended exceeded that recommended in the package insert. The FDA took that action after several children died as a result of being given the higher dosage. After the criticism, the FDA assured physicians that it had no intention of regulating physician prescribing.

In 1972 the FDA changed its mind and proposed a rulemaking proceeding to cover nonapproved prescribing. The agency, while admitting it had no direct authority over physicians, nevertheless proposed that "when an unapproved use of a new drug may endanger patients or create a health hazard," it was "obligated" to act by taking one or more of several enumerated actions. Again, important elements of the medical community vigorously attacked the FDA initiative. In an editorial headlined Eternal

1971), reprinted in Methotrexate Hearings, supra note 115, at 133. See note 290 and accompanying text supra.
279 For the reasons why not all physicians can evaluate drug information with equal expertise, see notes 104-05 and accompanying text supra.
280 See, e.g., Hearings on Quality of Health Care, supra note 59, at 105 (statement of W.N. Hubbard, Jr., M.D.).
281 H. Dowling, supra note 77, at 244-45. The original criticism appeared in Modell, FDA Censorship, 8 CLIN. PHARM. & THERAPEUTICS 359 (1967) and was answered in Ley, FDA Papers (Letter To The Editor), 8 CLIN. PHARM. & THERAPEUTICS 749 (1967).
282 H. Dowling, supra note 77, at 244-45.
283 Hauser, Medical Communications: Law, Ethics & Booby Traps, 9 CLIN. PHARM. & THERAPEUTICS 271 (1968).
284 Notice of Proposed Rule Making, supra note 48, at 16503.
285 Id. at 16504. The actions which the agency proposed it might take were: (1) revision of the drug package insert to require it to state a specific contraindication or warning against the unapproved usage, or to require it to state that the prescription should not be refilled, or to require it to state that the drug should be distributed only through specified channels such as hospital pharmacies, or to require it to state that the drug should be prescribed only by physicians with special qualifications; (2) to order a manufacturer to obtain and submit available data concerning the unapproved use including sponsoring clinical trials; (3) to approve the unapproved use if proper evidence were available; (4) to limit the distribution of the drug under the FDA's new drug and investigational new drug authority; (5) to require a patient package insert; or (6) to revoke the approval of the drug. Id.
Vigilance—the Price of Liberty, the American Medical Association voiced its criticism. The FDA also received a barrage of critical letters from physicians. Faced with this opposition, the FDA did not adopt any final version of its proposed rule.

The vigor of the medical profession’s opposition to even the most minor regulatory intervention in physician prescribing suggests the need to carefully weigh the choice between FDA and self-imposed regulation. The following discussion attempts to accomplish that result.

FDA-Imposed Prescribing Limitations.—In the proposed Drug Regulatory Act of 1978, the FDA has asked Congress to give it the authority, subject to several qualifications, to pose restrictions on what categories of physicians, designated by such factors as physician training and experience, and could prescribe certain drugs and what types of pharmacies, designated by categories such as hospital or retail, could dispense certain drugs. If Congress were to au-

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288 Letter from American Society of Hospital Pharmacists to FDA Commissioner Donald Kennedy, at 5 (Aug. 9, 1977).
289 The FDA could utilize its power to limit prescribing only if: (i) medical experts would say the drug could not be used safely without such limitations; (ii) the limitations could be expected within a reasonable period of time to render use of the drug safe; (iii) no other action which the agency might take would accomplish the same result. S. 2755, supra note 266, § 108(e)(1)(A)(i)-(iii), at S3878.
290 Id. § 108(e)(1)(B)(i)-(iii), at S3878.
authorize this proposal, it could be applied to nonapproved prescribing in the following manner.

The FDA would first have to decide whether prescription of a drug could be restricted in some manner without withdrawing it from channels where the approved use of the drug was necessary and useful. If the drug was used in the approved manner only in some identifiable location, such as hospital pharmacies, this could be accomplished.

Such action, of course, would deny the drug to anyone outside of the hospital context for use for any purpose, including any nonapproved purpose. Yet if some prescribing for the nonapproved purpose is desirable, the FDA could also limit the scope of such prescribing by restricting it to physicians with specialized training or experience. Access to the drug would thus be limited, but not entirely prohibited, in the hope that it would be used more safely than if it were generally available.

Several arguments have been advanced against giving the FDA the authority to allow limited use of drugs for nonapproved purposes. One argument is that under the proposed system patients would be deprived of "one of their most basic existing rights in the health care system"—the right to choose treatment with medications which a physician has judged appropriate. Moreover, some judicial authority exists from which to argue that such a "right" is legally protected. A recent federal district court decision held that for terminally ill cancer patients, there exists a constitutional privacy right to take laetrile. In the absence of evidence that laetrile is toxic, the court reasoned that the privacy right is not outweighed by any state interest in banning the use of laetrile. Even if a privacy right to

291 Under the proposed Drug Regulatory Reform Act of 1978, the FDA could restrict prescribing to certain physicians subject to some considerable and confusing limitations. See note 289 supra.

292 In many instances, a complete ban on nonapproved prescriptions would be undesirable. See note 177 and accompanying text supra.


take certain medications exists, the decision should have little or no applicability to the proposed prescribing limitations. Presumably the FDA would only seek to impose the restrictions where the toxicity of a drug posed a serious danger to patients, thereby requiring limited distribution of the drug. In such cases, the state interest would seem to outweigh any individual interests.

Physicians oppose granting the FDA the authority to regulate on a second ground. They argue that those factors which presently have led the FDA to be overcautious in approving drugs likewise would lead the agency, in the promotion of greater safety, to needlessly overuse its authority to limit prescribing.

Criticisms of the FDA’s drug decisions involve value judgments about which experts may differ. According to a recent governmental study, FDA critics have failed to establish that FDA caution in approving new drugs has harmed consumers. The qualifications contained in the legislation should promote reasonable decisions. Among other restrictions, the agency could use the power only as a last resort after trying other remedies and only if it obtained the approval of an independent group of consultants, including expert physicians.

The real difficulty with prescription restrictions is how to implement them. First, such restrictions could be used only when they would not withdraw the drug from locations or practices where it is used for an approved purpose. Even assuming this problem could be surmounted, there are still other management problems. If usage were limited to physicians having medical specialities or certain experience, pharmacists would have to perform a potentially burdensome policing function to decide whether a certain physician could prescribe a particular drug. Moreover, limiting certain drugs to particular physicians could cause considerable dissension in the

295 See notes 284-85 and accompanying text supra.
296 U.C.L.A. Comment, supra note 294, at 614-17. If courts were to find nonetheless that the privacy right outweighed the government’s interest in regulation in such instances, the ramifications would be considerable. Under such a holding, the FDCA itself, as well as other federal safety regulations, could be declared unconstitutional. It is assumed that the privacy right, if it exists, does not extend that far.
297 See, e.g., Archer, supra note 61, at 1398. It has been argued that such incorrect overcaution is possible since under the proposed legislation the FDA is given “virtually unbridled discretion” to restrict prescribing. Hearings on S. 2755, note 293 supra (statement of William Apple). For an analysis of this argument, see notes 298-99 and accompanying text infra.
298 REVIEW PANEL FINAL REPORT, supra note 54, at 26-30. See generally note 54 supra.
299 See note 290 supra.
300 One legislative proposal calls for the registration of physicians to implement a prescribing limitation program. S. 2697, 94th Cong., 1st Sess. § 405(b)(3) (1975). Under this system,
medical community, especially if the right to prescribe a drug gave the privileged physicians a considerable economic advantage. Perhaps for these reasons, the government has resisted proposals to reimburse differently trained physicians at different levels under Medicare and Medicaid.

If a drug were limited to hospital prescribing, discrimination among physicians could be avoided. All physicians, regardless of expertise, would be allowed to prescribe the drug. However, the patient may be safer for two reasons. First, an adverse reaction could be quickly recognized and treated in a hospital setting. Second, the FDA could condition prescription of the drug on the performance of necessary testing procedures.

Even choosing to limit prescribing to hospitals may be counterproductive. It has been argued that such restrictions would increase hospital usage at a time "when the focus of the health care system, health planners, and other reasonable agencies, is to reduce hospital utilization and return patients to the home and community environment for treatment." 

Peer Review Restrictions on Prescribing.—An alternative to FDA restrictions on physician prescribing is the establishment instead of a physician peer review mechanism which has the same effect. This concept has the support of three previous FDA Commissioners. One of them, Dr. Herbert Ley, Jr., has argued

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301 Letter from Michael Halberstam, M.D., to FDA Hearing Clerk (Aug. 12, 1977) [hereinafter cited as Halberstam Letter] (comments filed on REVIEW PANEL FINAL REPORT, note 54 supra); Letter from American Pharmaceutical Ass'n to FDA Hearing Clerk, at 10 (Aug. 12, 1977) [hereinafter cited as APA Letter] (comments filed on REVIEW PANEL FINAL REPORT, note 54 supra).

302 This kind of competitive friction already exists at times when some physicians, who are part of the drug testing process, are able to prescribe a drug, although it is not yet licensed, while other physicians cannot prescribe it. FOOD AND DRUG ADMINISTRATION, COMMISSIONER'S REPORT OF INVESTIGATION OF CHARGES 625 (1975).

303 Halberstam Letter, note 301 supra.

304 To solve this problem, the FDA could choose to restrict the drug to major medical centers or hospitals affiliated with medical schools where physicians might have greater levels of expertise. Such restrictions, however, would deny the drug to patients not located near the facility. Letter from Eli Lilly & Co. to FDA Hearing Clerk, at 7 (Aug. 12, 1977) [hereinafter cited as Eli Lilly Letter] (Comments on REVIEW PANEL FINAL REPORT, note 54 supra); APA Letter, supra note 301, at 9-10.

305 Halberstam Letter, note 301 supra.

306 Id.

307 Hearings on S. 2755, supra note 293 (statement of William Apple).

308 Hearings on the Quality of Health Care, supra note 59, at 18-19, 20 (statement of Charles
that there is ample precedent for such a use of peer review:

I for one have long accepted the concept that it would be unwise to have an abdominal surgeon perform neurosurgery on a member of my family except in the most extreme emergency. Fortunately, surgeons must utilize operating rooms and operating room privileges are rather well regulated by professional peer committees, so that I am not likely to have to face the hypothetical I mentioned. Unfortunately, there is no comparable mechanism to provide professional peer regulation of prescribing practices in this country. . . .

To determine whether peer review would be a viable method by which to address the problems of nonapproved prescribing, the following discussion examines two areas. First, existing peer review mechanisms are analyzed to determine what changes would be necessary to effectuate the necessary controls. Next, the possible effectiveness of those controls is assessed.

The most significant present system of peer review is the federal government's Professional Standard Review Organization (PSRO) system. Mandated by amendments to the Social Security Act, PSRO units now review medical services to determine whether they are medically necessary, whether the quality of care meets previously set professional standards, and in the case of inpatient facilities, whether the choice of the facility was appropriate. Review is by local physicians of their peers. Certain prepaid medical insurance programs also have created peer review mechanisms. Unlike the PSROs, however, most of the private programs are largely limited to the prevention of fraud and other cost control objectives.

Using their authority to engage in medical care evaluation studies designed to identify and correct deficiencies in the quality of health care, some PSROs have engaged in a review of physician

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Edwards, M.D.), 263-64 (statement of James Goddard, M.D.); Address by Herbert Ley, Jr., M.D., supra note 278, at 133.

309 Address by Herbert Ley, Jr., M.D., supra note 278, at 133.


314 Id. at 255.

315 Ball, supra note 111, at 583. Other PSRO functions include concurrent review of the appropriateness of institutional admissions and length of the patient's stay and institutional provider, practitioner, and patient profile studies, which involve a study of some medical area to determine methods of improvement. Id. at 583-84.
prescribing activities. The most active of these programs is that of the San Joaquin Foundation for Medical Care.

Under the San Joaquin system, all prescriptions filled for Medicaid patients in certain California counties are analyzed for certain characteristics. If, for example, a prescription exceeds certain limits previously set by the PSRO panel, such as twelve or more prescriptions within thirty days, the panel receives a report so the situation can be examined for evidence of possible drug abuse. Similarly, the system also records other deviations from preset standards for review by the PSRO committee. If necessary, aberrations are discussed with the appropriate physician.

A system similar to that of the San Joaquin Foundation could be used to monitor nonapproved prescribing. If the peer committee decided upon a standard that only physicians of certain experience or training should prescribe a drug for some nonapproved use, physician compliance could be monitored through a prescription audit. Moreover, it may not be necessary that the audit be a continuous one; spot checking may suffice.

Adoption of the San Joaquin model to review prescriptions for nonapproved purposes would involve a significant commitment to expand existing peer review mechanisms. Presently, most PSROs are concerned primarily with health care issues other than drug therapy and usually only in the context of institutional, rather than ambulatory, care. Moreover, any large scale monitoring system

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317 Hearings on Quality of Health Care, supra note 59, at 219-22; Peer Review Spurs Monitoring, supra note 316, at 195.

318 Hearings on Quality of Health Care, supra note 59, at 220-21.

319 Peer Review Spurs Monitoring, supra note 316, at 199.

320 Id.

321 Id. For a description of the other types of standards used, see Morgan, supra note 313, at 254-55.

322 Peer Review Spurs Monitoring, supra note 316, at 199.

323 Hearings on Quality of Health Care, supra note 59, at 254 (statement of Robert Talley, M.D.).

324 Peer Review Spurs Monitoring, supra note 316, at 195; Hearings on Quality Of Health Care, supra note 59, at 221 (statement of Robert Talley, M.D.).

325 The authorizing statute provides:

Notwithstanding any other provision of this part, the responsibility for review of health care services of any Professional Standards Review Organization shall be the review of health care services provided by or in institutions, unless such Organization shall have made a request to the Secretary that it be charged with the duty and function of reviewing other health care services and the Secretary shall have approved such request.

would require computers, posing the potential that the review would require a significant financial commitment.

Even if these necessary commitments were made, some aspects of the peer review system might limit its potential for effectiveness in this area. The most obvious constraint is that PSRO functions are limited to review of medical care paid for by Social Security. Further expansion of PSRO review, at additional cost, could be undertaken. However, even if the program were limited as it is presently, a sufficiently large number of physicians may be subject to review for some prescriptions to make the program effective nonetheless. Moreover, the influence of any PSRO actions could have a prophylactic effect of constraining physicians outside the review mechanism.

Whatever the scope of the program, another potential problem exists insofar as physicians, like most professionals, are unwilling to actively engage in any aspect of peer review which strongly suggests that some of their colleagues lack competence. As proof of the existence of such an ethic among physicians, critics of peer review point to the traditional difficulty malpractice plaintiffs have had in obtaining expert medical testimony in their behalf. Since there is independent evidence that such an ethic exists, PSRO groups may

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326 Hearings on Quality Of Health Care, supra note 59, at 220 (statement of Donald Harrington, M.D.).
328 Private insurers might be induced to include quality control features in their plans if the government undertook part of the costs of the peer review. Morgan, supra note 313, at 256. Otherwise, general peer review of prescribing might have to await some form of national health insurance.


The development of this ethic has been described as follows:

[This protection (of the inept) rests on very strong supports; the profession is a community. Doctors have all been rigorously socialized to view themselves in certain ways; they interact differentially with others like themselves; and they share a common fate. These conditions are conducive to a great solidarity, especially in the face of an attack on the key to their authority—confidentiality, secrecy and autonomy.]

Id.
330 See notes 197-98 and accompanying text supra.

Indicative of the strength of this ethic, before Congress adopted the PSRO legislation, the medical profession, besides minimum requirements for education and licensure, had not instituted any systematic mechanism for monitoring and evaluating the quality of care. Strosberg, Levine, & Mauet, Technology and the Governance of the Health Care Industry: The Dilemma of Reform, 2 J. HEALTH POLITICS, POLICY, & L. 212, 216 (1977). Moreover, the PSRO legislation produced substantial opposition from the medical profession. The American Medical
ignore some areas of health care in favor of other areas where review would not reflect as adversely on the profession.\footnote{332}

More than other PSRO potential activities, peer review of non-
approved drug prescribing could involve physicians in the kind of judgment of physician competence which they resist. In many in-
stances, a judgment by a PSRO panel merely means that a physician has exercised poor judgment in a given episode or group of epi-
sodes.\footnote{333} By comparison, effective policing of nonapproved pre-
scribing may involve the judgment that certain physicians should not prescribe certain drugs, a much more drastic interference with their medical practice.\footnote{334}

PSROs would be abetted in making a choice against reviewing nonapproved prescribing by the fact that under the statutory scheme, there is virtually no hierarchical control over local PSRO units.\footnote{335} Each component of the program (the local PSRO, statewide coun-
cils, a national council, and HEW) performs a distinct function\footnote{336}


\footnote{332} This ethic potentially could also lead to substantial noncompliance by individual physicians with recommendations of a PSRO unit. The Act, however, provides for substantial sanctions for noncompliance. 42 U.S.C. § 1320c-9(a) to (b) (1976). Moreover, experience with PSRO activities to date indicate that merely documenting wasteful or dangerous practices to physicians often is sufficient to prompt improvement. \textit{Peer Review Spurs Monitoring}, \textit{supra} note 316, at 199. Voluntary compliance is expected because once a PSRO agrees to adopt some standard for physician behavior, peer pressure will be an important motivating device. \textit{Hearings on Quality OfHealth Care}, \textit{supra} note 59, at 264 (statement of James Goddard, M.D.).

\footnote{333} Note, \textit{Federally Imposed Self-Regulation of Medical Practice: A Critique of the Professional Standards Review Organization}, 42 \textit{Geo. Wash. L. Rev.} 822, 842 (1974) ("The [PSRO] objective is to ensure that the practitioner who orders services for which a claim may be made against the government makes that decision in a reasonable manner . . . .").

The normal regard for physician sensitivity about judgments about peer competence is evidenced in the following description of the program by a HEW official:

Norms, criteria, and standards are to be used at each level of PSRO activity. The PSRO Program Manual contemplates their application in initial screening of cases to select those that require detailed review. . . . In applying those standards, however, some \textit{competent practitioners} may be subjected to further review because the particular circumstances of the case involved do not meet the criteria. . . . That case is then referred to peer review, which might determine that the [care given] was justified because of individual complications that were not considered when the criteria were developed.

\textit{Ball, supra} note 111, at 580-81 (emphasis added).

\footnote{334} See \textit{Ball, supra} note 111, at 580-81.

\footnote{335} \textit{Id.} at 578; Havighurst & Blumstein, \textit{Coping with Quality/Cost Trade-Offs In Medical Care: The Role of PSROs}, 70 \textit{Nw. U.L. Rev.} 6, 47-49 (1975).

\footnote{336} Local PSROs review the care being provided by peer physicians. \textit{See} notes 311-12 \textit{supra}. Statewide councils coordinate activities of local councils, disseminate and acquire in-
and interaction largely is limited to the exchange of information. \(^{337}\) For example, in controlling a local PSRO, HEW is primarily limited to revoking its charter to operate, a measure so drastic it seems unlikely to occur. \(^{338}\) HEW has interpreted the role of the national council, which is charged with determining whether local PSRO actions are in conformity with regionally derived standards, to extend only to consultation with local units, without any ability by the national council to enforce its decisions on the local units. \(^{339}\)

**Required Patient Education.**—The final method by which better use of existing prescribing information might be obtained would be to require patient education for any nonapproved use of a drug in one or both of two possible forms. There could be a patient package insert of a specific form for the nonapproved use—a drug label that would be given to the patient. Alternatively, or additionally, physicians could be required to obtain a specific form of informed consent for any drug prescribed for a nonapproved purpose. Each of these forms of patient education, as discussed below, could cause both physicians and patients to more carefully assess risk/benefit decisions.

**Patient Package Inserts.**—Under the present regulatory scheme, prescription drugs are exempted from bearing detailed consumer labels containing information about the risks and benefits of a drug on the theory that the physician makes the purchasing decision. \(^{340}\) Nevertheless, the FDA contends that for certain drugs it has the authority, and assist HEW in evaluating the performance of local units. 42 U.S.C. § 1320c-11(c) (1976). The national council advises the Secretary of HEW, disseminates information about standards adopted by other PSROs, studies the effectiveness of state councils and of the system generally. 42 U.S.C. § 1320c-12(e) (1976). See note 339 and accompanying text infra.

HEW coordinates these activities, 42 U.S.C. § 1320c-14 (1976), and performs certain limited supervisory functions. See note 338 and accompanying text infra. \(^{337}\) Ball, *supra* note 111, at 578-79.

\(^{338}\) 42 U.S.C. § 1320c-1(d)(2) (1976). HEW also is given two other methods to influence local PSROs, although neither would be of use in this situation. First, any person denied benefits or payment of $100 or more because of a PSRO ruling is entitled to a hearing before HEW. 42 U.S.C. § 1320c-8 (1976). This authority, however, does not allow HEW to positively influence adoption of standards, only to review their implementation. Second, the National PSRO Council's membership is appointed by the Secretary of HEW. 42 U.S.C. § 1320c-12(a) (1976). The Council, however, lacks control over local PSROs. See note 334 supra.

\(^{339}\) Havighurst & Blumstein, *supra* note 335, at 48-49. The PSRO enabling statute, 42 U.S.C. § 1320c-5(c) (1976), might allow greater control by the national council, but HEW has not so interpreted it. Havighurst & Blumstein, *supra* note 335, at 49. Nevertheless, HEW's position is sufficiently equivocal, *id.*, that some change might be made.

\(^{340}\) See note 22 supra.
authority to order that such detailed labels, usually in the form of a patient package insert, be disseminated to the consumer. Although this claim is under legal challenge, the agency has ordered that patient package inserts be provided for patients receiving prescriptions for oral contraceptives, intrauterine contraceptives (IUDs), postcoital contraceptives (DESs), and for all estrogen products.

The proposed Drug Regulatory Reform Act of 1978 would clarify the jurisdiction question by requiring patient informational labeling for all prescriptions unless the FDA could find that the labeling was not necessary "to protect the public health or to promote the safe and effective use of the drug product by patients." The labeling proposed by the act would inform the patient of directions for use, of precautions to be taken, of significant side-effects that could occur, and of warnings against unsafe use of the drug. In addition, the proposed labeling would tell the patients for which uses or indications the drug has been approved.

Under the proposal, however, physicians would retain discretion to decide that certain patients should not receive an insert. The FDA could withdraw physician authority to prevent dissemina-

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342 42 Fed. Reg. 37,636, 37,636 (1977); 40 Fed. Reg. 15,392, 15,393-94 (1975). The FDA argues that if a drug may not be approved or remain on the market as safe and efficacious unless patients are given informational labeling, then, under the broad grant of authority given it by Congress, it may order that such labeling be provided. Gardner, *supra* note 341, at 841-44. For an analysis of the validity of this viewpoint, see *id.* 343 See *Pharmaceutical Mfrs. Ass'n v. FDA*, Civ. No. 77-291 (D. Del., filed July 25, 1977); *Private Medical Care Foundation, Inc. v. Califano*, Civ. No. 77-0728-D (W.D. Okla., filed July 25, 1977).
350 *Id.* § 151(g)(1)(A), at S3891.
351 *Id.* § 151(d)(1), at S3892. This would make the act reasonably consistent with the prevailing standards in tort litigation concerning informed consent. See notes 208-09 and accompanying text *supra.* Although the physician owes the patient the duty to obtain informed consent, the physician in most instances retains a therapeutic privilege not to seek it when to do so would be medically counterproductive. See note 209 and accompanying text *supra.* Although there are limitations on the therapeutic privilege, *id.*, under the proposed legislation, the physician has complete discretion not to allow the patient to have the patient insert. S. 2755, *supra* note 266, § 151(d)(1), at S3892. The FDA's only option to limit this discretion is categorically to deny all doctors any such privilege.
tion of patient labels if “in light of the circumstances relating to the nature, use, or method of administration of [a drug, patient] labeling is necessary to assure the opportunity for an informed decision by a patient whether to use the drug product.”

Proponents of the package insert concept contend that it will improve the quality of therapy by increasing patient compliance with dosage instructions and patient awareness of necessary precautionary measures, including awareness of the possibility that there may be adverse effects which would require physician consultation. In addition, proponents of patient inserts argue that the inserts will allow patients to participate to a greater degree in decisions regarding drug therapy.

Any program which would lead to more rapid recognition and treatment of adverse reactions would help alleviate the problem of nonapproved prescribing. In addition, there may be another, more subtle effect. Patient interest in the nature of the prescribing decision may be greater than many physicians assume. If patient labeling caused patients to question physicians more actively about a prescription decision, physicians might be encouraged to reconsider the appropriateness of the decision. Professor Paul Freund has noted that effect in a related context. Where physicians doing research are required to obtain informed consent, Professor Freund believes the resulting physician-patient interaction operates as a “check” on physicians:

Not the least of the functions of consent is its reflexive effect on the management of the experiment itself. To analyze an experiment in terms of risks and benefits by way of presentation for consent is a salutory procedure for self-scrutiny for the investigator—like the preparation of a registration statement by a corporation issuing securi-

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352 S. 2755, supra note 266, § 151(d)(1), at S3892.
353 Gardner, supra note 341, at 844; Better Regulation Through Labeling, FDA CONSUMER, Feb. 1978, at 15 (Interview of FDA Commissioner Donald Kennedy) [hereinafter cited as Kennedy].

Studies have found that physicians normally overestimate the degree of compliance with their instructions and that physicians are not able to identify noncooperators. See, e.g., Caron & Roth, Patients' Cooperation With A Medical Regimen, 203 J.A.M.A. 922, 926 (1968).
354 Gardner, supra note 341, at 844. The patient would also be made aware of the necessity to avoid undesirable food or drug interactions and to take certain precautionary measures. Id.
355 Id. at 845.
357 See Maurizi, Commentary, in DRUG DEVELOPMENT AND MARKETING 51 (R. Helms ed. 1975).
ties.358

Despite the apparent advantages, many prominent medical organizations contend that the insert will be therapeutically counterproductive. These groups argue that the information in the insert will probably be misunderstood or will frighten patients. Either consequence will cause patients not to take the prescribed drug.359 Similarly, the Pharmaceutical Manufacturers Association, while generally supporting the concept of patient inserts, has contended that it will be very difficult to write an insert which can explain the nonapproved prescribing situation to patients.360

In response, defenders of patient inserts insist that the critics have underestimated the intelligence and good sense of patients.361 Little empirical testing has been conducted to determine which of these predictions of patient behavior is correct.362

If the critics are correct that for some patients a patient insert would be counterproductive, a decision against having patient inserts for that reason discriminates against those who could compre-

358 Freund, Legal Frameworks for Human Experimentation, 98 Daedalus 322-24 (1969), reprinted in J. Katz, Experimentation With Human Beings 603-04 (1975). It has been asserted that informed consent promotes the rationality of the physician's decision in another manner. Since the need to obtain consent forces the physician to talk with the patient on a personal level for additional time, there is less opportunity for the physician to disregard some of the interests of the patient. Capron, supra note 204, at 374-75. If patient inserts caused additional physician-patient consultation, it could also have this effect.

359 Eli Lilly Letter, supra note 304, at 5-6; Letter from American Medical Association to FDA Commissioner Donald Kennedy, at 11 (Aug. 12, 1977) [hereinafter cited as AMA Letter] (comments on Review Panel Final Report, note 54 supra); PMA Letter, supra note 274, at 26. The American Medical Association has observed: "Every physician engaged in primary care knows that frequently he prescribes a medication for a patient with psychosomatic or neurotic elements to his disease and doesn't wish the patient to be further concerned about the possibility of adverse reactions." Editorial, The Patient Package Insert, 223 J.A.M.A. 1089, 1089 (1975).

For a survey which found various attitudes by practicing physicians, see Carlova, Drug Package Inserts for Patients: Good Idea or Bad?, 515 Med. Econ. 140 (1974).

360 PMA Letter, supra note 274, at 11.

Critics of the patient package insert concept also argue that if it is used as evidence of negligence it potentially might increase the liability of health care providers for adverse reactions. See, e.g., Eli Lilly Letter, supra note 304, at 6. The criticism is without merit. The patient insert would contain roughly the same information as the present physician package insert. As a result, courts would presumably treat it in the same manner in terms of evidentiary acceptability. As previously noted, few courts have allowed any use of the physician package insert in any manner which has been damaging to physician malpractice defendants. See note 199 and accompanying text supra. Accord, Gardner, supra note 341, at 855-67.

361 See, e.g., Kennedy, supra note 353, at 15.

362 Cf. Zellmer, Editorial: Patient Package Inserts, 33 Am. J. Hosp. Pharm. 535, 535 (1976) ("Patients who are knowledgeable about their therapy and actively participate in it have a better chance for recovery.").
hend and not be frightened by the material they are given.\textsuperscript{363} Instead, it would be necessary to rely on the physician’s privilege to deny the insert to any patient who might have a counterproductive reaction to it.\textsuperscript{364} This may not, however, provide a complete solution. It is uncertain how well physicians can predict which patients might need protection.\textsuperscript{365} More importantly, perhaps cautious physicians would overuse the privilege not to provide the insert. In such cases, the FDA’s only remedy is a categorical decision to order the insert provided in all cases.\textsuperscript{366} Presumably the agency would be reluctant to take such action, since for most drugs there are probably some patients who should not receive an insert.

Distributional problems with the patient insert greatly compound the problems with patient behavior. Ideally, the insert would be distributed in the physician’s office to maximize the physician-patient interaction. Given the number of physicians’ offices, such a distributional scheme may be very burdensome.

A more efficient system would distribute the inserts at the pharmacy.\textsuperscript{367} However, with this location, since the patient will already have consulted with the physician, the physician would have to be recontacted if the patient has questions about information in the insert. Because any recontact would involve inconvenience and perhaps greater expense, physicians fear some patients may instead choose not to take the drug.\textsuperscript{368}

To solve the recontact problem, it has been proposed that the pharmacist counsel patients\textsuperscript{369} by answering questions within the pharmacist’s expertise\textsuperscript{370} and by referring the patient to the physician to answer others.\textsuperscript{371} Not surprisingly, the American Medical Association opposes any such role for pharmacists as an unwar-

\textsuperscript{364} See note 209 supra.
\textsuperscript{365} One survey found physicians greatly overestimated compliance by patients with drug usage instructions. Caron & Roth, supra note 353, at 923.
\textsuperscript{366} See note 352 and accompanying text supra.
\textsuperscript{367} For a description of how such a system could efficiently work, see Gardner, supra note 341, at 854 n.94; Zellmer, supra note 362, at 535.
\textsuperscript{368} Gardner, supra note 341, at 854. The patient’s difficulty in making recontact may be increased by the refusal of some physicians to answer questions over the telephone. \textit{Id.}
\textsuperscript{369} \textit{Id.} at 853-54.
\textsuperscript{370} Pharmacists receive at least five years of university training primarily oriented toward drugs and drug therapy and sometimes serve as therapeutic advisors at hospitals. \textit{Id.} at 854.
\textsuperscript{371} \textit{Id.} at 854-55.
If pharmacists are not to assume a counseling role, the only other answer to the distributional problem would be for the physician to discuss the information which later would be received in the insert with the patient during the office visit. For those patients who did not retain what was discussed, however, the same problems would arise. But other patients, who did retain the information, would benefit. Finally, if physicians used this method, they might be able to predict with greater accuracy whether a patient might misunderstand or be frightened by the information which would later be received and thereby order that no insert be provided.\(^\text{373}\)

Informed Consent.—The benefits of quicker recognition of adverse effects and increased physician self-scrutiny might also occur if physicians were required to obtain informed consent for prescription of a drug for a nonapproved purpose.\(^\text{374}\) In fact, physician self-evaluation would be more likely since physician-patient conversations would have to be initiated by the physician, rather than by patients.

Informed consent might also be considered a useful adjunct to the patient package insert. The informed consent requirement would place with the physician the responsibility to try to explain effectively the nature of the nonapproved prescription in instances where a patient’s age or education might otherwise make understanding of a package insert difficult.\(^\text{375}\) Similarly, to the extent that the patient might not understand the information imparted by the physician because of anxiety arising from the medical setting,\(^\text{376}\) the patient would have the package insert to read later to reinforce information which the patient had been given.

At present, there is little reason for physicians to disclose the nonapproved nature of a prescription to patients. As previously discussed, under the tort negligence system there is only a limited likelihood that such disclosures might be necessary.\(^\text{377}\) Governmental regulations and medical ethical codes, which call for expanded forms of consent, apply only to instances where a physician is engaged in

\(^{372}\) Id. at 853.

\(^{373}\) See note 359 and accompanying text supra.

\(^{374}\) See notes 353-55 and accompanying text supra.

\(^{375}\) See notes 361-62 and accompanying text supra.


\(^{377}\) See notes 225-39 and accompanying text supra.
some form of experiment.378

The proposed New Drug Regulatory Amendments of 1978 would change this situation. When a particular use of a drug would involve the risk of serious illness or injury, the FDA would be authorized to require informed consent in such form and manner as it might deem appropriate.379 If given this authority, the FDA could require physicians to disclose the nonapproved nature of a prescription as well as considerable educational information about the drug. That information could include the nature, purpose, and expected duration of the treatment, the hazards or side-effects potentially involved, the expected benefits, and the existence of alternative forms of therapy.380 The FDA could also require that the consent be written instead of oral.381

If the FDA ordered something approaching the scope of disclosure just described, it would greatly exceed what is presently required by the tort system and instead would be closer to what the agency requires for new drug experimentation.382 For this reason, medical organizations and physicians contend that proposals about informed consent such as this one are an unwarranted intrusion in nonexperimental medical practice.383

Yet because the FDA and courts stand in a different relationship to physicians, the boundaries set by the tort system may not be appropriate for nonapproved prescriptions. In considering what should be the scope of disclosure, courts face competing values. On the one side are the justifications for informed consent.384 On the

378 See Consent For Use of Investigation New Drugs (IND) on Humans: Statement of Policy, 21 C.F.R. § 310.102 (1977) (applicable to human experimentation to obtain FDA approval); Protection of Human Subjects, 45 C.F.R. §§ 46.101-.103 (1977) (applicable to human experimentation paid for by the federal government); Declaration of Helsinki, 11 WORLD MED. J. 281 (1964) (applicable to clinical research combined with professional care). But see AMERICAN MEDICAL ASSOCIATION, PATIENTS BILL OF RIGHTS, reprinted in J. GIBSON, supra note 17, § 11.4, at 269. The latter code, according to one authority, may offer broader protection for patients. J. GIBSON, supra note 17, § 11.4, at 270-71.

379 S. 2755, supra note 266, § 108(e)(2), at S3878.


381 Cf. 21 C.F.R. § 310.102 (1977) (requirements for written and oral consent for drug testing for FDA approval).

382 See id.

383 See, e.g., Letter from Smith Kline Corp. to FDA Hearing Clerk, at 11 (Aug. 11, 1977) [hereinafter cited as Smith Kline Letter] (Comments on REVIEW PANEL FINAL REPORT, note 54 supra).

384 See note 204 and accompanying text supra.
other side is a competing belief that those involved in the judicial system, due to a lack of training and experience, are ill-equipped to second-guess medical judgments.\textsuperscript{385} Of these two considerations, the latter, which gives considerable deference to medical judgments, has dominated judicial thinking.\textsuperscript{386}

By comparison, the FDA stands in a different relationship to physicians. First, the agency necessarily has expertise concerning medical judgments.\textsuperscript{387} Second, the proposed legislation requires the FDA to consult with its advisory committee, which includes representative medical experts, before ordering informed consent for any drug usage.\textsuperscript{388} Finally, it is likely that any decision to order informed consent would give physicians a therapeutic privilege to not seek such consent if to do so in individual cases would be medically counterproductive.\textsuperscript{389}

Nevertheless, there may still be problems with such a program. For example, there has been a prediction that some physicians faced with the prospect of liability for failure to adequately meet FDA-imposed requirements of informed consent, may choose not to prescribe a drug for a nonapproved purpose that they otherwise would have prescribed.\textsuperscript{390} If the consequence is that patients are denied a beneficial drug, the program could become counterproductive.\textsuperscript{391} Other physicians may react to whatever requirements are imposed by liberally using whatever therapeutic privilege is given to them to avoid seeking consent. Finally, even with good faith compliance by physicians, information might be misunderstood, leading to patient noncompliance with prescribed treatment.\textsuperscript{392}

\begin{footnotes}
\item[385] See Katz, supra note 200, at 140-41; DRAKE Note, supra note 202, at 703.
\item[386] This dominance is illustrated by the wholesale rejection of battery law as the basis of informed consent liability, which would have offered more protection to patients, in favor of a negligence theory, which offers less protection. Katz, supra note 200, at 165-67. Likewise, it is illustrated by such other judicial decisions as the movement to an objective, rather than a subjective, test of causation, and the universal adoption of the therapeutic privilege—both narrowing the protection of the patient. \textit{Id.} at 157; YALE Note, supra note 204, at 1564-70.
\item[387] Studies of the FDA indicate, however, that expertise could be improved. \textit{Review Panel Final Report, supra note 54, at 45.}
\item[388] S. 2755, supra note 266, § 108(e)(2), at S3878. The composition of the advisory panel is described at \textit{id.} § 173.
\item[389] Such a privilege is given under regulations governing the testing of new drugs on humans for FDA approval. See 21 C.F.R. § 310.102(g) (1977).
\item[390] U.S. CONGRESS, OFFICE OF TECHNOLOGY ASSESSMENT, \textsc{Achiving Safer, More Effective and Less Costly Utilization of Therapeutic Drugs} 252 (Draft of March, 1977) [hereinafter cited as \textsc{Office of Technology Assessment}].
\item[391] \textit{Id.}
\item[392] In seeking informed consent for drug experiments, patient understanding has proven to
\end{footnotes}
While all of these possibilities exist, the FDA should be able to take them into account in deciding what kind of action is appropriate in a given circumstance. If seen as a tool which can be effective if used in proper circumstances, rather than as a procedure to be routinely incorporated into medical practice, informed consent should have at least some viability regarding problems of nonapproved prescribing.  

**Improved Methods to Obtain Additional Prescribing Information**

In addition to better utilization of existing information, the possibility also exists of creating and disseminating additional information about a nonapproved use. After a nonapproved use becomes known, if the FDA could more rapidly make its decision as to approval or disapproval, an authoritative decision about the medical worth of the use would be available. If approved, vital prescribing information would be brought to the physician’s attention through the package insert (usually reprinted in the *Physician’s Desk Reference*) and the drug company promotion. A decision by the FDA might be hastened in either of two ways: by expediting the testing necessary for a FDA judgment or by expediting the judgment itself through a provisional approval mechanism. The feasibility of each method is assessed in the following discussion.

**Expedited Testing**—The FDA is often unable to approve a new use of a drug until long after the use becomes widespread because the sponsor of the drug, for various reasons discussed above, delays testing of the new use until after it becomes medically popular. As a result, the FDA is left in an awkward position. While the medical community castigates the agency for its failure to approve a use they regard as safe and effective, the FDA lacks the necessary data to reach any decision on that use.

The approval process for a new use of Propranolol illustrates this problem. Although the drug had been widely used for the nonapproved purpose of treating a form of heart disease, the sponsor

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be a problem even with patients who are employed and of middle income. Hassar & Weintraub, *supra* note 376, at 383.

393 *See Hearings on Quality of Health Care, supra* note 59, at 68 (statement of Marcia Greenberger); Klein, *What Should The Package Insert Be?*, 31 *ARCHIVES OF GENERAL PSYCH.* 735, 735-36 (1974).

394 *See* notes 25-27 and accompanying text *supra*.

395 *See* notes 75-79 and accompanying text *supra*.

396 *Hearings on Use of Advisory Committees, supra* note 56, at 130.
only commenced testing after the FDA asked it to do so.\textsuperscript{397} When by 1974 it did not appear the company would be able to finish its testing within a reasonable time, the FDA, faced with mounting medical criticism for its lack of approval, took the unprecedented action of approving the drug based on studies published in the medical literature.\textsuperscript{398}

To resolve this problem, it has been proposed that the FDA be given authority to obtain early testing of nonapproved uses. Under the proposed Drug Regulatory Reform Act of 1978, after consultation with its advisory committee of independent experts,\textsuperscript{399} the FDA could order a sponsor under certain circumstances to undertake safety or efficacy testing or both.\textsuperscript{400} Safety testing could be ordered whenever a drug reasonably could be expected to produce adverse effects.\textsuperscript{401} Efficacy testing could be ordered in instances of actual or expected nonapproved usage whenever such use either posed a safety risk, because of potential adverse reactions, or it could be expected that the use would be found effective.\textsuperscript{402} As an alternative to sponsor testing, the FDA would also be given authority to conduct this research for itself or to contract with a third party to perform it.\textsuperscript{403}

This proposed authority has been criticized on the ground that it would usurp the prerogative of drug companies to make their own research and investment decisions. If the FDA ordered testing, it could cause a company to undertake an investment in research which the company independently would have decided was undesirable.\textsuperscript{404} If frivolous research were undertaken by this method, investment funds could be diverted from more desirable and necessary research.\textsuperscript{405}

\textsuperscript{397} \textit{Interim Report: Expansion}, supra note 81, at 14 n.21.
\textsuperscript{398} \textit{Hearings on Use of Advisory Committees}, supra note 56, at 130.
\textsuperscript{399} S. 2755, supra note 266, § 108(h), at S3878-79. For the make-up of the panel, see id. § 178, at S3898.
\textsuperscript{400} Id. § 108(h), at S3878-79.
\textsuperscript{401} Id. § 108(h)(1), at S3878.
\textsuperscript{402} Id. § 108(h)(2), at S3878-79. In ordering either safety or efficacy testing, the FDA also would be given the authority to issue guidelines for any ordered investigation and a timetable for the testing. Id. § 108(h)(3), at S3879.
\textsuperscript{403} Id. § 179, at S3898. \textit{See also} H.R. 1603, 95th Cong., 1st Sess. § 8(b) (1977). \textit{Cf.} S. 630, 95th Cong., 1st Sess. § 3 (1977) (proposal that HEW test all new drugs); \textit{see generally}, Shapiro, supra note 19 supra.
\textsuperscript{404} \textit{See, e.g.}, \textit{Hearings on S. 2755}, note 293 supra (statement of Norman Dorsen); PMA Letter, supra note 274, at 25.
\textsuperscript{405} The Pharmaceutical Manufacturers Association has put the matter this way: "Certainly the manufacturer should not be penalized by being compelled to undertake a dangerous or commercially unjustified research investment, just because his marketed product has been mis-
The same criticism can be made of government testing, although the reason for this is not as obvious. If, based on testing done by itself or by contract, the FDA approved a new use of a drug, a sponsor potentially could be in a position to successfully sell the drug for the new use based on testing paid for by the government. To prevent such an economic windfall, the FDA would have to require that the sponsor not promote the drug for the newly approved purpose unless it first repaid the government for the costs of conducting the tests.

By imposing such a reimbursement requirement, the FDA could create a dilemma for itself. On the one hand, if the information concerning a newly approved use did not appear in the package insert, the program would be self-defeating. Unless the insert reflected the results of the testing, physicians might not learn of them and thus prescribing practices would not improve. On the other hand, if the package insert is changed to reflect the approval, the sponsor, even if it did not pay for the governmental data, would obtain at least some increased sales based on the insert.

In most situations, a sponsor would probably buy the government's data since it would want the ability to promote the drug through advertising other than the package insert. It cannot be assumed, however, that this would occur in every instance. It may be necessary, therefore, under a governmental testing program, to require a sponsor to purchase the test data any time the governmental testing proves the drug safe and effective.

Even if the sponsors were required to purchase the governmental data for any new approved use, there would still be a serious problem if most sponsors decided to allow the government to test for new uses. In such cases, the program would become a subsidization

prescribed or found useful for some new but unapproved indication.” PMA Letter, supra note 274, at 25.

The proposal that the FDA test or contract for the testing of new drugs or new uses has been criticized on other grounds. It has been argued that these procedures would put the FDA in the undesirable position of developing the very data which it would then have to review in order to make its regulatory decision. Such a conflict of interest, it is believed, could jeopardize the integrity of the FDA's decision. AMA Letter, supra note 359, at 12. Cf. Letter from Pfizer Inc. to FDA Hearing Clerk, at 56 (Aug. 15, 1977) (comments on REVIEW PANEL FINAL REPORT, note 54 supra).

The potential for such a conflict of interest could be resolved if the FDA would arrange for an appropriate governmental entity, such as the National Institutes of Health (NIH), to test or contract for testing of the nonapproved uses. See Shapiro, note 19 supra. Under such an arrangement, the only decision made by the FDA would be that the drug needed testing. Since this would not constitute any decision on the merits of the drug, no prejudgment should be involved.
of the pharmaceutical industry since the industry would be paying only for successful test results, not for tests which established that a use was not safe and effective. The companies would thereby have passed the risk of failure to the government.

For this reason, it can be assumed that in most situations a sponsor would allow the government to do the testing. The only risk an entity runs by so deciding is that it could itself have tested the drug in a more professional manner than the government. If the new use is disapproved because of faulty testing, the company would have lost, at least for a time, the ability to market an approved use. Yet this risk is minimal. The government would probably hire the very same persons whom the companies hire to do the testing—clinical pharmacologists at university teaching hospitals.

As a result of these problems, the sponsors would have to be required to pay for all testing costs, whatever the outcome of the tests, if there is to be a governmental testing program for nonapproved uses. Government testing then would share the same disadvantage as government-ordered testing. If the government undertook or ordered testing which was without merit, private companies, which would not have made the same decision, will have been taxed to pay for the research. The government would thereby usurp a company's prerogative to make its own investment decisions.

To partially resolve this disadvantage, it has been suggested that the FDA's authority to order or conduct such testing be limited to the time when it would be most justifiable—when the nonapproved usage has become widespread. In such a circumstance, since the company would probably be deriving a considerable financial reward from the sale of the drug for the nonapproved purpose, it could be argued that it more legitimately can be ordered to justify the safety and efficacy of that use. The intrusion would also be justified at that point because the danger posed to the public by the widespread use could be considerable.

Yet limiting the FDA's authority in such a manner could be counterproductive. Since drug testing is time-consuming, if test-
ing was not begun until a nonapproved use became widespread, the potentially dangerous use could continue for some time before the testing process could be completed. As a result, company investment prerogatives would need some other manner of protection.

The proposed Act, if amended, might offer the necessary protection. First, governmental testing, which under the proposed Act may be used at the FDA's discretion, could be subjected to the same constraints as FDA-ordered testing if it were to be used for the same purpose. Second, the constraints might be made more stringent. Instead of allowing FDA action regarding efficacy testing if there was actual or expected unapproved usage, the agency might be limited to situations where there was actual unapproved usage. If a further limitation was thought desirable, FDA action could be limited to situations where unapproved usage exceeded some minimum amount, based on appropriate criteria. The FDA's compliance with these criteria could be tested through the judicial review provided by the proposed Act.

If enacted, these changes would delay testing somewhat, but the testing would still come earlier than it would if postponed until the nonapproved use had become widespread. The changes, while not completely protecting companies from regulatory interference, would offer as much protection as is practicable.

*Expedited Approval.*—Whether or not the testing for a nonapproved use is relatively early or late in commencing, a final FDA decision may be further delayed. Because the standards under the law for approval are exacting and the FDA tends to interpret those standards strictly, a sponsor may not be able to convince the FDA that the testing establishes the new use as safe and effective.

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414 S. 2755, supra note 266, § 179, at S3898.
415 Id. § 108(h), at S3878-79.
416 See id. § 108(h)(2), at S3878-79. Such a restriction could, however, be disadvantageous. When some drugs are approved, the FDA, with great certainty, can predict they will be used for nonapproved purposes. Finkel, supra note 84, at 181, 182-83.
418 See note 11 and accompanying text supra.
419 See notes 12-19 and accompanying text supra.
One reason the FDA is motivated to strictly interpret the standards is that, once it approves a drug, the agency no longer has any legal control over it. As a former FDA Commissioner explained, this fact creates a conservative bias in the FDA: "Drug approval is now pretty much an all or nothing event. . . . Since approval is our 'last chance,' we properly now tend to want all data in hand to be absolutely certain of every detail before approving a drug."421

The Drug Regulatory Act of 1978 proposes to relieve this problem by allowing new uses of drugs, promising important therapeutic benefits, to be provisionally licensed under a standard of approval less rigorous than the standard for final approval. Because the approval would be only provisional, the sponsor would be required to complete testing in order to gain final approval.

In addition, since provisional approval would be under a less rigorous standard than final approval, the FDA would be given certain powers to protect the public. If additional protections were necessary, the proposed Act would allow the FDA to require that a patient package insert be given the patient, that there be prescrib-
ing limitations of the kinds discussed above, that informed consent be obtained from patients given the drug, that an adverse reaction reporting system be maintained for the drug, or that certain additional tests be conducted on the drug.

Supporters of the provisional approval concept argue that certain drug uses could be more quickly approved since the FDA would not need to be as cautious as under the existing system for final approval. If a new use could be quickly provisionally approved, the problems associated with widespread use for a nonapproved purpose would be eased. Authoritative information about use of the drug would be available to physicians through the package insert and through drug company promotion. Moreover, it has been suggested that a provisional approval process may encourage drug sponsors to submit applications for new indications at an earlier date because of the potential for expedited treatment of the application.

Some elements of organized medicine, like the American Medical Association, approve of the idea of earlier approval, but dislike giving the FDA any authority which would encumber or further inhibit use of the drug. However, unless the FDA is given that additional authority, provisional approval will probably not serve its purpose. Without the additional controls, the FDA would be in the same position regarding final approval. As a result, the agency would cautiously make its provisional decisions and little expediting would occur.

Another possible criticism of the provisional approval proposal is that it would escalate the new use of a drug. This would probably occur because authoritative prescribing information about the

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426 S. 2755, supra note 266, §§ 108(e)(1)(A), 110(d)(2), at S3878, S3881. For a discussion of the problems associated with imposition of such limitations, see notes 291-95 and accompanying text supra.

427 S. 2755, supra note 266, §§ 108(e)(2), 110(d)(2), at S3878, S3881. For a further description, see notes 374-93 and accompanying text supra.

428 S. 2755, supra note 266, §§ 108(g), 110(d)(2), at S3878, S3881. At present, the FDA has no such system. See notes 84-85 and accompanying text supra.

429 S. 2755, supra note 266, §§ 108(h), 110(d)(2), at S3878-79, S3881. The FDA, which maintains that it has the authority under the existing Act to order postapproval testing, has approved two drugs on the condition that additional testing be undertaken. Finkel, supra note 84, at 182-83. The authority of the FDA to impose such a condition, however, has not undergone legal challenge. Id. at 183.

For a discussion of the problems associated with FDA-ordered testing, see notes 404-06 and accompanying text supra.

430 See, e.g., Johnstone, supra note 47, at 179-80; Schmidt Address, note 81 supra.

431 AMA Letter, supra note 359, at 12.

432 Id.

433 OFFICE OF TECHNOLOGY ASSESSMENT, supra note 390, at 252.
use would appear in the package insert and elsewhere. The public danger could be an increased number of adverse reactions caused by the drug.

While such a risk would always exist, the proposed Act seeks to prevent the risk from reaching an unacceptable level. First, to gain provisional approval, a sponsor would bear the burden of proving that delaying issuance of the license until the sponsor could meet the final approval standards would pose a greater risk to patients in need of treatment than was posed by the potential for adverse reactions.434 Second, the FDA would be able to use the various powers given it under the proposed legislation to monitor and police any danger of unacceptable numbers of adverse reactions.435 Finally, it has been recommended, as a further precaution, that the agency's intention to provisionally approve a drug be announced in the Federal Register with ample time provided for public comment.436

CONCLUSION

Once it is determined that sole reliance on the tort negligence system to prevent nonapproved prescription injuries is not sufficient to protect the public, the choice of a preventative measure may depend on the seriousness of the health hazard posed. Some solutions, such as FDA dissemination of information, prescription limitations, or required patient education, could be implemented fairly rapidly if necessary. By comparison, expedited testing or approval are more time-consuming. Moreover, each of these various preventative efforts also varies in its effectiveness in improving the quality of physician risk/benefit decisions. Provision of existing or additional information can improve decisionmaking, but only if the information is utilized and understood. Required patient education may have a prophylactic effect of encouraging greater physician self-restraint, but prescription limitations may be more effective by limiting a drug's use to those physicians with the greatest expertise.

In addition, the choice of an appropriate remedy is further complicated by the possibility that, depending on the circumstances, characteristics associated with various solutions may rule them out. For example, expedited approval may depend on the FDA's ability to impose certain necessary restrictions, but those restrictions may be

434 S. 2755, supra note 266, § 110(a)(3), at S3880.
435 See notes 425-29 and accompanying text supra.
436 INTERIM REPORT: EXPANSION, supra note 81, at 19. Generally, the FDA does not issue a Federal Register notice announcing the approval of a new drug or new drug use, but instead usually issues a press release. Id. at 19 n.27.
undesirable in a given instance. Similarly, the restrictions on FDA-purchased or FDA-ordered testing recommended for protection of pharmaceutical investment prerogatives may hamper the use of this remedy.

Some of these problems, however, can be avoided by the use of multiple efforts. Slower efforts, such as expedited testing and approval, could be combined with more expeditious efforts such as patient education. Similarly, the distributional problems afflicting patient package inserts could be offset by physician discussion of the insert before the patient receives it at the pharmacy—a discussion which the FDA can mandate by requiring informed consent.

As a result of these considerations and because it is necessary that the various actions be coordinated, the wisest course of action would be to give the FDA the authority it seeks under the Drug Regulatory Amendments of 1978, with the changes previously suggested, so that the agency could choose those measures which would be most appropriate under the circumstances. Necessarily, this will impinge upon physician prescribing habits to an unprecedented degree. The prescription of a drug for a nonapproved purpose falls exactly between a FDA regulatory scheme intended to protect the public from the untested hazards of new drugs or drug uses and a strongly held ethic that physicians deserve substantial freedom to practice their craft. Unfortunately, if preventative efforts of meaningful importance are to be taken, both objectives cannot be met.

If faced with FDA actions in this area, physicians may choose to effectuate responsible peer review and thereby avoid the necessity for FDA actions. In the meantime, the FDA should first consider, consistent with other objectives such as timeliness and effectiveness, those efforts to resolve nonapproved prescribing problems which do not impinge on physician prescribing but instead provide the physician with existing or additional information. If greater protection is necessary, required patient education, which burdens the physician only with explaining the risk/benefit decision, is preferable to physician prescribing limitations. The latter remedy, which poses the greatest intrusion, should probably be limited to those instances where the nonapproved use of the drug can be considered an imminent hazard to the public.

Despite these various reasons for allowing the FDA to choose an appropriate remedy out of several options, the ethical preference is that, whatever other actions the FDA might take, the present FDA regulations on informed consent for large scale (Phase III) human
drug experimentation should apply to any drug prescribed for a non-approved use. The prescription of a drug for a nonapproved purpose is so comparable to such experimentation that it should be similarly treated.

Informed consent for new drug experimentation, intended both to treat the patient and to derive scientific information, is required for two reasons. First, it prevents patients from abdicating the decision to participate in the experiment to the physician when the physician has the dual motive of both treatment and experimentation. Second, it informs the patient that there are serious risks involved in participation because the outcome of the experiment may be in doubt. By comparison, informed consent of the same scope is normally thought not to be necessary for the strictly therapeutic use of a drug. In such a case the physician has only the motivation to treat the patient and “it is assumed that the benefits-risk calculation has been resolved decisively in favor of ‘benefits’ so that an individual physician can feel free to employ the procedure with his patients on the basis of his own judgment . . . .”

For the prescription of a drug for a nonapproved purpose, such an assumption cannot be made. Until there is FDA approval of a new use, the evidence has not been “resolved decisively” in favor of that use. But because this distinction is not presently made by physicians, some patients, who are being given the drug under IND testing intended to obtain FDA approval for the new use, fall under the FDA regulations on informed consent, while other patients, who are being given the same drug for the same purpose, do not. Presumably both groups of patients face the same risk. Hence, the only justification for the difference in treatment is that the experimenting set of physicians has a dual motive, while the therapeutic set of physicians does not.

This distinction should not be considered as controlling. Both reasons for informed consent are equally compelling and either should be sufficient to require the FDA-mandated disclosure. Moreover, even in the therapeutic situation, a physician may also be

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437 Because physician investigators may be in a position to improve their career status with successful research projects, there is a temptation to overreach ethical boundaries. “Man’s capacity to become joint adventurers in a common cause makes the consensual relation possible; man’s propensity to overreach his joint adventurer even in a good cause makes consent necessary.” P. RAMSEY, THE PATIENT AS PERSON 5 (1970), cited in J. KATZ & A. CAPRON, CATASTROPHIC DISEASES: WHO DECIDES WHAT? 83 (1975).


439 J. KATZ & A. CAPRON, supra note 437, at 170.
motivated by some sense of experimentation—a desire to informally determine the effects of the drug. But even if the increased patient risk alone is not sufficient to require such disclosure, there is another consideration. To the extent the matter is considered, it is believed that most patients assume that a prescribed drug has been approved by the FDA for the purpose prescribed. Necessarily, any such patient is deceived if the drug is taken even in part on the basis of this belief. As a result, any consent which is given must be considered as vitiated in such a situation.

Undoubtedly, for a time, a “civil liberties” approach to informed consent would cause great dislocation for many physicians. Moreover, as discussed above, a requirement of informed consent itself poses several problems. Nevertheless, a degree of honesty in this matter is owed patients and only in this manner can it be provided. If this proposal is combined with greater FDA authority of the kind recommended, the present anomaly of drug regulation may be eliminated to a satisfactory degree.

440 Such an approach may be endemic to lawyers and rejected for that reason by physicians. *See Jaffee, Law As a System of Control, in Experimentation With Human Subjects* 211-12 (P. Freund ed. 1970).