1972

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THE PROSUBSTITUTION TREND
IN MODERN PHARMACY LAW

Sidney H. Willig*

When the consumer reposes a high level of trust and confidence in the expertise of a provider of goods or services, the law commonly treats this vendor in a fashion different from the manner in which it treats other suppliers of goods and services. Accordingly, the law regulates the professions to a greater extent than other occupations. This scrutiny stems largely from the inability of the public to protect itself adequately in a situation where its members engage the professional on the understanding that he will put their interests before his own. Because the professional is deemed to be a fiduciary, the rule of caveat emptor does not apply. This is clearly the case with the professional pharmacist. He stands as a fiduciary for most transactions, and particularly in the case of prescription drugs, the public must trust the ability of the pharmacist to dispense properly those commodities on which health and life may depend.

Most patrons of commercial pharmacies assume that when they purchase a particular nonprescription article and ask the pharmacist for the item by brand name, they will receive the requested brand and no other. The consumer will generally be able to detect whether the pharmacist has complied with his request. Through advertising, recommendation, and other forms of promotion, the consumer will often have been apprised of the distinct nature of the commodity he seeks to purchase. Because brand name nonprescription pharmaceuticals are often packaged in a readily recognizable form, the consumer will usually be in a position to discern differences among items.

A different situation arises where the physician prescribes a particular product for a patient's use. The patient-buyer sees the product in only its final form, usually packaged by the pharmacist himself rather than by the manufacturer. As a result, the package received by the buyer is unlikely to bear the commercially distinguishing features which permit the buyer to protect himself in the nonprescription drug context. Barring an inordinate amount of technical knowledge on the part of the consumer, he will be unable to discern whether he has actually received the product that the physician has prescribed.

A discrepancy between the drug prescribed and the drug dispensed can result from either intentional or negligent action by the pharmacist. In the first instance, contrary to the ethics of his profession, an unscrupulous pharmacist may intentionally dispense an imitation or cheaper "equivalent" or even a nonequivalent item rather than the prescribed product. An intentional action of this variety will often be for the pharmacist's own economic benefit or that of another. In the second instance, the discrepancy is the result of an error by a careless pharmacist in dispensing the prescribed drug. Any act resulting in a variation between the prescription pharmaceutical requested and that pharmaceutical dispensed is technically known to the law governing pharmacy as "substitution." Both federal and state legislation have proscribed the practice of substitution. Undoubtedly both negligent and intentional substitution result from the actions of a small number of pharmacy practitioners. The problem is nevertheless one of great significance to pharmacists in general.

This article explores the legal problems presented to the practicing pharmacist by drug substitution. It delineates the practical and economic realities bearing on substitution and the arguments

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2 Id.
3 It has been stated that the practice we now call substitution dates at least to the eighth century B.C. The practice at that time involved substituting an entirely different compound which looked or tasted like the prescribed one. Id. at 758; Ulrich, The Generic Drug Dispute in Louisiana, 117 J. La. St. Med. Soc. 141, 142 (1965).
4 Ulrich, supra note 3, at 142-43; reports that the practice has been illegal at least since the year 1227 A.D. when Emperor Frederick II prohibited substitution without the consent of the prescribing physician. A discussion of the current state of antisubstitution law in the United States will be found in the text accompanying notes 103-52 infra.
5 Estimates vary as to the amount of substitution engaged in by practicing pharmacists. Galbally, supra note 1, at 758 n.2, cites a survey by the American Druggist Magazine finding that substitution in the prescription drug context had occurred in 3.7 percent of prescriptions filled in 1957, as compared with a 14.7 percent rate in 1953. A recent investigation by the Louisiana Department of Public Welfare, disclosed that in 24 percent of the drugstores audited a pharmacist was guilty of some irregularity in dispensing prescriptions. Ulrich, supra note 3, at 143-44.
both in favor of and against limited legal substitution. After describing the current status of the law on the subject and the various resultant liabilities of the pharmacist, the article then suggests means by which substitution might be made an acceptable practice in certain circumstances.

I. Substitution

In broadest terms, substitution may be defined as the replacement of an ordered or prescribed drug by another substance where the replacement is neither authorized by nor revealed to the person ordering or prescribing the item.6 The failure of the pharmacist to dispense a requested nonprescription item can result in various civil and other liabilities.7 Where a prescription article is involved, the person who has prescribed is generally not the purchaser. Both state and federal laws provide that many drugs may be prescribed only by authorized persons.8 Thus in the prescription drug context the prescriber is the physician, while the purchaser is the patient. Substitution occurs when the pharmacist replaces the item prescribed by the physician without the physician’s prior consent. Thus in both instances the proscribed act requires that (1) the dispensed drug differ from the order or prescription, and (2) that the replacement occur without the prior consent of the person ordering the article.9 This definition encompasses the situation in which the prescriber orders a particular brand name and the pharmacist replaces the requested brand name item with a similar or equivalent pharmaceutical having a different brand name.10

Within this general definition, a variety of circumstances can be hypothesized in which substitution will be held to have occurred. An analysis of these varieties of substitution is useful in consid-

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6 Galbally, supra note 1, at 758; Ulrich, supra note 3, at 142.
7 Liabilities to be incurred by the pharmacist in such a situation are discussed in the text accompanying notes 103–52 infra. See also Dunlap v. OakCliff Pharmacy, 288 S.W. 236 (Tex. Civ. App. 1926).
9 See, e.g., Galbally, supra note 1, at 758. Mich. Comp. Laws Ann. § 338.110(u) (1967) provides in part: “Substitute” means to dispense without prescriber’s authorization a different drug or brand of drug in place of the drug or brand of drug ordered or prescribed.
ering the need and possibilities for reform in substitution law. There may be policies weighing for the retention of substitution laws in some cases which are not present in others.

A. Negligent Substitution

The classic case of substitution is that of the pharmacist who negligently dispenses a commodity which differs from that ordered or prescribed. In this instance the erroneous substitution is unknown to patient, prescriber, and dispenser. It would seem that because none of the parties is aware of the substitution or able to consent to it in advance of dispensing the commodity, substitution of this variety should never be legally permissible.

B. Intentional Substitution

1. Known Only to the Pharmacist—A more perplexing problem is involved where the pharmacist intentionally replaces the prescribed drug with another. In this case, an intent to violate ethical principles and applicable law is involved. The intention to substitute may result from a number of motives, including considerations of the economic welfare of the patient and a desire on the part of the pharmacist himself for economic gain. His desire may be to charge the patient the price for a relatively expensive brand name product while actually dispensing a lower priced imitation, counterfeit, or equivalent. A pharmacist’s concern may also extend to the notion that by reducing the prices he charges his customers he will be able to compete with other pharmacists who engage in this unethical and illegal practice.

Intentional substitution may take another form. Upon receipt of a prescription for a brand name drug, the pharmacist may dispense a lower priced equivalent of the drug and charge the patient the lower price rather than the higher price of the brand name.


12 See, e.g., Wilcox v. Butt’s Drug Stores, 38 N.M. 502, 35 P.2d 978, 94 A.L.R. 726 (1934) (customer knew of substitution but had been misled by pharmacist as to nature of substituted item).

13 Galbally, supra note 1, at 762.

14 This was the technique allegedly employed in a recent Louisiana welfare fraud case. See Ulrich, supra note 3, at 141. See also Winthrop Chemical Co. v. Weinberg, 60 F.2d 461 (3d Cir. 1932).
There are considerable economic pressures on the pharmacist to follow this practice. His inventory position is considerably enhanced if he is able to stock only one brand of the article rather than a multitude of brand name equivalents.\textsuperscript{15} His competitive position vis-à-vis other commercial pharmacies may be maintained or advanced by offering the consumer-patient a lower priced drug.\textsuperscript{16} The commercial pharmacist must always live with the possibility that if he does not provide the lower priced item, his competition will. A further pressure bearing on the practitioner involves those who regularly deal with patients receiving some sort of public subsidy for medical care. In some instances public health service organizations will reimburse a pharmacist only on the basis of an average price list, even though the prescribing physician has requested a brand name pharmaceutical.\textsuperscript{17} These various economic pressures on the pharmacist place him, therefore, in an undesirable economic and professional position.

2. \textit{Known to the Pharmacist and Patient}—Other forms of substitution may be evident in which the prescriber does not consent to a replacement of the article he has ordered. The pharmacist may obtain the consent of the patient himself to substitute another, and presumably less expensive, commodity. In effect, the pharmacist and patient have combined their judgment to modify the physician's prescription. This presently violates both the spirit and the letter of Durham-Humphrey Act where the drug is one legitimately distributed only pursuant to prescription.\textsuperscript{18} Arguably, this course of action should be approved by law in order to allow economic considerations to influence the otherwise scientific problem of drug selection. Additionally, a pharmacist may request that a physician change his prescription in light of economic or clinical considerations. If the physician declines, the pharmacist is bound legally and ethically to honor this decision. If the pre-

\textsuperscript{15} With synthetic penicillin, for example, there are at least six different brand names. \textit{Administered Drug Prices}, supra note 11, at 223. If a pharmacist were able to carry only one of these brands in inventory (and not necessarily the least expensive), his cost savings could be substantial. Often the pharmacist will prefer to stock one well-known brand since physicians will more likely agree to a change to that brand.

\textsuperscript{16} At least two situations can be envisioned here: first, simply in terms of added sales volume that may result from a lower level of prices; second, where the pharmacist is out of stock on a particular item and must either substitute or forgo a sale.

\textsuperscript{17} For example, Kentucky reimburses druggists on the basis of a list of average prices. \textit{Task Force on Prescription Drugs, Current American and Foreign Programs} 59 (HEW 1968) [hereinafter cited as \textit{Task Force Current Programs}]. Ninety-five per cent of all prescriptions in the United States are written by brand name. Ulrich, \textit{supra} note 3, at 141. In instances where reimbursement for a brand name prescription is on some sort of average price basis, the pharmacist faces a choice of substituting, refusing to fill the prescription, asking the patient to absorb the difference, or absorbing the difference himself.

scribing physician approves, substitution is no longer in issue because the pharmacist has in effect received a new prescription.

3. Known to the Pharmacist and a Third Party—Under some circumstances substitution may occur at the request of a third party. The most controversial of these arrangements arises where a public authority is paying for prescriptions to be received by the patient. The public authority may instruct the physician or pharmacist that prescriptions are to be filled only with the least expensive product available and may also ask the physician so to prescribe. Similarly, the public authority may reimburse the pharmacist only on the basis of an average price list.19 Whether the directive is to a pharmacist employed by the authority in its own pharmacy or to an independent commercial practitioner, the ethical and legal problems are similar, even though there is a vast difference in the economic pressures faced by each.20

Finally, a variety of substitution by consent is often employed under what is known as a formulary organization system. Often employed by large hospitals, this arrangement commonly involves a committee of physicians, administrators, and pharmacists that decides which drugs will be used in the hospital. When a physician prescribes a brand name, generally on a blank which bears a legend stating the pharmacist may choose the formulary equivalent unless the doctor specifies contrarily, the pharmacist dispenses the equivalent drug selected for use at the hospital21 Such a system requires prior consent from all physicians in the health service unit. This formulary system may not fall within the general definition of substitution because the physician-prescriber has consented in advance to all substitutions by agreeing to the hospital by-laws as well as by often using the hospital prescription blank described previously. Yet he has not consented to each

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19 This method was employed as to physicians by Louisiana after the investigation conducted by the Department of Public Welfare. Ulrich, supra note 3, at 141. It has also been employed in California. TASK FORCE CURRENT PROGRAMS, supra note 17, at 39–52. An average price system of reimbursement is also used in Kentucky. See id. at 53–61. For a detailed summary of these reimbursement systems, see id. at 37. See generally COMPTROLLER GENERAL OF THE UNITED STATES, REVIEW OF PRICING METHODS USED BY VARIOUS STATES IN THE PURCHASE OF PRESCRIBED DRUGS UNDER FEDERALLY AIDED PUBLIC ASSISTANCE PROGRAMS (1967).

20 The economic pressure on the pharmacist appears to be increasing every year. It has been estimated that combined federal and state expenditures for public assistance payment programs totaled 200 million dollars in 1968, as compared with approximately eighteen million dollars in 1957. TASK FORCE CURRENT PROGRAMS, supranote 17, at 36.

21 For discussions of the operation and legal implications of the hospital formulary system, see Woods, Hospital Formularies—Possible Liability Risks for Injuries to Patients, 19 BUS. LAW. 1007 (1964); Statement, Guiding Principles on the Operation of the Hospital Formulary System, 21 AM. J. HOSPITAL PHARMACY 40 (1964); TASK FORCE ON PRESCRIPTION DRUGS, FINAL REPORT 38–40 (HEW 1969) [hereinafter cited as TASK FORCE FINAL REPORT].
individual substitution in an "informed" manner because in practice only the pharmacist or purchasing agent may know the exact drug available for the prescription order.

It should be evident that all varieties of substitution may not deserve uniform legal treatment. In the instance of negligent substitution, it can be persuasively argued that current anti-substitution laws serve a valid purpose in holding pharmacists to a high standard of care by deterring and punishing substitution that occurs without the consent or knowledge of any of the parties to the transaction. In the case of intentional substitution undertaken by the pharmacist for his benefit alone, a similar conclusion is appropriate since the pharmacist is essentially perpetrating a fraud. In contrast, where the practitioner substitutes a lower priced equivalent and charges the patient for the less expensive pharmaceutical, the pharmacist may really be tempering the physician's scientific judgment with a consideration of economic factors. This concern for economic factors may serve the pharmacist's economic interests, but it is purportedly also in the patient's economic interest. Most physicians believe, however, that the patient's primary interest is a health interest. Furthermore, because the physician is the patient's primary agent in serving that interest, tampering with the physician's judgment without his knowledge is a dangerous activity. The patient at least ought to be made aware of the pharmacist's decision and be able to ratify it. While this may not satisfy the present state and federal statutes, it at least indicates nonfraudulent conduct by the pharmacist.

The focus of this article is the legal and practical problems involved in substitution where demonstrably equivalent drugs are involved. It has been argued that this variety of substitution should be legally permissible. Presumably, only that substitution which occurs when the drug prescribed and the drug dispensed are truly equivalent should be eligible for permission. It is possible that substitution of this sort may also be useful where the substitution is authorized by a third party who pays for the prescription.

II. PHARMACEUTICAL EQUIVALENCE

The most frequently discussed issue in the substitution controversy is that of the equivalence of the two drugs involved in any particular case. Considerable debate has been generated on the existence of so-called "generic equivalency." The argument

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22 See text accompanying notes 64-94 infra.
for substitution in limited instances rests on the proposition that when a physician prescribes a brand name product, about 20 percent of the time there are equivalent and possibly less expensive products which would be appropriate for use in treatment.

When a pharmaceutical is compounded, there will always be a chemical name to describe the active ingredient or ingredients contained. The chemical name conveys information concerning the structure and components of the compound. Because the chemical name is not often conducive to facile communication, the same compound usually will bear one or more generic names. The generic name is also commonly referred to as the usual, nonproprietary, established, or official name. Finally, the manufacturer may compose a proprietary or brand name for his form of the generic product. Frequently this brand name is protected by a trademark. This trade name represents an attempt by the manufacturer or distributor to distinguish his product from other similar or even identical products. The debate over substitution has centered on whether the law should permit generic name or other brand name drugs to be substituted for the prescribed brand name.

23 Administered Drug Prices, supra note 11, at 223. For example, the chemical name of a synthetic penicillin is alphaphenoxyethyl penicillin potassium. Id.


25 The Federal Food, Drug, and Cosmetic Act § 502, 21 U.S.C. § 352 (1970), terms this the "established name." See also Task Force Final Report, supra note 21, at x; Ulrich, supra note 3, at 142. The generic name for synthetic penicillin is the same as the chemical name, as identified in note 23 supra. This drug bears the additional generic names of potassium penicillin 152 and phenethicillin potassium. While the chemical name often presents problems of communication, it does have the advantage of expressing the relationship to similar compounds. This relationship is often not expressed in the generic name. Administered Drug Prices, supra note 11, at 223–24.

26 Task Force Final Report, supra note 21, at x; Ulrich, supra note 3, at 142. The trade names for the synthetic penicillin discussed are Syncillin (produced by Bristol), Darcil (Wyeth), Alpen (Schering), Chemipen (Squibb), Dramcillin-S (White), and Maxipen (Roerig). Bristol and Wyeth also characterize their brands by the generic name potassium penicillin 152, while Schering, Squibb, and White also use the ordinary name phenethicillin potassium for their brands. Roerig uses the generic name alpha-phenoxyethyl penicillin potassium. Administered Drug Prices, supra note 11, at 223–24.

drug. This raises the unavoidable factual and technical issue of whether a given generic drug is equivalent to the particular brand name pharmaceutical.

Although much of the literature has framed the issue in terms of generic equivalents, the Department of Health, Education, and Welfare (HEW), in its study of prescription drugs, has rejected the use of that term. In its place, the study employs the terms chemical equivalent, biological equivalent, and clinical equivalent. As to the significant relationships among these terms, the HEW Task Force on Prescription Drugs has succinctly stated the problem as follows:

Given two drug products containing essentially the same amount of the same active ingredient in the same dosage form—that is, two chemical equivalents—will they produce essentially the same clinical effects?

The answer to this question has been debated in the literature and no concrete answer has emerged. The Food and Drug Administration, as the sole unit within HEW with actual knowledge of manufacturing procedure and drug product quality control assurance, has steadfastly refused to give a generally affirmative or negative answer, preferring to consider each product on an individual basis. The HEW Task Force appears to be the first organization to undertake a systematic study of the clinical equivalency problem. Ideally, any study of the issue should seek to

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30 TASK FORCE FINAL REPORT, supra note 21, at x. The Task Force rejected the shorthand "generic equivalent" for the persuasive reason that its meaning has been completely confused by the literature.

31 "Chemical equivalents—Those multiple-source drug products which contain essentially identical amounts of the identical active ingredients, in identical dosage forms, and which meet existing physico-chemical standards in the official compendia." Id.

32 "Biological equivalents—Those chemical equivalents which, when administered in the same amounts, will provide essentially the same biological or physiological availability, as measured by blood levels, etc." Id.

33 "Clinical equivalents—Those chemical equivalents which, when administered in the same amounts, will provide essentially the same therapeutic effect as measured by the control of a symptom or a disease." Id.

34 Id. at 31.

35 Significant issues of public policy, governmental drug policy, regulation of the drug industry, drug standards, and drug marketing turn on the answer to this question. DRUG PRESCRIBERS, supra note 29, at 22.
determine the relationship between chemical and clinical equivalency. The Task Force decided, however, that this would be impractical from a testing point of view.\footnote{For the direct determination of clinical equivalency, the ideal method would be the comparison of two or more drug products, containing the same active ingredients, in the same tablet or capsule or other dosage form, in the same amounts, and measurement of their relative effects in human patients in the alleviation of symptoms or the control of a specific disease. Except perhaps in rare instances, such a comparison is impractical. It would be time-consuming and costly. It would be complicated not only by human differences but by differences in the symptoms or diseases under consideration. Furthermore, it would involve human experimentation under conditions in which an unexpected lack of clinical equivalency might well have serious adverse results. Id. at 23.} Therefore the Task Force used the premise that a study of the relationship between chemical equivalents and biological equivalents could serve as a proxy for a study of the chemical-clinical relationship.\footnote{This necessarily assumes that biological equivalency will in most cases correspond with clinical or therapeutic equivalency. To support this assumption, the Task Force found that there is general agreement among pharmacologists that in the case of most drugs—certainly those taken orally for their effects in the blood, the liver, the brain, or other internal organs—their therapeutic effectiveness will be substantially related to the absorption of the active ingredient into the blood stream. Thus, if two preparations yield the same blood concentration of active ingredients, they will presumably yield the same therapeutic effect. Id.} This position has not been found to be acceptable to the agency or to the Food and Drug Administration. The Food and Drug Administration has only recently finished the awesome task of reviewing all prescription drugs marketed under federal drug laws. In its review of drug efficacy the agency concluded that each manufacturer must submit documentation as to the efficacy of his own product, regardless of the chemical likeness to others.

In order to assess the relationship of chemical equivalence to biological equivalence, a number of factors must be considered.\footnote{The drug must present the required concentration, be released from the dosage form into residual granules, dissolve within a reasonable period of time, and be absorbed and delivered to the appropriate part of the body in an adequate concentration. Id.} These factors bearing on physiological availability are substantially influenced by the manner in which the pharmaceutical is formulated.\footnote{Solubility, particle size, crystal form, tablet compression, additives (adjuvants), and age of the drug are factors to be considered. Id. at 24. See also National Pharmaceutical Council, The Importance of Pharmaceutical "Know-How" (n.d.); Sadove, What is a Generic Equivalent?, AM. PROFESSIONAL PHARMACIST, Feb., 1965, at 23–29.} Beginning in 1967, the Task Force began limited biological equivalency trials for selected drugs. After approximately one year of testing, the Task Force had concluded that, "on the basis of available evidence, lack of clinical equivalency among chemical equivalents meeting all official standards has
been grossly exaggerated as a major hazard to the public health.40 Further testing was to be carried out on a high priority basis. Significantly, at this writing five years later, the results of this research are not yet available41 but will hopefully be a comprehensive and objective consideration of the problem.

A. Proequivalence Arguments

Those who have advocated that chemical equivalents are often clinically or therapeutically equivalent have used a number of arguments to support this proposition. Where chemical equivalents have been used on a wide-scale basis over a long period of time, these advocates urge that there have been few reports to the effect that clinical results differ significantly.42 This has been the case in a number of foreign health systems which employ limited forms of substitution in situations where the drugs are arguably equivalent.43 Similarly, some public sector experience in the United States has enhanced the argument that clinical nonequivalence is not as serious a concern as has been suggested.44 Chemical equivalents have been employed in some instances by the Public Health Service, Veterans' Administration, and the Department of Defense procurement services. However, the last, as the single largest federal purchaser of drugs and devices, has a substantial number of inspectors who independently monitor the manufacturers submitting bids. They also independently sample and test the product before use. These services further have their own specifications which the product must meet. On the basis of these specifications and testing, the Department of Defense procurement services reject an average of 40 percent of all bids, even though the particular product may actually be on the market for public use.45

The issue of clinical equivalence is of course a concern in the hospital formulary system where limited substitution has worked

40 Task Force Final Report, supra note 21, at 31.
41 After extensive investigations, it appears that no conclusive findings have yet been reported.
42 Task Force Final Report, supra note 21, at 31-32.
43 See, e.g., Task Force Current Programs, supra note 17, at 140 (Australia), 143 (Belgium), 146 (Canada), 171 (Denmark), 174 (France), 179 (Great Britain), 183 (Netherlands), 186 (New Zealand), 189 (Norway), 192 (Sweden), 196 (West Germany). In a number of these countries, the use of chemical equivalents has not raised serious questions regarding the lack of clinical equivalency.
44 See, e.g., Task Force Final Report, supra note 21, at 31-32; Task Force Current Programs, supra note 17, at 3-134.
45 See Task Force Final Report, supra note 21, at 31-32; Task Force Current Programs, supra note 17, at 4, 18-19.
Risk-taking in a hospital population is minimized, however, by constant patient contact with nurses and clinical pharmacists as well as physician supervision. Therefore, the comparability of this system with nonhospital situations is far less than perfect. Those who suggest that clinical equivalence of chemical equivalents is a common occurrence nevertheless point to these systems employing substitution to demonstrate that the organizations using these systems are satisfied that equivalence does occur.

It is often pointed out that all drugs approved to be marketed in the United States must meet the requirements of the national drug compendia such as the United States Pharmacopeia and the National Formulary. This argument is not entirely accurate. A manufacturer of a given product may send it to market without running any compendial tests. It is only when the manufacturer is involved in an enforcement proceeding that government agencies check whether these requirements have been complied with. The assertion of this argument, however, is that once a product has met the compendial standards of chemical equivalence, substantial therapeutic equivalence must follow. One must bear in mind, however, that the compendia do not advise as to manufacture, but simply offer minimal quality-control monographs. In using the compendial designations on his product, the manufacturer is only agreeing that if and when his product is tested, it will meet these minimal criteria. Yet because in actuality his product is rarely sampled and tested, the Task Force has found that compliance with compendial standards may not be sufficient. Some examples of nonequivalence have been reported. Most recently, government analysts have been dismayed by the lack of clinical efficacy and bioavailability of various brands of Digitoxin which all presumably met the compendial standards for this cardiac maintenance product. Authorities affiliated with the compendia state that these instances are few in number and the answer to the problem lies in more rigid specifications. It is asserted that the problem should be approached with a view to finding standards to

46 See text accompanying note 21 supra.


48 Task Force Final Report, supra note 21, at 34.

49 "The existing standards do not provide complete assurance of clinical or biological equivalency." Drug Prescribers, supra note 29, at 26.
identify those drugs which are not equivalent.\textsuperscript{50} Regrettably, these are after-the-fact detection procedures which ensue following a notice of complaint or drug failure. Public safety demands a better inspection system to deter more forcefully manufacturer unconscionability.

\textbf{B. Antiequivalence Arguments}

Those who suggest that the relationship between chemical equivalents and clinical equivalents is tenuous and at this time largely unknown raise several arguments.\textsuperscript{51} Not all chemicals which are substantially equivalent produce identical clinical results. The use of therapeutically nonequivalent products would thus jeopardize the quality of health care in general as well as in specific cases. There are a number of well-documented examples which have shown that with generic equivalents, the same clinical results were not obtained.\textsuperscript{52} The number of such examples has been variously rated from five to over 200.\textsuperscript{53} This demonstrated lack of correspondence between chemical and therapeutic equivalents results from a number of technical factors which are not reflected in purely chemical terms.\textsuperscript{54} As an example, this author was recently shown an antibiotic sample rejected by the Federal Defense Procurement Agency which had passed certification on an \textit{in vitro} basis but when tested \textit{in vivo} by their bacteriologists exhibited zero efficacy.

Consideration of the problem in terms of mere nonequivalence perhaps understates the problem. It has been suggested that the problem should be seen in terms of demonstrably \textit{equivalent} drugs rather than demonstrably \textit{nonequivalent} pharmaceuticals. Proponents of nonequivalence argue that it is a matter of burden of proof and that it should not be assumed that different pharmaceutical products are equivalent simply because they have not been demonstrated to be nonequivalent.\textsuperscript{55}

Antisubstitution groups also assert that brand name manufacturers have more efficient and reliable quality control than other

\textsuperscript{50} \textit{Id.} at 26–27; \textit{TASK FORCE \textsc{Final Report}}, \textit{supra} note 21, at 34.


\textsuperscript{52} \textit{See, e.g., Drug Prescribers, supra} note 29, at 27.

\textsuperscript{53} \textit{Id.}


\textsuperscript{55} \textit{Drug Prescribers, supra} note 29, at 27.
manufacturers. They also maintain that brand name manufacturers have often exceeded the standards of the official compendia, and as a result their product should not be equated with those products which only meet the minimum criteria of formulation and manufacture.\(^5\)

C. Additional Comment: The HEW Task Force Report

In concluding that the dangers of clinical nonequivalency were exaggerated,\(^5\)\(^7\) the HEW Task Force made several findings. First, while the problem of nonequivalence does not even arise for most pharmaceuticals and although the number of reported examples of clinical nonequivalency is small, such examples cannot be ignored. Second, because 80 percent of the widely used prescription drugs are under patent for seventeen years or enjoy licensure by the Food and Drug Administration, they cannot be legally duplicated. Third, for the remaining one-fifth of the popular prescription drugs, exact clinical equivalency is not crucially important. Those few where exact clinical equivalence is of great importance should be studied carefully in this context. Fourth, nonequivalency may be more widespread than reported. Fifth, although some chemical equivalents are not therapeutically equivalent, there may be therapeutic value in each of the different compounds. Sixth, consideration should be given to raising the standards of the official compendia where lack of clinical equivalence has been shown. Seventh, some chemical equivalents may produce different side effects.\(^5\)\(^8\)

Although the technical answer to the problem of clinical equivalence is by no means clear, it is fair to say that at least in some instances, commodities which are chemically identical will produce therapeutic results which are not significantly different. All chemical equivalents are certainly not equivalent in the clinical sense; furthermore the number of nonequivalents is probably sufficiently great that we cannot ignore the problem. Among drugs in common use, however, it is almost certain that a significant number of clinical equivalents exist, even if the effort has not yet been made to document that fact. It is in these situations that substitution may be a procedure which the law may seek to allow or to encourage.

\(^5\) See id.; Sadove, supra note 39, at 25.
\(^7\) See text accompanying note 34 supra.
\(^8\) DRUG PRESCRIBERS, supra note 29, at 27–28.
III. The Substitution Debate

The discussion of whether substitution should be a permissible practice operates within two constraints. First, the issue of substitution arises only in those instances where the prescriber has a choice of at least two equivalent products. In a large number of instances, not only is the brand name protected by trademark, but the underlying chemical composition is protected by a patent. Of the most frequently used prescription drugs, 80 percent are covered by a patent. The HEW Task Force's Master Drug List included the 409 drugs most frequently used by elderly people. Of these, almost 300 were protected by a patent and produced by only one manufacturer. For these pharmaceuticals, the issue of substitution was not present. In the remaining 116, however, the drug was available under generic or brand names from more than one supplier. Notwithstanding the fact that the Food and Drug Administration requires separate proof of safety and efficacy for each one individually, it is for these drugs that substitution is both a legal and practical issue. Second, it can be reasonably argued that substitution should be permissible only where the two or more products from which a prescriber can choose are therapeutically equivalent. The only body with expertise sufficient to warrant this is the Federal Food and Drug Administration, and they are presently unprepared to undertake the task, let alone the warranty. At the same time, clinical proof of acceptability is virtually the exclusive purview of the medical profession. To argue that a nonequivalent product should be permitted to be substituted would be to defeat the goal of rational prescribing.

A. Prosubstitution Arguments

The most often heard and perhaps most persuasive argument in favor of substitution in cases of substantial therapeutic equivalence is cost. The decision to prescribe an appropriate drug should include economic as well as scientific considerations. One of the constituent elements of rational prescribing is a consideration of relative costs. Foremost among factors contributing to the fail-

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59 For an analysis of the roles played by patents in the drug industry, see ADMINISTERED DRUG PRICES, supra note 11, at 105–54.
60 DRUG USERS, supra note 29, at 36.
61 Id.
62 Id.
63 "Rational prescribing—Prescribing the right drug for the right patient, at the right time, in the right amounts, and with due consideration of relative costs." TASK FORCE FINAL REPORT, supra note 21, at x.
64 For a definition of rational prescribing, see id. That cost is a factor which should be
ure to consider costs when prescribing is the fact that "[h]e who orders does not buy; and he who buys does not order." In essence, the consumer must buy and the pharmacist must dispense only what the physician has prescribed. Because this unique relationship exists, the drug manufacturers aim their advertising at the physician rather than at the ultimate consumer. Furthermore, the large manufacturers spend a considerable amount of money in order to distinguish their products from other brand names. Much of this promotional expense is aimed at maximizing the use of brand names and minimizing the use of generic names. It is generally admitted that the overall market for drugs is fixed in the sense that the demand for all drugs considered together cannot be significantly increased as it can be with other commodities. Nevertheless, it would seem evident that the real purpose of these promotional expenses is to maintain or to enhance market position for particular brand names vis-à-vis competitors. Arguably, this amount of promotional expense is excessive and adds unduly to the price of prescription drugs. For large manufacturers, approximately 24 percent of the sales dollar goes to advertising expenses, 13 percent to profit, and 13 percent to taxes. However, scaled into the drug pricing considered in prescribing is well recognized. Drug Prescribers, supra note 29, at 4; Goodman, The Problem of Drug Efficacy: An Exercise in Dissection, in P. Talalay, Drugs in Our Society 53 (1964). Statement of Seymour Blackman, cited in E. Kefauver, In a Few Hands: Monopoly Power in America 18 (1963); See also Task Force Final Report, supra note 21, at 12. In 1959 and 1960 Senator Kefauver’s Subcommittee on Monopoly and Antitrust held hearings on “administered prices.” One target of his investigation was the drug industry. His findings are summarized in Administered Drug Prices, supra note 11. Senator Kefauver condensed these voluminous hearings in a book, which in part considers the drug industry. E. Kefauver, In a Few Hands: Monopoly Power in America 8-79 (1965). Administered Drug Prices, supra note 11, at 155. The Kefauver Committee estimated that the drug industry spent $750 million in 1958 for promotional expenses. For the twenty-two largest manufacturers, this represented 24 percent of the price of goods sold. Id. at 157. Id. at 231–34. One industry spokesman, Francis C. Brown of the Schering Corporation, has summarized the problem in the following fashion: “Senator, . . . we can’t put two sick people in every bed when there is only one person sick.” Hearings on S. Res. 57 Before the Subcomm. on Antitrust & Monopoly of the Senate Comm. on the Judiciary, 86th Cong., 1st & 2d Sess., pt. 14 at 7888 (1959–60) [hereinafter cited as Senate Hearings]. Senator Kefauver’s investigations were continued by Senator Nelson. See Hearings on Competitive Problems in the Drug Industry Before the Subcomm. on Monopoly of the Senate Select Comm. on Small Business, 90th Cong., 1st & 2d Sess., 91st Cong., 1st & 2d Sess. (1967–70). See E. Kefauver, supra note 65, at 11–22. Senate Hearings, supra note 69, pt. 14, at 8205 (remarks of Mr. Blackman). Administered Drug Prices, supra note 11, at 157. For a comprehensive analysis of the American and Canadian drug industries, see Steele, An Economic Analysis of Recent Attempts to Alter the Laws Regulating the Prescription Drug Industry: The Canadian Investigation and Its Relevance for the United States, 6 Houston L. Rev. 666 (1969).
structure are the costs of research and innovation, the losses for maintaining on the market drugs which are vital for rare conditions (but infrequently sold), products liability insurance, and the like.

In contrast to brand name drugs, many chemically equivalent preparations are therefore understandably available at lower costs than their brand name counterparts. Extensive documentation is offered to illustrate the savings gained by the public from either substitution of chemical equivalents or prescribing on a generic name basis. For sixty-three drugs on HEW’s Master Drug List, the HEW Task Force found that a change to generic prescribing would save 55 percent at the wholesale level and from 20 to 35 percent at the retail level, depending on the pharmacist’s mark-up. This corresponds with an annual savings at the retail level of from 30 to 40 million dollars on total annual expenditures by the public of 150 million dollars for these sixty-three pharmaceuticals. Total annual expenditures by the public on all prescription drugs were reported to be 2.3 billion dollars in 1966. Even if the highest standards of health care would permit substitution in only a fraction of all transactions, the savings to the public would be significant. The precise amount to be saved has, of course, been debated, and the more extreme situations of price differentials have been indicated. Although these wide variations are not always present, the HEW Task Force concluded that important savings could be realized, even though the amount was uncertain. The advocates of generic drugs argue that the consumer

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73 The HEW Task Force found that of the approximately 400 drugs on its Master Drug List, sixty-three could be obtained at "a cost distinctly lower than that of the brand-name product." TASK FORCE FINAL REPORT, supra note 21, at 36. Twenty-three drugs could only be obtained at the same or a higher cost. Id.

74 Id. By implication the same savings would result if substitution were permitted in these instances.

75 This represents a savings of 6 to 8 percent on the total spending for the 400 drugs on the Master Drug List, which spending came to more than 600 million dollars at the time of the HEW Task Force Study. Id.

76 DRUG USERS, supra 29, at 19.

77 See, e.g., TASK FORCE FINAL REPORT, supra note 21, at 36–37.

78 For example, Meticolten ($8.50 per 30) is available under the generic name prednisone ($2.58 per 30); Serpasil ($7.06 per 100) is available under the name reserpine ($2.91 per 100). TASK FORCE FINAL REPORT, supra note 21, at 36. In 1961 McKesson & Robbins sold prednisone by generic name for approximately $3.00 per 100 (retail price). At the same time Schering sold its brand name for almost $30 per 100 (retail price). E. Kefauper, supra note 65, at 12. In the case of dextroamphetamine, the difference in price can be as much as a factor of twenty. E. Kefauper, supra note 65, at 18. In a competitive bidding situation, as where the Defense Medical Supply Center buys generically, the manufacturers have offered lower prices. Id. at 20–23.

79 Specifically, the Task Force said:

The Task Force finds, therefore, that the use of low-cost chemical equivalents can yield important savings, especially in the case of patients with
should benefit from savings gained from the substitution of generic drugs. These savings would reflect lower research costs, lower promotional costs, and lower profits among manufacturers of equivalents.

Another factor to be considered is the success produced by the systems which have used some form of generic prescribing or generic substitution. There have been relatively few reported difficulties in both foreign programs and federally operated systems in this country.

A number of states have also employed various systems under combined federal and state programs such as Medicaid. Substitution by prior consent has also been very successful in hospitals using the formulary system. The latter does not necessarily require use of less expensive drugs. Often the hospital stocks one of many well-regarded brands and that is the extent of their substitution, while they save on volume purchases and reduced inventory.

Another reason that has weighed at various times in favor of substitution in cases of equivalence has been the rapidly increasing number of drugs on the market. In previous years 300 to 500 new brand names flooded the market every year. Although within the past two years some decline has occurred, it has become increasingly difficult for doctors to familiarize themselves with these products. Moreover, most physicians learn pharma-

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80 The HEW Task Force found that much of the funds spent by the large manufacturers on research "provide only minor contributions to medical progress," since only 10 to 25 percent of new drugs every year represent new chemicals. Task Force Final Report, supra note 21, at 8.

81 See text accompanying notes 66-72, supra. See also Task Force Final Report, supra note 21, at 9.

82 The Task Force found that the drug industry was characterized by an "exceptionally high rate of profit... [which] is not accompanied by any peculiar degree of risk." Task Force Final Report, supra note 21, at 14. The twenty-two largest manufacturers of drugs net an average 13 percent profit after taxes. Administered Drug Prices, supra note 11, at 157. Testimony before Senator Kefauver's Subcommittee indicated that it is these high profits which make the drug industry "Wall Street's 'fair-haired boy.'" Senate Hearings, supra note 69, pt. 14, at 8205.

83 See generally Task Force Current Programs, supra note 17, at 136-205.


85 See Task Force Current Programs, supra note 17, at 32-134; see also Task Force Final Report, supra note 21, at 44-45 for projected savings from using chemical equivalents in these programs.

86 Task Force Final Report, supra note 21, at 39-40. See also, Administered Drug Prices, supra note 11, at 238-44.

87 Administered Drug Prices, supra note 11, at 225.

88 Id. at 225-26.
Substitution of Pharmaceuticals in medical schools on the basis of generic names. In light of these factors, it may make more sense for physicians to prescribe generically or permit substitution by the pharmacist of generically equivalent drugs.

Finally, the lower priced generic equivalents must meet the same chemical standards of the national compendia required of the brand names when tested. Thus the use of proven generic equivalents where possible does not subject the patient to inferior care. Furthermore, the majority of drug manufacturers, both large and small, whether producing brand or generic name pharmaceuticals, use proper methods to insure a high quality product. Recalls for substandard drugs have involved not only the smaller manufacturers but all types of producers. Furthermore, it is claimed that the boast of the brand name manufacturers that their products exceed the necessary standards may be largely irrelevant.

To summarize, the advocates of substitution argue that where every reasonable assurance can be given that two pharmaceuticals are equivalent, relative cost should be the determinative factor. With appropriate regulations and a thorough up-to-date generic compendium the pharmacist would be in a proper position to decide this issue. To permit substitution of an equivalent pharmaceutical under such conditions, groups such as the American Pharmaceutical Association have argued, would reduce the cost of equivalent health care without jeopardizing the quality of treatment received by the patient.

B. Antisubstitution Arguments

The primary argument of those who oppose substitution where drugs are equivalent centers around the quality of the pharmaceutical product. They contend that in meeting compendial stan-

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89 Id. at 226.
91 TASK FORCE FINAL REPORT, supra note 21, at 9. The HEW Task Force reported that the cost of an adequate quality control system was 2.4 percent of sales for large firms and somewhat less for the smaller companies.
92 Id.
93 ADMINISTERED DRUG PRICES, supra note 11, at 231.
95 On the issue of drug quality, see generally Perloff, Anti-Substitution Law Repeal—Pro
iards, manufacturers of generic name drugs exercise little quality control. One set of data often cited pertains to the relative rates of regulatory confiscation between the major manufacturers and the smaller producers, who tend to produce only generic drugs. From 1950 to 1960, the Food and Drug Administration (FDA) examined approximately 8,000 drug samples which represented the output of the twenty-eight firms producing almost 90 percent of the prescription drugs sold in the United States. A total of four legal actions against these firms was instituted during this period. In contrast, the FDA also examined over 8,000 samples from the 1,200 other firms in the industry. Among these firms, the agency instituted almost 500 actions for violations by 235 firms. These statistics are employed to support the proposition that "the likelihood of legal action resulting from composition violations is over 100 times greater if the drugs are manufactured by the smaller companies, which includes all the 'generic houses.'" This greater likelihood is presumably a result of the lower levels of standards and quality control in the generic houses. Thus, it is argued, when a physician's order for a brand name is the object of substitution and the patient receives a less expensive brand or generic name, the probability that the patient will be subjected to a less effective and possibly a harmful drug is greatly increased.

Another concern is the relationship among the physician, the pharmacist, and the patient. Not infrequently, a physician will prescribe a particular brand name on the grounds that it has a special feature which other products which are chemically equivalent do not have. To permit substitution in this context deprives the physician of his ability to prescribe a drug which he feels is necessary for its unique qualities. In effect, to permit the pharmacist to substitute another drug upon a consideration of costs measureably decreases the certainty of therapeutic effect that the physician seeks. Undoubtedly, physicians are hesitant to delegate their professional responsibility in this fashion; in some instances this feeling may be well founded on technical considerations.

The prescribing physician has the duty to decide whether the patient's health and well-being will be affected adversely by a particular product; he therefore must consider whether a product is compounded with ample quality control. He further must consider factors bearing on the bioequivalence of the product he


96 Senate Hearings, supra note 69, pt. 22, at 12114, 12147.
97 Ulrich, supra note 3, at 148.
selects. Arguably, a pharmacist simply does not have the expertise to consider those factors which may interfere with any correspondence between chemical and therapeutic equivalence. The pharmacist is not able to analyze the reliability or reputation of the manufacturer as is the physician. Since the pharmacist is neither trained to prescribe nor allowed to render his own prescription, he should not be able to overrule the physician's choice. Quite clearly the ordinary patient lacks the knowledge to appreciate the subtle differences among pharmaceuticals. As a result, the patient is not prepared to give a knowledgeable and voluntary consent to the substitution of a different product.

The administrative costs to be incurred in establishing a system of substitution are substantial. It is estimated that a system for substitution could not be effective until at least two years after legislation is approved. Furthermore, there is no guarantee that any administrative or legislative system would be able to insure that substitution would be permitted only in cases of therapeutic identity. Because very few valid clinical trials have been carried out, it is not clear that a sufficient number of identical drugs would be found to justify the extensive expense involved. Those who oppose substitution tend to doubt that there are a great number of these truly therapeutically equivalent drugs and believe that equivalence should be well demonstrated before any substitution is permitted.

The number of organizations that have opposed substitution initiated by the pharmacist or coerced generic prescribing is indeed formidable. They argue that the evidence available indicates that substitution in general is inconsistent with superior health care. And, admittedly, where substitution or generic prescribing is detrimental to the health or well-being of the patient, this practice cannot be permitted or encouraged.

IV. State of the Law: Pharmacist's Liability

Under present law the pharmacist who supplies a patient with a therapeutic equivalent to the brand name prescribed by the physician is confronted by a variety of liabilities. He may be subject to administrative, criminal, and civil sanctions, regardless of the fact

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98 Galbally, supra note 1, at 764.
99 Ulrich, supra note 3, at 141-42.
100 TASK FORCE FINAL REPORT, supra note 21, at 44.
101 See text accompanying notes 52-55 supra.
102 See, e.g., Editorial: Drug Names, 190 J. AM. MED. ASSOC. 542 (1964); Fishbein, Editorial: Generic Names, 33 POSTGRADUATE MEDICINE 524 (1963).
that the substituted drug is therapeutically equivalent to the prescribed drug. Furthermore, the practicing pharmacist is regulated by both the federal and state governments.

A. State Administrative Liabilities

Because the practice of pharmacy bears directly upon the public health, safety, and welfare, the field is within the scope of the state's police power. The common pattern of state regulation requires that professional pharmacists be licensed. The licensing requirements usually pertain to professional education and experience, as well as satisfactory performance on an examination and evidence of good character. A pharmacy typically cannot do business without the direct supervision of a licensed pharmacist. Violations of the prohibitions against substitution can lead to various actions by the state board of pharmacy against the pharmacist. A fine may be assessed, and under some circumstances the pharmacist's license to practice may be suspended or revoked. Because this sanction is often imposed by an administrative proceeding before the state board of pharmacy, the nature of the practice in question and the action taken by the board are frequently not disclosed to the general public.

A threshold problem in the administrative regulation of pharmacy is the difficulty of discovering when substitution has occurred. Discovery in the nonprescription context requires only that the vendee learn that he has not received the ordered item. Where the buyer has presented the pharmacist with a prescription, however, it is highly unlikely that the purchaser will recognize that he has received something other than that which the physician has prescribed, unless he has an abnormal reaction to the substituted drug. In the majority of cases, neither the patient nor the physician will suspect that substitution has occurred. The pharmacist may have dispensed an item which purports to be of the same composition as the prescribed item and is

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103 See, e.g., Milligan v. Board of Registration in Pharmacy, 348 Mass. 491, 204 N.E. 2d 504 (1965); State Bd. of Pharmacy v. Matthews, 197 N.Y. 353, 90 N.E. 966 (1910).
105 See statutes cited in note 104 supra.
identically colored and shaped.\textsuperscript{109} If the substituted drug is equivalent to the dispensed drug in some fashion, the only discernible therapeutic differences may be in potency, in rate of achievement of blood levels, or in dissolution times and disintegration rates. Generally, only a truly unskilful job of substitution will trigger suspicion. As a result, the task of discovery falls on experts such as physicians, pharmacologists, and other pharmacists,\textsuperscript{110} operating in conjunction with trained law enforcement personnel.\textsuperscript{111} Moreover, the problem in discovering cases where substitution has occurred arises not only in the administrative context but also where a buyer seeks a judicial remedy against a pharmacist.

Administrative agencies may discover the substituting pharmacist by other means as well. An inspection of a pharmacist's inventory may reveal to officials that a pharmacist is engaging in substitution. The presence in inventory of large amounts of chemically equivalent products which physically resemble popular and quick-moving brand names will often raise suspicion. In such a case investigators will typically have the pharmacist fill decoy prescriptions for a brand name and then subject the drug to chemical analysis. If testing reveals that the prescription was in fact the subject of substitution, appropriate administrative or criminal proceedings will be instituted.

\textbf{B. Criminal and Other Governmentally Initiated Actions}

\textit{1. Under State Law—The pharmacist who intentionally or negligently dispenses a prescription drug other than the item ordered faces criminal penalties on at least two different legal bases: substitution per se and misbranding. A number of states specifically define substitution to include brand name substitution.\textsuperscript{112} Typically such substitution constitutes a criminal offense\textsuperscript{113} conviction of which may result in a jail sentence.\textsuperscript{114} Statutes usually

\begin{footnotesize}
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\item \textsuperscript{109}See, e.g., Winthrop Chemical Co. v. Weinberg, 60 F.2d 461 (3d Cir. 1932).
\item \textsuperscript{110}Statutes often provide for the services of trained personnel to aid in discovery. See, e.g., N.Y. EDUC. LAW § 6804 (McKinney 1972).
\item \textsuperscript{111}See, e.g., Ulrich, supra note 3, at 143–44, for a discussion of the means used to discover substitution and other irregularities, in a scheme to defraud the Louisiana Department of Public Welfare.
\item \textsuperscript{112}See, e.g., MICH. COMP. LAWS ANN. § 338.1101 (1967). The relevant portion of the statute is set out in note 9 supra. See also N.J. STAT. ANN. § 45:14–16 (1963); N.Y. EDUC. LAW § 6816 (McKinney 1972); PA. STAT. ANN. tit. 63, § 390–5(8) (1968).
\item \textsuperscript{113}See, e.g., MICH. COMP. LAWS ANN. § 338.1117(1) (1967); N.Y. EDUC. LAW § 6816 (McKinney 1972).
\item \textsuperscript{114}See, e.g., N.Y. EDUC. LAW § 6816 (McKinney 1972).
\end{enumerate}
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empower the state board of pharmacy to refer cases to the appropriate prosecuting attorney or attorney general.\textsuperscript{115}

In most states, the substituting pharmacist confronts criminal liabilities under the state misbranding\textsuperscript{116} or adulterating\textsuperscript{117} statutes. In states which proscribe substitution per se, liability for misbranding is in addition to liability for substitution.\textsuperscript{118} Violations for misbranding or adulteration will typically occur where the physician has prescribed a particular brand and the pharmacist dispenses a different brand while labeling the container with the elements of the original prescription. As with substitution, a violation of the misbranding or adulteration statutes can result in a fine or jail sentence\textsuperscript{119} as well as the administrative actions previously discussed.\textsuperscript{120}

In addition to administrative and criminal liabilities, the substituting pharmacist may be subject to other governmentally initiated action. Drugs which have been misbranded or adulterated may be subject to seizure by the state.\textsuperscript{121} The pharmacist may further be subject to an injunction to prevent introduction of misbranded or adulterated items into commerce.\textsuperscript{122}

2. \textit{Under Federal Law}—Violations of federal law may be concurrent with violations of state law. The Federal Food, Drug and Cosmetic Act\textsuperscript{123} includes no definition of substitution.\textsuperscript{124} The federal statute includes substitution within the definition of misbranding. The Act prohibits the misbranding or adulteration of any drug moved by interstate commerce\textsuperscript{125} and the delivery of such drug through the means of interstate commerce.\textsuperscript{126} Violation

\textsuperscript{116} E.g., Mich. Comp. Laws Ann. §§ 335.1, 335.4, 335.10 (1967); N.Y. Educ. Law §§ 6811(10), 6815(2)(b) (McKinney 1972); Pa. Stat. Ann. tit. 35, §§ 780–4(b), 780–4(c), 780–14 (1964). It should be noted that the offense of misbranding is often included in the state food and drug act (which applies to others as well as pharmacists), while substitution is usually defined in the state code which regulates professional pharmacists.
\textsuperscript{118} Compare Michigan statutes cited in notes 112 and 113 supra, with Michigan statutes cited in note 116 supra.
\textsuperscript{120} See text accompanying notes 107–108 supra.
\textsuperscript{124} This may be attributable to the fact that the Act does not aim to regulate the pharmacist himself, this aspect being largely a matter of state concern.
\textsuperscript{126} Id. § 301(c), 21 U.S.C. § 331(c) (1970).
of these provisions can result in fine or imprisonment.\textsuperscript{127} Where the pharmacist labels a substituted drug with a prescription label meant by the prescriber to cover the actual product he prescribed, the pharmacist is labeling in a false or misleading manner in violation of the Act.\textsuperscript{128} He is also dispensing an imitation and offering a drug for sale under the name of another drug in violation of the Federal Act.\textsuperscript{129} Although the Act exempts the pharmacist from some of the labeling requirements,\textsuperscript{130} it specifically does not exempt pharmacists from those labeling requirements noted above.\textsuperscript{131} Because virtually all prescription drugs with which the pharmacist deals have traveled through interstate commerce, a pharmacist is exceedingly likely to be subject to the Act.\textsuperscript{132} The statute further provides that any drug which must be used under the supervision of a medical practitioner may only be dispensed upon the prescription of a physician.\textsuperscript{133} Dispensing a drug contrary to this provision is an act which “results in the drug being misbranded while held for sale.”\textsuperscript{134} A pharmacist who dispenses an item different from that prescribed may violate this section because he has dispensed a drug without a prescription for that drug.

Violations of these federal provisions may result in other actions in addition to criminal penalties. As under state law, the drugs are subject to seizure if they are determined to be misbranded under federal law.\textsuperscript{135} The pharmacist may also be subject to an injunction under the Act.\textsuperscript{136}

\section*{C. Civil Liabilities}

Where a pharmacist dispenses a drug other than that called for in the prescription and the patient suffers injury as a proximate result of this substitution, the pharmacist may be held liable in a civil action for damages.\textsuperscript{137} The most prominent theory used

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\textsuperscript{127} Id. § 303.21 U.S.C. § 333 (1970).
\textsuperscript{128} Id. § 502(a), 21 U.S.C. § 352(a) (1970).
\textsuperscript{129} Id. § 502(i), 21 U.S.C. § 352(i) (1970).
\textsuperscript{134} Id.
\textsuperscript{137} For a comprehensive survey of the pharmacist’s civil liabilities see Kamm, The Liability of the Pharmacist in the Role of Drug Product Selector, ILL. PHARMACIST, Jan., 1971, at 19–22.
\end{footnotesize}
against the substituting practitioner is negligence. The typical case involves the situation where the pharmacist erroneously substitutes a harmful or ineffective item for the one prescribed.\footnote{See, e.g., Gault v. Poor Sisters of St. Frances Seraph, 375 F.2d 539 (6th Cir. 1967); Troppi v. Scarf, 31 Mich. App. 240, 187 N.W.2d 511 (1971), \textit{motion for leave to appeal denied}, 385 Mich. 753 (1971); Duensing v. Huscher, 431 S.W.2d 169 (Mo. 1968).} Because a patient entrusts his life and health to the skill and judgment of the pharmacist, the pharmacist is held to the highest standard of caution and care.\footnote{Krueger v. Knutson, 261 Minn. 144, 152, 111 N.W.2d 526, 532 (1961).} This exceptional duty of care applies in the dispensing of both nonprescription\footnote{See, e.g., \textit{id.}} and prescription items.\footnote{See, e.g., \textit{People's Service Drug Stores, Inc. v. Sommerville, 161 Md. 662, 158 A. 12 (1932); Troppi v. Scarf, 31 Mich. App. 240, 187 N.W.2d 511 (1971), \textit{motion for leave to appeal denied}, 385 Mich. 753 (1971).} It is clearly a breach of this duty where the pharmacist erroneously supplies a drug different from that prescribed or ordered, and he will be held liable for any damages incurred as a result of this breach.\footnote{See \textit{Potter v. Krown Drugs, 214 So. 2d 198 (La. Ct. App. 1968); Brown v. Marshall, 47 Mich. 576, 11 N.W. 392 (1882); MacKay v. Crown Drug Co., 420 P.2d 883 (Okla. 1966); Highland Pharmacy v. White, 144 Va. 106, 131 S.E. 198 (1926).} The pharmacist may also be held liable on a warranty theory. It has been stated that “a druggist who sells a prescription warrants that . . . he will compound the drug prescribed.”\footnote{See \textit{id.}} Moreover, “the written order or prescription [is] the basis of the bargain.”\footnote{See \textit{People's Service Drug Stores, Inc. v. Sommerville, 161 Md. 662, 158 A. 12 (1932); Troppi v. Scarf, 31 Mich. App. 240, 187 N.W.2d 511 (1971), \textit{motion for leave to appeal denied}, 385 Mich. 753 (1971).} If the pharmacist either intentionally or negligently substitutes another drug for the prescribed one, he will have breached this warranty and be liable for consequent injuries.\footnote{McLeod v. W.S. Merrell Co., 174 So. 2d 736, 739 (Fla. 1965).} Although this warranty is characterized as implied, the pharmacist may additionally express warranties on which he may be held liable, as where the compound dispensed is represented to have certain qualities.\footnote{Jacobs Pharmacy Co. v. Gipson, 116 Ga. App. 760, 762, 159 S.E.2d 171, 173 (1967).} Injured parties have not frequently used warranty theory as a basis for their claims.\footnote{Intentional substitution in this context may be found to be fraud as well as a breach of warranty. Additionally it has been reported that research done by legal counsel for the American Pharmaceutical Association has revealed no reported cases seeking to hold a pharmacist liable for intentional substitution. Hawkins, \textit{Drug Product Selection—The Pharmacist's Responsibility, Mich. Pharmacist, Aug.}, 1971, at 16.}

An alternative basis for the pharmacist's liability for damages resulting from substitution is that violations of drug and pharmacy
laws are tortious per se. In Orthopedic Equipment Co. v. Eutsler,\textsuperscript{148} plaintiff sought to hold the manufacturer of a surgical nail liable for injuries that resulted from the misbranding of the device. Plaintiff established that the misbranding was a violation of the Federal Food, Drug, and Cosmetic Act and sought to have the violation held to be negligence per se. The Court of Appeals for the Fourth Circuit upheld the trial judge’s instruction that a violation of the Federal Act was negligence per se in Virginia.\textsuperscript{149} Similar reasoning could be applied to the pharmacist who has misbranded a drug with resulting injury. Often the pharmacist will have violated both state and federal law by his substitution, and if the Eutsler rationale were followed, these violations would be sufficient to construct a prima facie case.\textsuperscript{150} Thus the pharmacist who substitutes an equivalent for the prescribed drug always faces the possibility of a civil suit by an injured patient. In reality, however, intentional substitution has not generated much case law. The case law on point has largely evolved from suits charging egregious negligence in filling a prescription.\textsuperscript{151} That intentional substitution has not often been litigated may be a result of several factors. First, the difficulty of discovering the act is great where the prescribed and dispensed items are substantially equivalent. Second, because many acts of intentional substitution involve substantially equivalent products, it is unlikely that damages will be discernible to anyone but a physician. Finally, the matter may be dealt with in most cases on the administrative level where unreported sanctions take the form of warnings or license suspensions. Even if civil liability does not usually fall on the substituter, it does play an important part in the pharmacist’s view of the problem.\textsuperscript{152}
expressed by the parties to the debate\textsuperscript{154} are considered and met. Any modification of the law must then operate within constraints. First, substitution should only be permissible where there is evidence to indicate that the products from which the pharmacist may select are therapeutically equivalent. Second, the pharmacist must be given a reliable means by which he can determine that products are therapeutically equivalent. Third, steps must be taken to assure that all drugs which would be used in a substitution system meet the highest standards of composition, as guaranteed by effective quality-control systems. Fourth, a system allowing substitution would probably require a means whereby the physician could indicate that no substitutions should be made because of peculiarities in individual cases of which the pharmacist may be unaware. Fifth, any reform must avoid placing the pharmacist in a position in which his actions, although complying with state law, violate federal law, or vice versa. Sixth, new means must be provided for allocating the infrequent, yet inevitable, losses which will be generated by a substitution system. These and perhaps other considerations must be accounted for if substitution is to be consistent with superior health care.

Recent legislation in Kentucky\textsuperscript{155} establishing a system permitting substitution deserves consideration to determine the extent to which the legislation meets the concerns noted above. The Kentucky act establishes a nine-member Drug Formulary Council consisting of representatives of the medical and pharmacy professions, the public, and the state government.\textsuperscript{156} The Council is directed to prepare a formulary "of drugs and pharmaceuticals with their generic or chemical names, if any, that are determined by the Council to be therapeutically equivalent to specified brand name drugs and pharmaceuticals."\textsuperscript{157} The formulary will then be distributed to pharmacists and periodically revised.\textsuperscript{158} Section 7 of the act permits parties who are aggrieved by any act of the Council to seek judicial review in state court.\textsuperscript{159} The act specifically permits a pharmacist who has received a prescription for a brand name to dispense an equivalent listed in the formulary.\textsuperscript{160}

\textsuperscript{154}See part III B supra.


\textsuperscript{156}Ch. 126, §5, [1972] Ky. Acts 559-60.

\textsuperscript{157}Id., § 6, at 560.

\textsuperscript{158}Id., § 6, at 561.

\textsuperscript{159}Id., § 7, at 561.

\textsuperscript{160}Id., § 8(1), at 561, provides:

\begin{quote}
When a pharmacist receives a prescription for a brand name drug for which
He must dispense an equivalent upon the patient's request and is subject to a fine if he fails to do so. The label on the dispensed drug must bear the names of both the prescribed and the dispensed drugs. The act also permits the prescribing physician to indicate on the prescription that no substitution should be made, and the pharmacist must honor the prescription as written. The last section of the act provides that where a physician has forbidden substitution a patient must be reimbursed by any health care insurance contractor at the brand name rather than generic name price. The act finally provides that the system was enacted with the "intent . . . that all citizens of Kentucky may be assured of high quality medicine at a reasonable cost."

The Kentucky act permits substitution only where therapeutic equivalence has been determined. Presumably the Council may draw on current investigations done by the federal government in this regard as well as by its own investigation. It is likely, however, that large sums of money will be needed for clinical trials. It is probably most appropriate that this be done on the federal level in order to avoid duplication of effort. The act also gives the pharmacist a reliable means to determine where equivalency exists. The language and operation of the act itself do nothing to regulate the quality of manufacture of pharmaceuticals. Drug quality may be enforced, however, by preventing certain drugs from being listed in the formulary. The act does not provide for large-scale inspection of processing and manufacturing facilities; nor does it provide for continuing improvement in the approved national compendia from which the standards of composition are.

161 Id.
162 Id. § 9, at 561. Presumably this is aimed at preventing the pharmacist from refusing to substitute because his profit may be greater on more expensive drugs than it is on less expensive equivalents.
163 Id. § 8, at 561.
164 Id. §§ 8, 9, at 561. Section 8 (2) provides in pertinent part:
If, in the opinion of a practitioner, it is to the best interest of his patient that an equivalent drug should not be dispensed, he may indicate in the manner of his choice on the prescription "Do Not Substitute," except that the indication shall not be pre-printed on a prescription.
165 Id. § 13, at 562. The intent here must have been to prevent the type of pressures to which pharmacists and patients are currently subjected by both substitution laws and reimbursement policies of health insurance or public health care organization.
166 Id. § 11, at 562.
167 The HEW Task Force recommended that clinical investigation be carried out on the federal level on a high priority basis. TASK FORCE FINAL REPORT, supra note 21, at 33.
drawn. As with clinical trials, these activities are perhaps more appropriate on the federal level in view of the fact that responsibility for these activities is currently centered there.\(^{168}\) The legislation as enacted also permits the physician to override the pharmacist's choice.

A major difficulty with the Kentucky act is that the pharmacist still may be liable for misbranding under federal law. Although the labeling provisions of the act will presumably remove some federal liabilities for misbranding,\(^{169}\) the pharmacist may still be liable for dispensing the substituted drug without a prescription.\(^{170}\) This problem may be avoided, however, by arguing that the pharmacist has not dispensed a drug without having received a prescription for \textit{that} drug because by state law a prescription for a brand name automatically includes a prescription for all equivalent pharmaceuticals listed in the formulary unless the physician specifies otherwise.

A final difficulty is that the act makes no provision for allocating losses that may result from the operation of the system. As an example, assume that the Council has concluded that two brand names are equivalent. Assume further that a physician writes a prescription for Brand X, and its "equivalent" Brand Y is dispensed. If the patient is injured as a result, does he have a claim for relief, and if so, against whom? The pharmacist has certainly not been negligent, and presumably a law similar to that enacted in Kentucky removes the prescription as the basis of the bargain. In effect the pharmacist has only filled the prescription as required by law and with all due care. He cannot be held liable for performing all that the law requires.\(^{171}\) If the damage is the result of a defect in the product, surely the manufacturer will be liable. The question remains, however, what will the duties and liabilities of the Council and the state be. The question may well go unlitigated, as has the issue of the liability of the intentional substitutor;\(^{172}\) yet it is a difficulty that should not be overlooked.

Although the Kentucky system has not been in operation long enough to produce any definitive results,\(^{173}\) it promises to be a significant experiment in the law regulating pharmacists. It raises

\(^{168}\) The HEW Task Force generally advocated more quality-control-oriented action by the federal government. See \textit{Task Force Final Report}, supra note 21, at xi-xx.


\(^{171}\) See \cite{McLeod v. W.S. Merrell Co.}, 174 So. 2d 736 (Fla. 1965).

\(^{172}\) See text accompanying notes 151-52 \textit{supra}.

\(^{173}\) The statute was enacted on March 27, 1972.
Substitution of Pharmaceuticals

anew the specter of liability as "certifiers" for those who formu-
larly assert preference or equivalence in the event of subsequent
patient disservice because of demonstrable nonequivalence or
inefficacy. The act answers many of the criticisms of those who
oppose legal substitution. It does, however, leave gaps in the
areas of testing, certification responsibility, inspection, and quality
control.

VI. Conclusion

This article has sought to consider the practical and legal impli-
cations of drug substitution. It has further sought to summarize
the arguments bearing on any review of present substitution laws.
In so doing it has attempted to highlight the important problems
which are presented in this context.

Some of the answers to these problems undoubtedly lie in
increased federal administrative and legislative attention to assur-
ing quality pharmaceutical products as the cornerstone of pharma-
cy services throughout the nation. Another answer lies in educat-
ing the medical and pharmacy practitioner, along with elements of
the public, as to what truly comprises pharmaceutical manufac-
turing quality.

In any context, legal reform must reflect the socio-political
goals and economic needs of those who are governed. In in-
stances such as health law, those goals and needs are inextricably
involved with complex scientific issues. As this article has sought
to illustrate, any change in the legal system relating to pharmaceu-
ticals must be predicated on considerations of scientific validity.